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Лекар-преподавател
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Университетска болница „Лозенец“

Конкурс за заемане на академичната длъжност „Доцент"
в област на висшето образование
7. «Здравеопазване и спорт»,
Професионално направление
7.1. Медицина /Патоанатомия и цитопатология/
- един ново щатно място на
Университетска
Болница „Лозенец“
обявен в ДВ, бр 24 от 16.03.2018 г.

Резюмета на представените за участие в конкурса научни трудове, на основание чл 110 от Правилника за условията и реда за придобиване на научни степени и заемане на академични длъжности в Софийски Университет „Св. Климент Охридски“

гл. ас. Станислав Филипов дм

Дисертационен труд
Образователна и научна степен "доктор"
Професионално направление Медицина 7.1

„Подход при хирургично лечение на пациенти с първичен хепатоцелуларен карцином (експериментални и клинико-морфологични аспекти)"

Дата на защита	*Език на основния текст*	*Библиография*	*Общ обем на дисертационния труд*
28.07.2016	Български	461 *(бр. заглавия)*	216 *(бр. страници)*

Организация в която е защитен дисертационния труд
Висше училище : Софийски Университет „Св. Климент Охридски"
Факултет : Медицински факултет

СОФИЙСКИ УНИВЕРСИТЕТ „СВ.КЛИМЕНТ ОХРИДСКИ“
МЕДИЦИНСКИ ФАКУЛТЕТ
КАТЕДРА ПО ХИРУРГИЧНИ БОЛЕСТИ , АКУШЕРСТВО И ГИНЕКОЛОГИЯ

Д-р Станислав Минчев Филипов

Подход при хирургично лечение на пациенти с първичен хепатоцелуларен карцином /експериментални и клинико-морфологични аспекти/

Д и с е р т а ц и я за присъждане на образователната и научна степен “ДОКТОР”

Научна специалност: “Медицина”, шифър 03.01.37

Научни ръководители:
Доц. д-р Здравко Йорданов Лазаров, дм
Проф. д-р Спиро Михайлов Константинов, дм

София, 2016

Година	Списание	IF	RG Impact
2003	Folia Biologica (Praha)	0,5	0,60
2004	Journal of Neuroimmunology	2,704	
2007	Inflammation	1,292	
2014	International Journal of Immunopathology and Pharmacology	2,507	1,77
2014	Journal of biological regulators and homeostatic agents	2.04	
2016	Food and Chemical Toxicology	3,778	2.52
2017	TOXICOLOGY MECHANISMS AND METHODS	1,595	1,28

Година	Списание	IF	Публикации
2003	Folia Biologica (Praha)	0,5	1
2004	Journal of Neuroimmunology	2,704	1
2007	Inflammation	1,292	1
2014	International Journal of Immunopathology and Pharmacology	2,507	3
2014	Journal of biological regulators and homeostatic agents	2.04	1
2016	Food and Chemical Toxicology	3,778	1
2017	TOXICOLOGY MECHANISMS AND METHODS	1,595	1
	Общо		**19,43**

2003

Cellular Localization of NGF and NGF Receptors in Aged Human Thymus

(human thymus / involution / NGF / p75^{NTR} / TrkA / immunoreactivity / epithelial cells / microscopy)

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Abstract. Recent evidence indicates that some thymic cells of developing and adult laboratory animals express the neurotrophin NGF and its low-affinity p75^{NTR} and high-affinity TrkA receptor. Less is known as to whether the thymus of adult and aged humans express these markers. We hypothesize that the presence and distribution of immunopositive cells for NGF and NGF receptors undergo some alterations during the involution of human thymus. Specimens from normal thymuses of old individuals were obtained from autopsy and surgery cases, and examined immunocytochemically at the light and transmission electron microscopic level. The immunoreactivity of NGF, p75^{NTR}, TrkA and cytokeratin was found in the epithelial thymocyte microenvironment. Our results provide the first ultrastructural evidence for NGF/receptor immunocytochemical localization in human thymus. They suggest a possible immunotrophic/immunoregulatory role of the NGF-p75^{NTR}-TrkA system for T-cell development in human thymus during senile involution.

Neurotrophins are a family of proteins including nerve growth factor (NGF), brain-derived neurotrophic factor, neurotrophin-3 (NT-3) and NT-4/5 (Sofroniew et al., 2001). NGF is the prototypic member of this family (Levi-Montalcini, 1987). Conceived originally as no more than a growth and survival factor for certain neuronal cells, within the last 50 years increasing information was accumulated showing that NGF also exerts effects on non-neuronal cells, particularly immune cells (reviewed by Aloe et al., 1997a; Aloe and Micera, 1999). The thymus is one recent example of this neuroimmune framework.

The thymus undergoes age-related (physiological, chronic) involution during postnatal development (Von Gaudecker, 1978; Bodey et al., 1997; Turke, 1997; Rodewald, 1998; Goya and Bolognani, 1999). Recent evidence indicates that thymic epithelial cells (TEC), a cellular component that plays an important role in the development and differentiation of T cells, produce NGF and express both low- and high-affinity NGF receptors, p75 neurotrophin receptor (p75^{NTR}) and tyrosine kinase A (TrkA) receptor, respectively (Pescarmona et al., 1993; Aloe et al., 1997b; Parrens et al., 1998; Garcia-Suarez et al., 2000, 2001; Turrini et al., 2001; Yoon et al., 2003). We hypothesize that the presence and distribution of NGF- and NGF receptor-immunopositive cells undergo some alterations during the thymic involutionary process. As a first step in testing this hypothesis we examined these biomarkers' immunoreactivity (IR) in the thymocyte microenvironment of aged human thymus. Here we report structural and ultrastructural data about the cellular localization of NGF, p75^{NTR} and TrkA in human thymus during its age-related involution.

Material and Methods

Specimens from thymuses of old (aged 70–82 years) (N=9) and from young (aged 12–20 years) (N=4) individuals were obtained from autopsy and surgery cases. The thymuses collected have had no pathological disorders. Four kinds of antibodies (Ab), namely anti-NGF rabbit polyclonal Ab (NGF H-20, sc-548, Santa Cruz Biotechnology, Santa Cruz, CA), anti-p75^{NTR} monoclonal Ab (NGFR p75 ME 20.4, sc-13577, Santa Cruz

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Abbreviations: IR – immunoreactivity, NGF – nerve growth factor, PBS – phosphate-buffered saline, p75^{NTR} – p75 neurotrophin receptor, TEC – thymic epithelial cell, TEM – transmission electron microscopy, TrkA – receptor tyrosine kinase A.

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Short communication

Altered levels of nerve growth factor in the thymus of subjects with myasthenia gravis

Barbara Stampachiacchiere[a], Tsvetana Marinova[b], Kamelia Velikova[c], Stanislav Philipov[c], Ivan S. Stankulov[d], George N. Chaldakov[d], Marco Fiore[a], Luigi Aloe[a,*]

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Abstract

We have previously reported that nerve growth factor (NGF), a polypeptide known for its neurotrophic activities, is also involved in the differentiation and survival of immune cells, and that NGF and its high-affinity receptor are present in the thymus. We here demonstrate that the thymus of humans affected by myasthenia gravis (MG) contains significant concentrations of NGF. These observations support our hypothesis of a role for NGF in the thymus and suggest that the changes observed in the thymus of subject with MG may have functional significance.

Keywords: NGF; Thymus; Myasthenia gravis; Mast cells; Epithelial cells

In spite of its name, nerve growth factor (NGF) is increasingly reported to exert a biological function outside its classical domain which is the nervous system (Levi-Montalcini 1987; Aloe et al., 2001). Thus, NGF can act on cells of the immune system, including thymic cells (Aloe et al., 1994, 2001; Laurenzi et al., 1994). Also, the thymus of rodents produces NGF and its level changes during physiological events, such as pregnancy and aging (Aloe et al., 1997; Hannestad et al., 1997; Turrini et al., 1998). NGF administration in rodents causes hypertrophy of thymic epithelial cells (Abramchik et al., 1988), and the thymus of TrkA (the main NGF receptor) gene knockout mice undergoes accelerated regression (Garcia-Suarez et al., 2000). Using biochemical, molecular, immunohistochemical and immunogold electron microscope methodologies, we report that resident thymic cells, such as epithelial cells and mast cells of healthy subjects and of subjects affected by myasthenia gravis (MG), are able to produce NGF.

Thymus samples were taken from MG autopsy cases ($n=4$), or from subjects ($n=4$) who died by car accident ($n=1$) or strangulation ($n=3$), and were used as controls. MG subjects suffered by MG for at least 5 years, received corticosteroid treatments and showed anti-AchR positivity. Histologically, MG thymuses displayed hyperplasia follicularis ($n=3$) and adiposus syndrome ($n=1$) characteristics. MG patients died by car crash ($n=1$), suicide ($n=2$) or after 2 months of pneumonia ($n=1$). Control thymuses were without any pathological changes with structural and morphological features of their ages. MG diagnostic criteria were carried out according to Sternberg (1996).

The thymus was removed at the Department of General and Clinical Pathology, Medical University, Sofia, and at the Division of Cell Biology, Department of Forensic Medicine, Medical University, Varna, Bulgaria. This study was approved by the Ethical Committees of the hospitals and Informed consent was asked and obtained by the parents in accordance with the Helsinki Declaration.

Thymic tissue was homogenized in extraction buffer (see Bracci-Laudiero et al., 1992), centrifuged at 8500 rpm at 4 °C and the supernatant used for NGF and mRNA Trk-A analyses. Levels of NGF were measured by a highly sensitive two-site

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Nerve Growth Factor Immunoreactivity of Mast Cells in Acute Involuted Human Thymus

Tsvetana Marinova,[1] Stanislav Philipov,[2] and Luigi Aloe[3]

Abstract—The acute involution of the thymus is induced by either exogenous or endogenous factors, including some infections (infection type involution). The present study was focused on both detection and immunocytochemical analysis of NGF immunopositive mast cells in child thymus with acute infection-induced involution. Autopsy thymus specimens from children with infection diseases (Sepsis, Encephalomyelitis, Varicella) were examined at light and electron microscopic level and compared to normal infantile thymuses. We observed a redistribution of NGF immunopositive mast cells in infection-affected child thymus, which lobular architecture was collapsed. A positive correlation between the degree of the involutive changes, increased distribution and enhanced NGF immunoreactivity of mast cells was defined. The possible involvement of NGF immunopositive mast cells in the process of acute thymus involution is discussed.

KEY WORDS: NGF immunoreactivity; mast cells; thymus.

INTRODUCTION

Both mast cells and NGF have been reported to be involved in neuroimmune interactions and tissue inflammation [1, 2]. The known actions of NGF on nerve and immune cells suggest that mast cells-derived NGF may control adaptive/reactive response of the nervous and immune systems toward noxious tissue perturbations [3, 4]. NGF, a well-characterized neurotrophic factor that acts on the nervous, endocrine and immune system, is also produced and stored in the thymus [5, 6]. It is a powerful endogenous mediator which play a crucial role acting on a variety of non-neuronal cells, including mast cells, both mast cells growth and degranulation [7, 8]. NGF induces an increase in the number of mast cells in the peripheral tissues of developing rats, as well as histamine release in fully differentiated mast cells [1, 9]. Mast cells are amine-storing cells with heterogeneous histological, biochemical and functional properties [10, 11]. They are actively involved not only in the physiological but also in the pathological events in the thymus [2, 7]. Mast cells respond functionally (via specific receptors) to an enormous range of neuroactive components including NGF [1, 4].

The acute (age-independent, spontaneous, transient, pathological, accidental) involution of the thymus is induced by either exogenous or endogenous factors, including some infections (infection type involution) [12, 13]. This type of involution is associated with an initial trigger and relatively "acute" mechanism, i.e.,

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Abbreviations: NGF, nerve growth factor; MC, mast cells.

2008

Acta morphologica et anthropologica (13)

Professor Marin Drinov
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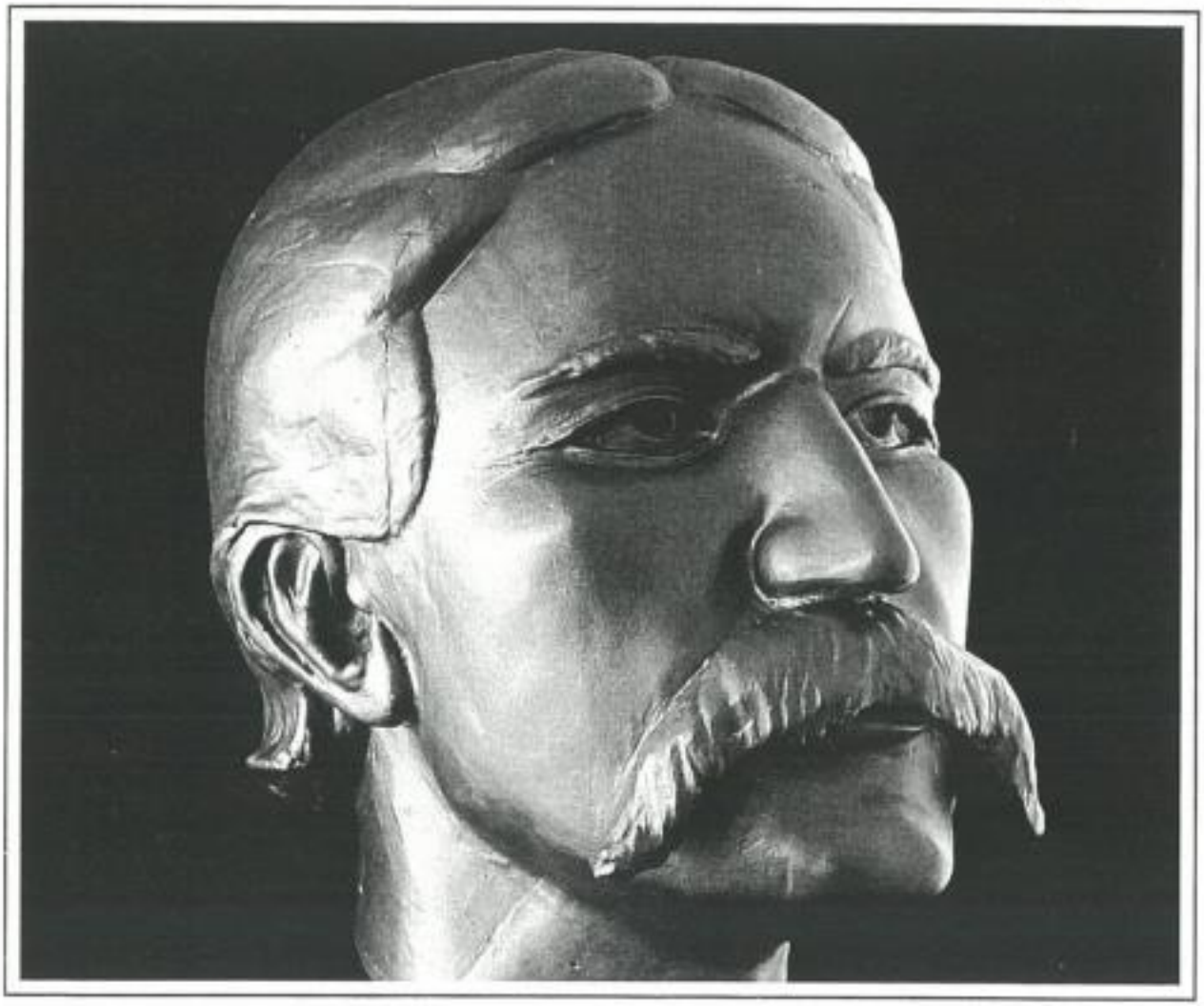

Institute of Experimental Morphology and Anthropology with Museum
Bulgarian Anatomical Society

Acta morphologica et anthropologica, 13
Sofia • 2008

Epithelial Cells and Macrophages of Aged Human Thymus Possess IGF-I Immunoreactivity

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****Anatomical Institute, University of Cologne, Germany*

The presence and distribution of insulin-like growth factor I (IGF-I) immunoreactivity in the aged human thymus were investigated both at light and electron microscopic levels. IGF-I immunoreactive cells were observed in the structurally preserved regions of the chronic involuted thymus. Presenting novel data for presence of IGF-I immunopositive epithelial cells and macrophages, we conclude that the aged human thymus is still capable to govern some "beneficial" microenvironment events, including IGF-I signalling mechanisms. The latter might be involved in the local regulation of T cell development and plasticity of thymocytes-epithelial cells interactions during aging.

Key words: IGF-I immunoreactivity, human thymus, chronic involution.

Introduction

Accumulating evidence shows that adult mammalian thymic cells express insulin-like growth factor I (IGF-I) immunoreactivity [1, 2]. Astonishingly, despite the generally acknowledged roles of IGF-I in the ontogeny [1, 7, 8], generation and survival of T-cells [3, 6, 10], little is known about the exact time course of IGF-I occurrence during the age-related thymic involution and the decline of immunoreactivity [4, 5, 9].

This is why, in the present study we concentrated our efforts to perform a detailed temporo-spatial analysis of IGF-I expression in the aged human thymus.

Material and Methods

Specimens from thymuses of old (aged 66-82 years) (n=14) and young (aged 2-27 years) (n=10) individuals were obtained from autopsy and thoracic surgery cases, and examined immunocytochemically at light and transmission electron microscopic level. The thymuses collected have had no pathological disorders. Three kinds

2010

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Sofia • 2010

Anatomy Teaching – Application of Innovation Methods in Higher Education

E. Tsankova, Ch. Chouchkov, S. Philipov

Faculty of Medicine, St. Kliment Ohridski University of Sofia

It is our duty to do something more to rouse the interest to science in young people, not only to stimulate them for professional scientific work but also to make them informed citizens [1].

Dr Philippe Busquin
European Commissioner for Research

As a fundamental science, Human anatomy represents an important part of the scientific basis of medicine. It is a fundamental medical subject that requires a prolonged study, and huge terminology knowledge, which consists of an essential knowledge perimeter; terminology training; an interdisciplinarity; a suggestiveness; and specific inventory. The use of innovative didactical methods, such as discussion in small groups, didactical and role-playing games, phantoms practical education, multimedia education etc. in Faculty of Medicine of Sofia University "St. Kliment Ohridski" is presented. The innovative techniques, consisting of development and application of new pedagogical methods include new teaching technologies for education optimization, increase in effectiveness and motivation of the students. Creating a motivation for enhancing the effectiveness in the teaching process results in an increased scientific interest and creates a novel view of the medical education.

Key words: human anatomy teaching, innovation methods, inquiry, medical education.

Topical Issues

A globalization in medicine and a tendency of integration of fundamental and clinical science and practice are observed lately [2]. A tendency of application of innovative educational methods as problem based education, as well as an education in small groups, distant education, continuing education through whole life etc., is recommended [2-4].

As a fundamental science, human anatomy represents an important part of the scientific basis of medicine. Topical issues regarding innovations in teaching medicine and in attaining knowledge depends on developing a system of effective teaching and education methods. That requires the learner to be placed in the middle of this process and change in teaching and education by introducing innovations to be made.

2013

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Central Medical Library

ONCOGENIC BALANITIS

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Summary. The so-called „oncogenic balanitis" is a not so rare nosological entity, whose pathogenesis is related in most cases to infection with oncogenic strains of the human papilloma viruses (HPVs). In the early stages of the disease the clinical presentation of the infection with some oncogenic or high risk human HPVs is often non-specific, contributing to its persistance for a long time, often misdiagnosed as a candidous or bacterial balanitis. Clinically the lesions may also be confused with lichen planus or lichen sclerosus, as well as penile eczema or psoriasis. Local and/or systemic therapy with corticosteroids can lead to unmasking of the symptoms and rapid progression of the disease, with potential risk of malignant transformation. Additionally, some patients decline a biopsy, further hampering the confirmation of the diagnosis. In all these problematic cases a diagnostic PCR examination of material taken from lesional skin could be of help for the diagnosis of Bowen's disease, erythroplasia Queyrat, consequently preventing its progression to invasive squamous cell carcinoma. We present a rare case of erosive and partially verrucous balanitis, in which HPV 56 strains were identifed by PCR in repeated samples from lesional skin. Additionaly, HPV 16 was also identified in the second sample. The clinical findings were entirely consistent with erythroplasia of Queyrat but histopathological examination was not possible. A local therapy with imiquimod was started. After complete clinical recovery a vaccination with Gardasil was additionaly planned with the hope that the patient would be protected from possible recurrence due to the generation of cross-immunity against HPV 56. Due

РЕНТГЕНОЛОГИЯ РАДИОЛОГИЯ

ПРАВОПРИЕМНИК НА "ИЗВЕСТИЯ НА БЪЛГАРСКОТО РЕНТГЕНОЛОГИЧНО ДРУЖЕСТВО"

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РЕНТГЕНОЛОГИЯ РАДИОЛОГИЯ
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АДРЕС ЗА КОРЕСПОНДЕНЦИЯ:
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Тумор на дивертикул на пикочен мехур

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Intradiverticular tumor of the bladder

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Резюме. Дивертикулите на пикочния мехур представляват херниране на мукоза през мускулен дефект на стената на пикочния мехур, с което се обяснява липсата на контрактилна способност, и представляват терен на уринарна стаза с предпоставка за развитие на конкременти и инфекции. Мнозинството от дивертикулите се развиват вторично вследствие на затруднена евакуация на съдържимо в пикочния мехур (стриктури или тумори на уретрата). Тънките стени на дивертикула благоприятстват инвазията в съседни структури, което прави прогнозата на тумори в дивертикул по-лоша. MP изследването след цистоскопия е метод на избор за по-нататъшно уточняване на формации на пикочния мехур по отношение на инфилтрацията на стената и особено в случаи на „замаскиране" на тумор, облитериращ остиума на екстравезикалния дефект, приемани като солидни маси.

Ключови думи: ДИВЕРТИКУЛИ И ТУМОРИ НА ПИКОЧНИЯ МЕХУР. МР

Abstract. The diverticula are mucosal outpouching of the bladder not having the muscle layer and contractile activity; so they are a place of urine stasis resulting into complications like stone formation and urinary tract infection. The majorities of bladder diverticula are acquired, secondary to bladder outlet obstruction. Carcinoma arising within urinary bladder diverticula has a poorer prognosis than do neoplasms that originate within the main bladder lumen because the thinner diverticular wall would allow earlier spread. MR is the method of choice after cystoscopy for staging infiltration of the bladder wall and especially in the cases when a intradiverticular tumor can be missed cystoscopically when tumor invasion has spread into the lumen of the bladder and can be misinterpreted as a solid mass.

Key words: BLADDER DIVERTICULA. BLADDER TUMORS. MR

Въведение

Карциномът на пикочния мехур след този на простатата е вторият често срещан тумор на отделителната система сред мъжете и представлява 2% от всички неоплазми. Този тип злокачествено заболяване е със съотношение мъже/жени 4:1 и се среща по-често при възрастни мъже.

Честотата на преходноклетъчни карциноми е най-висока – 90% от малигнените заболявания на отделителна система, в 5-10% се срещат сквамозоклетъчни и аденокарциноми, а в останалите по-редки случаи – саркоми и метастази.

Две трети от туморите са повърхностни и папиларни, а останалите се манифестират с инфилтрация в мускулната стена и извън нея.

Лечението и прогнозата зависят от дълбочината на туморната инвазия в стената на мехура, регионалната лимфна инвазия, наличието на далечни метастази и хистологичния вариант на тумора [14].

Anorectal malignant melanoma in a hemorrhoidal nodule: a diagnostic and therapeutic problem

Georgi Tchernev, Kristina Semkova, Stanislav Philipov, Radoswet Gornev, Julian Ananiev & Uwe Wollina

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Anorectal malignant melanoma in a hemorrhoidal nodule: a diagnostic and therapeutic problem

Georgi Tchernev · Kristina Semkova · Stanislav Philipov · Radoswet Gornev · Julian Ananiev · Uwe Wollina

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Summary Anorectal malignant melanoma (ARMM) is an extremely rare condition, often misdiagnosed and mistreated until development of metastatic disease. Clinical presentation mimicking hemorrhoids is a well-known pitfall. We present a male patient with hemorrhoidal nodules who was referred to the policlinic of dermatology for management of anal pruritus. A dark macule was detected over one of the hemorrhoidal nodules histologically verified as melanoma. Subsequent CT and PET/CT showed lymph nodes involvement and the patient underwent wide local excision (WSE) followed by abdominoperineal resection (APR). The rarity of ARMM does not allow for establishment of a validated staging system, placebo-controlled treatment trials and management guidelines adoption. The current treatment for the condition is surgical excision, using different techniques according to the stage of the disease and depth of invasion. The prognosis and overall survival are poor, but recent genetic studies give promising results for molecular targeting. Awareness for this disease is indispensable, as early recognition could result in improved survival and quality of life.

Keywords Anorectal malignant melanoma · Wide local excision · Abdominoperineal resection

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Anorektales malignes Melanom in einem Hämorrhoidalknoten: ein diagnostisches und therapeutisches Problem

Zusammenfassung Das anorektale maligne Melanom (ARMM) ist ein sehr seltener Tumor, der häufig fehldiagnostiziert und -behandelt wird bis es zur Metastasierung kommt. Das klinische Mimikry von Hämorrhoiden ist eine solche recht gut bekannte Situation. Wir berichten über einen männlichen Patienten mit einem Hämorrhoidalknoten, der ab die Poliklinik für Dermatologie mit der Diagnose eines Pruritus ani überwiesen wurde. Bei der klinischen Untersuchung fand sich eine dunkle Makel auf einem der Hämorrhoidalknoten, der sich histologisch als Melanom herausstellte. Nachfolgende CT- und PET/CT-Diagnostik zeigte einen Lymphknotenbefall. Der Patient wurde mit einer ausgedehnten

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EARLY ONSET BASAL CELL CARCINOMA: SURGICAL APPROACH

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Summary. Basal cell carcinoma (BCC) is the most frequent non-melanoma skin cancer. Only 5-15% of BCC cases can be found in patients aged 20-40 years (so-called early onset). The early onset BCC is characterized by active and aggressive tumour growth, clinically presenting in most of the cases as a morpheaform, locally infiltrating or recurrent BCC. Despite the advances in the study of the pathogenesis of this tumour, surgery remains the most used, most effective and most suitable treatment modality. We describe a case of a 39-year-old woman who developed an early onset BCC of the nasolabial fold. After the subsequent surgical excision an excellent cosmetic result was achieved.

Key words: *Basal cell carcinoma, early onset, surgery, excision*

INTRODUCTION

Basal cell carcinoma (BCC) is the most frequent non-melanoma skin cancer [1, 2]. According to different authors the frequency of BCC accounts to 70-85% [1, 2]. BCC affects different kind of people with high prevalence in individuals with type 1 or type 2 skin [1, 2]. Usually BCC occurs in patients after their 40's. Only 5-15% of BCC cases can be found in patients aged 20-40 years [1].

The clinician should also remember that BCC is one of the main features of Gorlin syndrome (Basal cell nevus syndrome) [3]. In this autosomal dominant inherited syndrome the patients could develop hundreds of invasive tumours on the area of the face, trunk and extremities [3]. Additional symptoms are mental retardation,

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HPV-ASSOCIATED PENILE PIGMENTED LESION

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Summary. HPV infection is involved in the etiology of a number of nonmalignant, premalignant and malignant cutaneous lesions. One of them is the so-called giant condyloma of Buschke-Löwenstein type (Buschke-Löwenstein tumor, BLT), which sometimes can imitate clinically other tumors or tumor-like conditions. Clinicians face a particular challenge in cases of BLT where, clinically, the lesions demonstrate a permanent brown hyperpigmentation in parallel with the dermatoscopic lack of the characteristic melanocytic network, globules or regression zones. There are uncommon clinical presentations with solitary, sharply demarcated pigmented lesions. In these cases the histopathological verification of the lesion is obligatory and the most efficient treatment method in the early period of the disease is the complete surgical excision. We report a case of a 74-year-old man who was admitted to the University Hospital "Lozenetz" in connection with profuse variceal bleeding of the esophagus associated with liver cirrhosis of unknown etiology. He underwent a consultative examination at the department of dermatology because of suspected advanced stage melanoma of the prepuce. Computed tomographic analysis indicated diffuse bone metastases located in the small pelvis and femur, as well as metastatic disease in the left inguinal lymph nodes. However, the subsequent histopathologic

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СЛУЖЕБНА БЕЛЕЖКА

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Additional Possibilities for Evaluation of cell pathological alterations: Comparative Study of reproduced elements of liver lobular segment in experimental (in vitro) model and tissue specimens of hepatocellular carcinoma (HCC).

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Abstract

Hepatocellular carcinoma is the fifth most common cancer and the third leading cancer killer in the world. Apoptosis occurs as part of tissue remodeling and avoids stimulation of inflammatory pathways. Pathological apoptosis may actually amplify the inflammatory process. Hepatocellular apoptosis is also a regular feature of the major inflammatory hepatic diseases.

The acute myeloid (eosinophilic) leukemia cell line EOL-1 and the hepatocellular carcinoma cell line HEP-G2 were used for the development of an *in vitro* model for hepatocyte stress. Cell survival of hepatocytes after co-culturing with PMA differentiated EOL-1 cells was estimated using the MTT assay. Patient samples were evaluated morphologically after staining.

No influence on the vitality of HEP-G2 cells was registered after co-cultivation with both differentiated and undifferentiated EOL-1 cells. Absence of such effect explains the low degree of infiltration of stimulated eosinophils toward organized clusters of hepatoma cells. Appearance of increased number of vacuoles in particular cells under treatment with activated eosinophilic cells is the consequence of the cellular adaptation toward probable inflammatory stress. This increases the capability of the hepatic cells to survive. The cell culture experiments showed high degree of correlation with the histological findings in tissue samples from the patients with primary hepatocellular carcinoma.

Key words: HEP G2 cell line, *in vitro* stress model, liver autophagy, hepatocellular carcinoma (HCC)

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ДЕРМАТОФИБРОМИКСОМ НА ИНГВИНАЛНАТА ГЪНКА ИМИТИРАЩ АКСЕСОРНА МАМИЛА: ХИРУРГИЧНО ЛЕЧЕНИЕ

Чернев Г., Чокоева А., Филипов С., Ананиев Ю.

Резюме:

Дерматофибромиксомът е рядък бенигнен тумор, който най-често се отстранява хирургично и налага обсъждането на редица диференциални диагнози с цел потвърждаване на хистогенезата му.

Представяме рядък случай на пациентка с туморна формация в ингвиналната област, с клинични данни и характеристика близка до тези за аксесорна мамила, хирургично ексцизирана и доказана хистологично като дерматофибромиксом.

Ключови думи: *дерматофирбомиксом, ингвинална област, хирургична ексцизия*

DERMATOFIBROMYXOMA OF THE INGUINAL FOLD MIMICKING ACCESSORY MAMMILLA: SURGICAL APPROACH

Tchernev G., Chokoeva A., Philipov S., Ananiev J.

Abstract: *Dermatofibromyxoma is a rare benign tumor which most often surgically removed and requires consideration of a number of differential diagnoses, in order to confirm its histogenesis.*

We present a rare case of a female patient with tumour formation in the inguinal region, with clinical manifestation and characteristics similar to those of accessory mammilla,which was surgically excised and histologically established as dermatofibromyxoma.

Key words: *dermatofibromyxoma, inguinal fold, surgical excision*

Въведение

Дерматофибромиксома представлява рядък бенигнен тумор разположен по-често по крайниците на човешкото тяло и състоящ се от умерена клетъчна пролиферация с фибробласт-подобни клетки и миксоиден и/или колагенен матрикс в дермата и в съчетание с хиперкератоза на надлежащия епидермис (1). Основна характеристика на тумора е наличието на солитарна нодуларна лезия и бавен растеж в дермата и подкожната тъкан.

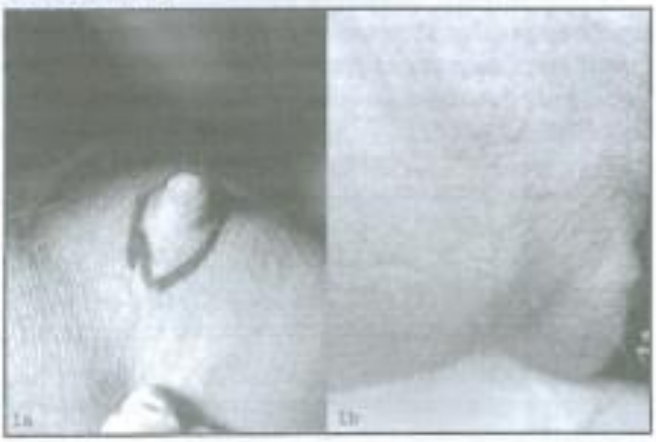
Ние представяме случай на пациентка с не голяма туморна формация в ингвиналната област, с макроскопска характеристика близка до тази на аксесорна мамила, хирургично ексцизирана и доказана хистологично като дерматофибромиксом.

Case report

Анамнеза и находка

Касае се за пациентка на възраст 62 години постъпващ в поликлиниката по повод на налична лезия в областта на дясна ингвиналната гънка, датираща от няколко години. Липсват данни за прекомерна употреба на алкохол и системна медикация, както и съпътстващи заболявания или инфекции.Не съобщава за вредности от битов и професионален характер.

Ингвинално се намери не голямо кожно образуване под формата на проминираща лезия с еластична консистенция и седефен цвят и с диаметър около 15 мм без зачервявания или пигментации около нея (Фиг.1a). Под локална анестезия се извърши елипсовидна ексцизия с поле на оперативна сигурност от 1 см и адаптиране на раневите ръбове с първичен кожен шев (Фиг.1b).



Лечение и хистологични данни

След извършване на ексцизия се проведе биопсично изследване. В материала се различава епидермис и дерма със съответната находка: в епидермиса - хиперкератоза и акантоза, репаративна епидермална хиперплазия и единична - солитарна инфундибуларна кератинова киста; в дермата сред обилен миксоиден матрикс се наблюдава нискостепенна колагенизация

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Conference Paper · June 2014

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Mid-IR Laser Tissue Ablation with Little Collateral Damage Using a Laser Tunable in the Water Absorption Peak

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Abstract: A comprehensive experimental study of mid-IR laser tissue ablation within the water absorption peak is presented. A novel all-solid-state table-top sub-ns mid-IR laser designed for efficient tissue ablation have been used for observation of wavelength-dependent effects on the ablation of hard and soft tissue.

OCIS codes: (170.1020) Ablation of tissue; (170.3890) Medical optics instrumentation

1. Introduction

An ultimate goal of minimally invasive laser surgery is to incise or remove a defined volume of tissue by laser ablation, while leaving the adjacent tissue biologically viable. Besides, minimizing collateral damage to adjacent tissue structures is vitally important when ablating in close proximity to nerve or other neural structures. The laser ablation characteristics and collateral damage effects depend on the optical absorption properties of the tissue and subsequent energy dissipation on distinct time scale. The optical absorption properties of tissue are governed by the electronic, vibrational, and rotational structures of the constituent biomolecules, thus they are dominated by the absorption of water, lipids and proteins, all of which show absorption bands in the mid-IR range. Tunable mid-IR lasers have an advantage over ultraviolet and visible or near-IR lasers. Water has sharp absorption peak around 3,000 nm, while lipids around. Changing the wavelengths of the laser would allow to fine-tune laser tissue interactions (penetration depth and density of the absorbed energy), minimizing the collateral heating effects in a tissue-specific manner. Hence, intense laser radiation tuned to specific absorption bands in this spectral region has the potential for carrying out selective ablation and is therefore of great relevance for advanced surgical procedures. In addition, tunable mid-IR lasers can optimize the laser tissue interaction for ablation and/or coagulation, i.e. the suppression of bleeding.

Here we demonstrate efficient tissue ablation using a novel all-solid-state table-top mid-IR laser tunable within the water absorption peak (3,000 to 3,500 nm) as a valuable alternative of mid-IR Free Electron Lasers (FEL). Comparative studies of the ablation process in different types of tissues and at different wavelengths across this biologically important spectral region have been carried out for the first time.

2. Experimental design

A sub-nanosecond, short cavity, singly resonant optical parametric oscillator (OPO) was constructed and its radiation was amplified in a highly efficient optical parametric amplifier (OPA), which was based on large aperture periodically poled stoichiometric lithium tantalate (PPSLT). The OPO uses a 20 mm long, 10 mm wide, and 3.2 mm thick PPSLT crystal with three poled zones with different domain inversion periods (30.2, 30.3 and 30.4 μm). The OPA stage employed a similar 37 mm long crystal. The pump source for the two frequency conversion stages was a diode-pumped master oscillator power amplifier system, providing 35 mJ pulses with high beam quality ($M_x^2 \times M_y^2$=1.3 × 1.1), 1.4 ns pulse duration at 0.5 kHz repetition rate. The maximum output idler energy from the system was 5.7 mJ with a pulse duration of 1.4 ns and the idler conversion efficiency in the OPA stage was 19%. By changing the temperature of the two PPSLT crystals from 40 °C up to 265 °C and by employing the three domain inversion periods, continuous tunability of the laser from 3 to 3.5 μm was achieved.

The repetition rate of the laser pulses was 500 Hz and the selected radiant energy per pulse was 3.0, 2.9, and 2.3 mJ at 3, 3.32, and 3.47 μm radiation wavelength, respectively. The focused beam spot has and elliptic shape with dimensions of 350 × 250 μm and had a near Gaussian beam profile. By advancing the stage by 2 mm/s continuous groves were created in the tissue. During the irradiation, the sample surface was kept at the focal point of the laser beam.

14 year-old female patient with rounded dark brown lesion in the breast area: Melanoma or nevus?

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14-jährige Patientin mit rundlicher dunkelbrauner Läsion im Bereich der Brust: Melanom oder Nävus?

14 year-old female patient with rounded dark brown lesion in the breast area: melanoma or nevus?

P. K. Penev, G. Tchernev, A. A. Chokoeva,
S. Philipov, J. Ananiev, U. Wollina

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Angiomyolipoma of the Helix without Signs of Systemic Involvement: Successful Surgical Approach

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LETTER TO THE EDITOR

ANGIOMYOLIPOMA OF THE HELIX WITHOUT SIGNS OF SYSTEMIC INVOLVEMENT: SUCCESSFUL SURGICAL APPROACH

G. TCHERNEV[1], S. PHILIPOV[2], J. ANANIEV[3], M. GULUBOVA[3], A.A. CHOKOEVA[4], C. TANA[5] and U. WOLLINA[6]

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Cutaneous angiomyolipoma (AMP) of the ear is an extremely rare benign mesenchymal tumour. Angiomyolipomas are the most common benign tumour of the kidney and could be associated in 20% of the cases with the tuberous sclerosis complex (TBC), in which condition, most of the patients have several angiomyolipomas affecting both of the kidneys. We report the rare case of a 66-year-old female who had an asymptomatic, solitary, nodule on the helix of the right ear for several years, which was histologically assessed as angiomyolipoma. There were no clinical signs of the tuberous sclerosis complex (TBC) or renal AML. A surgical excision was performed with an excellent therapeutic result. In contrast to renal AMLs or PEComas, which are often invasive and may involve regional nodes, cutaneous AMLs are solitary, non-invasive, and not associated with tuberous sclerosis, and are curable by simple elliptical excision.

We present the case of a 66-year-old female who had an asymptomatic, solitary, nodule on the helix of the right ear for several years (Fig. 1a). The physical examination revealed an exophytic tumour formation, covered with slightly lobulated skin (Fig. 1a). The patient was otherwise in good health and had no clinical signs of the tuberous sclerosis complex (TSC) or renal AML. Instrumental and imaging diagnostics did not shown evidence of involvement of other organs or systems in the human body. All laboratory investigations were within normal range.

The diagnosis of cutaneous angiomyolipoma was based on the histopathological examination of the lesion (Fig. 2 a-d). Fragments from the epidermis and papillary derma were observed in the same. Low-stage hyperkeratosis and acanthosis with pseudo epiteliomatous hyperplasia were also established. Mature adipocytes were represented in zones, with peripheral demarcation from the fibrous capsule. A presence of vascular network of capillaries was also observed. Within the various parts of the obtained materials the presented vessel network varies in size.

Key words: cutaneus angiomyolipoma, angiomyolipoma of the ear, tuberous sclerosis complex, renal AMP, PEComas

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LETTER TO THE EDITOR

WRONG MELANOMA THICKNESS MEASUREMENT: CHECK IT OR LEAVE IT?

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Cutaneous malignant melanoma (CMM) is one of the most aggressive forms of skin cancer, accounting for about 90% of deaths from cutaneous neoplasms, and its incidence has increased significantly in recent years. According to the 2012 European criteria for diagnosis and treatment of malignant melanoma, diagnosis should be based on the combination of clinical features, dermoscopic data and histological examination, preferably after excisional biopsy. Tumour thickness and other parameters for local staging according to the AJCC classification should be included in the pathology report. Although many factors influence the prognosis and course of the disease, it has been established in a number of studies that tumour thickness is the most important parameter. Therapy of malignant melanoma in its initial stages mostly consists of wide local excision with 1 to 2 cm margins, and sentinel lymph node biopsy that is usually performed in cases of tumours with a thickness greater than 1 mm. We present the case of a 58-year-old Bulgarian male with cutaneous superficial spreading malignant melanoma, in which, after complete excision, histological examination established an inaccurate tumour thickness (0.7 mm), with consequent inadequate staging and further management. After reassessment of the results in another institution (as well as their confirmation by two additional independent histopathology laboratories in our country – 1.92 mm), in the National Oncological Hospital where the patient was initially evaluated, sentinel lymph node biopsy was not performed, contrary to the generally accepted European and World standards. With the present case we raise some current issues regarding diagnosis and therapy of Bulgarian patients (not only in the case presented) with malignant melanoma in the 21st century, and discuss the urgent need for external quality control procedures and standardization of the histopathologic reporting, which is of paramount importance in the staging and subsequent management of these patients.

Cutaneous malignant melanoma (CMM) is one of the most aggressive forms of skin cancer, accounting for about 90% of deaths from cutaneous neoplasms (1). Although it represents only about 3 to 5% of all skin cancers, malignant melanoma represents a serious public health problem as its frequency is increasing more rapidly than any other cancer in the world (1, 2). If in 1930, the risk of developing

Key words: diagnosis, surgical excision, malignant melanoma, treatment, SLNB, tumour thickness

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EDITORIAL

THE "MYSTERY" OF CUTANEOUS SARCOIDOSIS: FACTS AND CONTROVERSIES

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The reason why the cutaneous form of sarcoidosis is well known in the literature is because of its spectrum of manifestations granting it the fame of a Great Imitator. The mystery shrouding the pathogenesis of this rare cutaneous disease is still there (in spite of the fundamental progress of the various diagnostic methods in current day medicine). The production of the morphological substrate – the epithelioid cell granuloma – which is considered to be characteristic of skin sarcoidosis, could, however, also be the end result of a reaction to i) various specific infectious agents such as Leishmaniasis cutis, coccidioidomycosis, etc., ii) certain residual bacterial or other mycobacterial antigens which, at the moment of setting the diagnosis are - by definition - non-infectious but still immunogenic, as well as iii) different tumor antigens in lesional tissue or other location. Often, differentiating between sarcodiosis and a sarcoid-like reaction, based on the updated criteria for cutaneous sarcoidosis, is problematic to downright impossible. A future characterization of the genetic signature of the two conditions, as well as the implementation of additional mandatory panels for i) the identification of certain infectious or ii) non-infectious but immunogenic and iii) tumor antigens in the epithelioid cell granuloma (or in another location in the organism), could be a considerable contribution to the process of differentiating between the two above-mentioned conditions. This will create conditions for greater accuracy when setting the subsequent therapeutic approaches.

Key words: sarcoidosis, sarcoid like reaction, genetic signature, bacterial antigens, tumor antigens

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Macrophages and dendritic cells in the development of liver injury leading lo liver failure

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LETTER TO THE EDITOR

MACROPHAGES AND DENDRITIC CELLS IN THE DEVELOPMENT OF LIVER INJURY LEADING TO LIVER FAILURE

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Liver failure (LF) continues to be a serious problem due to different underlying disorders. Not only hepatocytes but Kupffer cells (KCs) and dendritic cells (DCs) are of importance in this instance. We wanted to investigate the possible role of KCs and liver DCs in the development of liver injury in patients with liver failure. Liver specimens from 23 patients who died after liver failure were examined for the presence and distribution of CD68-positive KCs and CD83-positive DCs by immunohistochemistry. The distribution of the CD83-positive DC in the sinusoidal and the periportal spaces was not even. While 39.1% of patients had a high sinusoidal density of CD83-positive cells, 60.9% demonstrated a high density of CD83-positive cells in the periportal tract. The number of CD83-positive DCs in periportal tracts in patients with advanced liver fibrosis (n = 5) were high, while those with mild liver fibrosis (n = 18) had low numbers of mature dendritic cells ($\chi 2=4.107$; $p=0.043$). In addition, all patients with intensive fibrosis had low counts of CD68-positive KC's in portal tracts *vs* patients with mild fibrosis of which 67% had high counts ($\chi 2=6.97$; $p=0.008$). In seven of the patients with moderate steatosis (87.5%) low numbers of CD68-positive KCs were found in sinusoids, in contrast to those with severe steatosis, where 12 patients (80%) had high KC counts ($\chi 2=13.4$; $p<0.001$). The distribution and number of CD68-positive KC and CD83-positive DC reflect the progression of liver fibrosis leading to liver failure.

Liver failure is defined by the American Association for the Study of Liver Diseases (AASLD) and the European Association for the Study of the Liver (EASL) as an "acute deterioration of pre-existing chronic liver disease usually related to a precipitating event and associated with

Key words: liver failure, Kupffer cells, dendritic cells

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DISCLOSURE: ALL AUTHORS REPORT NO CONFLICTS OF INTEREST RELEVANT TO THIS ARTICLE.

Рентгенология и Радиология

ПРАВОПРИЕМНИК НА "ИЗВЕСТИЯ НА БЪЛГАРСКОТО РЕНТГЕНОЛОГИЧНО ДРУЖЕСТВО"

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Вретеновидно-клетъчен тумор на млечната жлеза

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Spindle cell tumor of the breast

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Резюме. Вретеновидно-клетъчните тумори са рядък подтип на карцинома на млечната жлеза и спадат към категорията на метапластичните неоплазми на гърдата.

Представяме клиничен случай от практиката. Ще разгледаме образните и хистологичните характеристики на този вид тумор и образните методи за диагностика.

Обикновено се представят като добре отграничени формации с образуване на големи кистични компоненти. Хистологично доминиращи са слоеве от вретеновидни по форма клетки и компоненти, както при сквамозия и инвазивния дуктален карцином. Въпреки саркоматозните си характеристики вретеновидните клетки произхождат от епитела на млечната жлеза.

Метод на избор за диагностика на този тип тумор е мултимодалният подход, включващ ехомамография, мамография, МР мамография, кор-биопсия и КТ за стадиране.

Ключови думи: ВРЕТЕНОВИДНО-КЛЕТЪЧЕН ТУМОР. КАРЦИНОМ. ХИСТОЛОГИЯ. ЕХОМАМОГРАФИЯ. МАМОГРАФИЯ. МР МАМОГРАФИЯ. КОР-БИОПСИЯ. КТ

Abstract. Spindle cell breast carcinoma is a rare subtype of breast cancer, that falls within the general category of metaplastic breast carcinoma.

We present a case of spindle cell carcinoma of the breast and review its radiological appearance, pathophysiological characteristics and radiological methods for diagnosis.

Spindle cell carcinoma frequently forms a large and well-circumscribed tumor with gross cyst formation. Histologically, its dominant component is of sheets of spindle shaped cells, and it includes such contiguous carcinoma components as squamous differentiation or invasive ductal carcinoma. Despite the sarcomatous features, spindle cells are likely to be derived from epithelial cells of mammary glands.

The method of choice in the diagnosis of these tumors is a multimodal approach including US, mammograms, MR, „cor" biopsy and CT for staging.

Key words: SPINDLE CELL TUMOR. CARCINOMA. HISTOLOGY. US. MAMMOGRAM. MR. "COR" BIOPSY. CT

Efficient Tissue Ablation using a Laser Tunable in the Water Absorption Band at 3 microns with little collateral damage

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Efficient Tissue Ablation using a Laser Tunable in the Water Absorption Band at 3 microns with little collateral damage

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ABSTRACT

Lasers can significantly advance medical diagnostics and treatment. At high power, they are typically used as cutting tools during surgery. For lasers that are used as knifes, radiation wavelengths in the far ultraviolet and in the near infrared spectral regions are favored because tissue has high contents of collagen and water. Collagen has an absorption peak around 190 nm, while water is in the near infrared around 3,000 nm. Changing the wavelength across the absorption peak will result in significant differences in laser tissue interactions. Tunable lasers in the infrared that could optimize the laser tissue interaction for ablation and/or coagulation are not available until now besides the Free Electron Laser (FEL). Here we demonstrate efficient tissue ablation using a table-top mid-IR laser tunable between 3,000 to 3,500 nm. A detailed study of the ablation has been conducted in different tissues. Little collateral thermal damage has been found at a distance above 10-20 microns from the ablated surface. Furthermore, little mechanical damage could be seen in conventional histology and by examination of birefringent activity of the samples using a pair of cross polarizing filters.

Keywords: laser-tissue interaction, near-infrared, laser, ablation, surgery

1. INTRODUCTION

Over the last decades the introduction of lasers has advanced several medical disciplines and opened completely novel treatment opportunities in medical areas such as neurosurgery, cardiology, dentistry, urology, or dermatology [1-4]. The procedures and the methods for medical treatment and research take advantage of a wide variety of laser-tissue interaction mechanisms, including photothermal, photomechanical and photochemical interactions [4, 5]. Recently, there has been increasing interest in the use of lasers in the infrared (IR) region. For this range the penetration depth of the radiation changes drastically [6]. Changing the wavelengths of the laser would allow one to fine tune laser tissue interactions (penetration depth and radiant energy density), minimizing the collateral heating effects in a tissue specific manner. Moreover, the latest solid-state laser technology ensures small and compact design and fiber optic delivery options. Hence, these lasers are indispensable for minimally invasive surgery. Currently, there are several commercial IR lasers available that have individual (fixed) single wavelength output and thus, their application range is strongly limited to specific surgical tasks performed at those specific wavelengths. In other words, some lasers are ideal for tissue cutting in fluid-filled spaces, while others for kidney stone fragmentation or coagulation of the tissue etc. [4]. Instead of using multiple separate laser units – which is practically impossible – it would be economically and practically efficient to combine the many characteristic features each laser system provides into a *single compact table-top laser instrument*. Here we present the results obtained with such a novel laser.

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Multiple primary cutaneous melanomas in patients with FAMMM syndrome and sporadic atypical mole syndrome (AMS): What's worse?

Georgi Tchernev, Julian Ananiev, José-Carlos Cardoso, Anastasiya Atanasova Chokoeva, Stanislav Philipov, Plamen Kolev Penev, et al.

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Multiple primary cutaneous melanomas in patients with FAMMM syndrome and sporadic atypical mole syndrome (AMS): What's worse?

Georgi Tchernev · Julian Ananiev · José-Carlos Cardoso · Anastasiya Atanasova Chokoeva · Stanislav Philipov · Plamen Kolev Penev · Torello Lotti · Uwe Wollina

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Summary Atypical Mole Syndrome is the most important phenotypic risk factor for cutaneous melanoma, a malignancy that accounts for about 80% of deaths from skin cancer. Since early diagnosis of melanoma is of great prognostic relevance, the identification of Atypical Mole Syndrome carriers (sporadic and familial) is essential, as well as the recommendation of preventative measures that must be undertaken by these patients.

We report two rare cases concerning patients with multiple primary skin melanomas in the setting of a familial and a sporadic syndrome of dysplastic nevi: the first patient is a 67-year-old patient with a history of multiple superficial spreading melanomas localized on his back. The second patient presented with multiple primary melanomas in advanced stage in the context of the so-called sporadic form of the syndrome of dysplastic nevi—AMS (atypical mole syndrome). In the first case, excision of the melanomas was carried out with an uneventful post-operative period. In the second case, disseminated metastases were detected, involving the right fibula, the abdominal cavity as well as multiple lesions in the brain. The patient declined BRAF mutation tests as well as chemotherapy or targeted therapies, and suffered a rapid deterioration in his general condition leading to death. We classified the second case as a sporadic form of the atypical mole syndrome, associated with one nodular and two superficial spreading melanomas.

There are no data in the literature to allow us to understand if, in patients with multiple primary melanomas, there is any difference in terms of prognosis between those with and without a family history of a similar phenotype. To answer this and other questions related to these rare cases, further studies with a significant number of patients should be carried out.

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Relapsing advanced metatypical basal cell carcinomas (MTBCC) of the face: Surgical modalities

Georgi Tchernev · Anastasiya Atanasova Chokoeva · Plamen Kolev Penev · Julian Ananiev · Andreas Nowak · Yousef Bayyoud · Stanislav Philipov · José-Carlos Cardoso · Uwe Wollina

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Relapsing advanced metatypical basal cell carcinomas (MTBCC) of the face: Surgical modalities

Georgi Tchernev · Anastasiya Atanasova Chokoeva · Plamen Kolev Penev · Julian Ananiev · Andreas Nowak · Yousef Bayyoud · Stanislav Philipov · José-Carlos Cardoso · Uwe Wollina

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Summary Metatypical basal cell carcinoma (MTBCC) represents a high-risk type of cutaneous tumour. We report about three different patients with relapsing advanced large MTBCC: one of the scalp and two of the cheek region. Such patients required in most of the cases a complex surgical approach to achieve a stable and complete remission.

In the first presented patient a combination of flaps and grafts has been performed. We describe tailored surgical approaches. By this contrivance it is possible to treat even elderly patients with exposed bone after complete excision effectively and safe. Interdisciplinary team work is for the benefit of these patients.

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Дистални стенози на лява предна десцендентна артерия – оперативен мениджмънт, клинични корелации и хистологичен профил

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Distal stenosis of left anterior descending coronary artery – surgical management, clinical correlation and histological profile

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Дистални стенози на лява предна десцендентна артерия – оперативен мениджмънт, клинични корелации и хистологичен профил

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Резюме

Въведение

Стенозите на лявата предна десцендентна коронарна артерия (ЛАД) са обект както на интервенционални, така и на хирургични намеси. Настоящото проучване има за цел да провери пригодността и качеството на дисталния край на лявата *a. mammaria interna* (АМИ) при употребата ѝ за кондюит, когато са налице дистални или каскадни стенози на ЛАД и таргетната зона за реваскуларизация е именно дисталният ѝ край.

Изложение

Извършването на байпас с АМИ към ЛАД е отдавна утвърден златен стандарт в сърдечната хирургия. Наличието на каскадни или дистални стенози на ЛАД налага поставяне на подобен байпас в апико-дисталните части на съда – там, където луменът не е толкова голям, колкото в проксималните сегменти. От своя страна това изисква и добра дължина на АМИ за реализирането на такъв байпас, без да се подлага графтът на излишна тракция.

Материали и методи

В настоящото проучване са включени 17 болни (13 мъже и 4 жени), оперирани в клиниката по кардиохирургия към УБ „Лозенец" по повод исхемична болест на сърцето и с данни за таргетна зона за байпас в средните към дисталните сегменти на ЛАД. Дисталните отдели на АМИ се резецират (1–3 сантиметра) и се подлагат на хистологично изследване.

Заключение

Преходът на ЛИМА (лява вътрегръдна артерия – left internal mammary artery) от еластична в мускулна артерия става още в нейния дистален

Abstract

Introduction

Left anterior descendent artery (LAD) stenosis is managed either percutaneously or surgically. Our study aims to confirm whether the distal part of the left internal mammary artery (LIMA) is appropriate to be used as a conduit for revascularization of distal LAD stenoses.

Objectives

LIMA to LAD anastomosis is the most commonly used bypass graft in coronary surgery. However multiple or distal LAD stenoses require revascularization to be performed using the distal parts of the LIMA, where the vessel lumen is not as wide as in the proximal segment. Further to that, optimal distal grafting requires sufficient length of the artery to avoid unwanted traction of the graft.

Materials and methods

The current study includes 17 patients (13 men and 4 women) who have been diagnosed with Coronary artery disease (CAD) and a targeted zone for anastomosis in the middle to distal LAD, and have undergone surgery in the department of Cardio-thoracic surgery at UH Lozenetz. Distal LIMA segments were resected (1–3 cm) and sent for histological examination.

Conclusions

LIMA transition from elastic type of artery to muscular type of artery occurs in its distal segment before its bifurcation. Thus it is recommended to

МЕТАТИПИЧЕН БАЗАЛНОКЛЕТЪЧЕН КАРЦИНОМ НА НОСА – ОПИСАНИЕ НА КЛИНИЧЕН СЛУЧАЙ

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METATYPICAL BASAL-CELL CARCINOMA OF THE NOSE: DESCRIPTION OF A CLINICAL CASE

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МЕТАТИПИЧЕН БАЗАЛНОКЛЕТЪЧЕН КАРЦИНОМ НА НОСА – ОПИСАНИЕ НА КЛИНИЧЕН СЛУЧАЙ

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Резюме:

Базалноклетъчният карцином (БКК) е най-честата злокачествена кожна канцероза. Множествени са причините, водещи до възникването му, като най-важните са свързани с интензивното ултравиолетово лъчение и светлия тип кожа при засегнатите пациенти. Той съставлява приблизително 80% от всички немеланомни кожни карциноми. Метатипичният БКК е рядка подформа, в която се съчетават клинични и хистопатологични признаци едновременно на БКК и сквамозноклетъчния карцином, като рискът от метастазиране на лезията се оценява общо на не повече от 5%. Клиничната картина е по-скоро нетипична, което води до грешна интерпретация, а нерядко и до грешен диагностичен и терапевтичен подход. Нетипичната клинична картина на засегнатите пациенти често се оказва и основен проблем, водещ при някои пациенти и до летален изход. Представяме случай на метатипичен базоцелуларен карцином на носа, лекуван първоначално с криотерапия, електрокаутер и локална деструктивна терапия, без да бъде взета хистология. Последвалата прогресия на тумора и проведената хирургична ексцизия доказаха наличието на метатипичен базоклетъчен карцином. Постигнат бе отличен естетичен резултат.

Ключови думи: метатипичен базалноклетъчен карцином, елипсовидна ексцизия, хистологична верификация

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Summary:

Basal-cell carcinoma (BCC) is the most common malignant cutaneus cancer. The causes leading to its occurrence are various, as the most important of them are associated with the intense ultraviolet light and the bright skin type in the affected patients. It accounts for approximately 80% of all non-melanoma skin cancers. Metatypical BCC is a rare subform of BCC which combines the clinical and histopathological features of BCC and squamous cell carcinoma, simultaneously, while the risk of metastasis in these lesions is assessed in approximately 5%. The clinical manifestation is rather atypical, leading to misinterpretation, not infrequently with an inadequate diagnostic and subsequent therapeutic approach. The atypical clinical features, manifested in the affected patients are often a major problem, leading to fetal outcome in some of the cases. We present a case of metatypical basal-cell carcinoma of the nose, initially treated with cryotherapy, electrocauterization, as well as local destructive therapy, without

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TWO CASES OF LIPOSARCOMA IN THE THIGH AREA

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Abstract

The liposarcoma are not rare in the thigh area. Two patients both men, 56 and 39 years of age were operated within a few months because of giant liposarcoma in the left thigh region. The liposarcoma of these patients was strikingly similar. Upon suspicion of malignancy, resection of the tumor without prior diagnostic biopsy is recommended**.** The early postoperative period of both patients passed smoothly. The full range of movement was achieved in left hip and knee joints. Operative wounds healed *per primam intentionem*. Up till now, several months after tumors removal, both patients have no data of local or distant metastases.

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Key words: *Excisio en bloc*, liposarcoma, malignant tumor, limb sparing surgery

Introduction

The liposarcoma involves heterogenic group of sarcomas in which cells differentiate in lipoblasts and lipocytes and according to many authors it is the most frequent sarcoma of the soft tissues. The tumor prevails in males when it is localized in the limbs and it is very rare prior to 20 years of age. Histological varieties of adipose tumors are presented in Table 1.

Table 1. Adipocytic tumors according to WHO 2013

Intermediate (locally aggressive)
Atypical lipomatous tumour / well differentiated liposarcoma
Malignant adipocytic tumors
Dedifferentiated liposarcoma
Myxoid liposarcoma
Pleomorphic liposarcoma
Liposarcoma, not otherwise specified

Well differentiated and purely myxoid liposarcomas are low-grade, while pleomorphic and dedifferentiated types are high-grade malignant tumors. Metastases are exceptional in well differentiated liposarcoma, and frequent and early in pleomorphic and dediferentiated type (1). The dedifferentiated types, metastasize to more than 50% of the cases and predominantly in the left lung. Into deep tissues of extremities, the tumor can remain undiagnosed for long time and highly differentiated forms can undergo dedifferentiation (2). Differential diagnosis between liposarcoma, lipoma, spindle and pleomorphic lipoma should be done (3). Limb sparing surgery is the recommended treatment for liposarcomas. The postoperative radio- and chemotherapy and adjuvant

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In vitro and *in vivo* toxicity evaluation of cationic PDMAEMA-PCL-PDMAEMA micelles as a carrier of curcumin

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ABSTRACT

Polymeric micelles have attracted significant attention because of their potential application as promising drug-delivery systems. In the present study cationic micelles, based on triblock copolymer poly(-dimethylaminoethyl methacrylate) - poly(e-caprolactone) - poly(dimethylaminoethyl methacrylate) were prepared and loaded with curcumin. *In vitro* cytotoxicity of empty and curcumin loaded polymer micelles was investigated on two cell culture models, human hepatoma cell line HEP G2 and freshly isolated rat hepatocytes, following their viability and lactate dehydrogenase (LDH) leakage. MTT dye reduction assay and LDH release study showed that empty cationic micelles did not cause significant changes in cell viability and membrane integrity at the concentration range from 10.0 to 80.0 μg/ml. Our special attention was focused on the effects of empty and curcumin loaded micelles on oxidative stress markers malondialdehyde (MDA) and reduced glutathione (GSH). The increase in the micelles concentration to 100 μg/ml was accompanied by GSH depletion and increased levels of MDA production in isolated rat hepatocytes. The *in vivo* toxicity of polymeric micelles was examined in male *Wistar* rats. The results showed that neither single (7.5 mg/kg, i.p.), nor repeated (3.5 mg/kg, i.p., 14 days) exposure to empty or curcumin loaded polymeric micelles induced any toxicity changes, e.g. hematopoietic and liver tissue damages.

1. Introduction

With the growing application of polymeric materials as drug carriers the concerns of their safety are increasing, but the current understanding on the toxicity of these carriers, especially the newly synthesized is very limited. Among various polymers, cationic polymers are attractive nanocarriers mainly because of their potential in gene delivery (Lin et al., 2008; Layman et al., 2009; Qiao et al., 2010). In addition, cationic polymers could lead to improved interactions between nanoparticulate systems and cell membranes. However, various studies have reported the toxicity of some cationic polymers (Fischer et al., 2003; Lv et al., 2006). According to some studies, the high concentration of amino groups can result in high cytotoxicity, whereas the presence of poly(-ethylene glycol) (PEG) reduces the relative concentration of amino groups and cytotoxicity of polycationic carriers (Van de Wetering et al., 1997; Van de Wetering et al., 1998). Zhang et al. evaluated cytotoxicity of branched polyethylenimine and linear poly(ethylene glycol monomethyl ether)-block-poly(ε-caprolactone)-block-poly(2-(dimethylamino)ethyl methacrylate) (mPEG-PCL-PDMAEMA) copolymer on two cell lines (Zhang et al., 2010). The study reported less toxicity of mPEG-PCL-PDMAEMA copolymer compared to branched PEI, probably due to the presence of mPEG and PCL. In another study, copolymerization of PDMAEMA with methacrylated chondroitin sulphate led to significantly improved cell viability compared to PDMAEMA (Lo et al., 2013).

Poly(2- (dimethylamino)ethyl methacrylate) is an example for cationic polymer widely studied as carrier of gene and drug delivery systems (Verbaan et al., 2005; Karanikolopoulos et al., 2010).

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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

მცხოვრებ მოზარდებში. ნატარებული კვლევის შედეგად ქ. აქტობეში მცხოვრებ პირობითად ჯანმრთელ მოზარდების 72%-ში გამოვლინდა ოსტეოპენია. ძვლის ქსოვილის მინერალური სიმკვრივის (ძმს) მაჩვენებლები ორი ეთნოსის წარმომადგენლებში (ყაზახები და რუსები) არ განსხვავდებოდა ერთმანეთისაგან. ძმს-ს მიხედვით, ბიჭებში ოსტეოპოროზის მაჩვენებელი 1.5-ჯერ მაღალი აღმოჩნდა გოგონებთან შედარებით. გამოკვლეულებში ძვლის ქსოვილის რემოდელირება განპირობებული იყო ოსტეოხინთეზის და ოსტეორეზორბციის მარკერებით PINP და β-Cross Laps, შესაბამისად, მათი მკიერი კორელაციური კავშირით ($r=0.8$) დაქვეთებული და ნორმალური ძმს-ის პირობებში. ძმს-ის დაქვეთება ყაზახეთის მოზარდებში გამოიხატებოდა β-Cross Laps-ის მაჩვენებლის და პუმორული რეგულატორის (პარათირეოიდული ჰორმონი) მომატებით, რომლებიც პასუხისმგებელია ოსტეორეზორბციაზე ძვლის ქსოვილის რემოდელირების პროცესში.

NEVUS FLAMMEUS ASSOCIATED WITH DYSPLASTIC NEVI AND LICHEN SCLEROSUS: THE FIRST REPORT IN THE MEDICAL LITERATURE

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Nevus flammeus or port-wine stain is a congenital cutaneous venulocapillary malformation of unknown pathogenesis, in which the presence of dilated blood vessels leads to a reddish-purplish patches or plaques, sometimes evolving later into nodular lesions [10]. Lichen sclerosus et atrophicus is a chronic, inflammatory skin disease of unknown etiology, characterized by hardened, discrete or confluent pruritic atrophic papules with ivory-porcelain-white discoloration and keratotic plugs, microscopically showing epidermal hyperkeratosis, atrophy, superficial dermal edema, homogenization of collagen and mid-dermal inflammation [11]. Dysplastic nevus is perhaps one of the most controversial concepts in dermatology and dermatopathology, usually defined as a junctional or compound benign melanocytic proliferation with various degrees of architectural disorder and cytological atypia. It is often clinically manifested by such atypical features as heterogenous color and irregular borders. Although there is a poor correlation between the degree of clinical and histopathological atypia [11]. Variaety of theories of diverse origin raise the question of a potential genetic background for these three entities. Higher rates of lichen sclerosus have been reported among twins and within the same family [11]. Port-wine stains were shown to be caused by mutations in the *GNAQ* gene and to be associated with *RASA1* or as a part of such syndromes as Sturge-Weber or Klippel-Trénaunay-Weber [2]. Furthermore, the genetic background of dysplastic nevi in the context of the dysplastic nevus syndrome (also known as Atypical Mole Syndrome (AMS), Familial Atypical Multiple Mole-Melanoma (FAMMM) syndrome and "B-K mole syndrome") has been also well investigated [12].

To the best of our knowledge, despite being reported in different contexts and with different associations and manifestations, co-existence of these three diseases has never reported until now. Thus, the purpose of this report is to present a rare case of such association, discussing the possible pathogenic link between the three entities. Although this combination could be only a fortuitous occurrence, we cannot exclude that it could result from common pathogenic mechanisms thus corresponding to a defined entity.

Material and methods. *Case report.* A 28 year-old white male patient presented to our clinic complaining of pruritus and increased sensitivity in the area of the penile prepuce. Examination of the genital area revealed the presence of erythema and confluent ill-defined papules on the prepuce and coronal sulcus (Fig. 1d). Whole body dermatological examination discovered a unilateral form of nevus flammeus (NF) along almost the whole length of the right lower limb (Fig. 1a,b,c,e) and two nevi with atypical clinical features, one located on the mid back and the other on the medial aspect of the fifth toe, the latter coinciding with an area involved by the nevus flammeus (Fig. 1e). Because

Melanoma in situ (MIS) in a patient with atypical mole syndrome (AMS): with aggressiveness to success?

G. Tchernev, A. A. Chokoeva, T. Lotti & S. Philipov

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Melanoma in situ (MIS) in a patient with atypical mole syndrome (AMS): with aggressiveness to success?

G. Tchernev · A. A. Chokoeva · T. Lotti · S. Philipov

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Dear editors,
Malignant melanoma is an extremely aggressive tumor, which is responsible for approximately 80 % of the mortality caused by cutaneous tumors in general [1]. The lowest invasive variant of melanoma is the so-called melanoma in situ (MIS), accounting for approximately 27 % of all melanomas [2]. This noninvasive lesion is in fact a precursor to invasive disease, which highlights the obligation for their careful and regular follow-up [2].

We present a case of a 52-year-old white male patient, presenting to the dermatologic unit for surgical removal of a pigmented lesion with a long-lasting history, which recently became more pronounced, causing moderate discomfort and itching. Arterial hypertonia was reported as an accompanied disease, well-controlled with medicines. Family history was negative for dermatologic diseases.

The patient was second to third phenotype. Multiple pigmented lesions (>50) were clinically established all over his body, most of them clinically atypical. The attention was focused on 2 lesions, located on the left upper part of the back—one of them was brownish to black colored tumor with elliptic shape and irregular borders, slightly elevated above the skin surface, rounded by erythematous ring, measuring 2.5/1.5 cm in diameter, highly suspicious for malignant melanoma, while the other located more proximately was reddish to brown colored oval-shaped nevus with sighs of dysplasia (Fig. 1a). Elevation of the lymphocytes count was established from the conducted laboratory blood tests (30.2), while no pathologic abnormalities were revealed on the imaging diagnostic procedures. An elliptic surgical excision was performed under local anesthesia; the pigmented tumor was removed with 1 cm field of surgical safety in all directions and depth to the underlying muscle's fascia (Fig. 1b, c and d).

Histological examination of the removed suspicious lesion revealed the diagnosis of melanoma in situ, in confirmation to our clinical observations. The other removed lesion was verified as junctional nevus.

Both genetics and environment factors are implicated in the malignant transformation of the melanocytes, as the presence of multiple melanocytic nevi, dysplastic nevi and atypical mole syndrome (AMS), are among the most important [1]. According a study by Bataille et al., atypical naevi consist the highest relative risk for development of cutaneous melanoma, with an odds ratio of 28.7 ($P < 0.0001$) for

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Case Report

Subungual Exostosis in a Young Soccer Player

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Keywords: Surgery; exostosis; nail; verruca vulgaris; treatment outcome

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Abstract

BACKGROUND: Subungual exostosis is a relatively uncommon, benign osteocartilaginous tumor of the distal phalanx of the toes or fingers in young adults, considered as a rare variant of osteochondroma. Differential diagnoses include subungual verruca (viral wart), pyogenic granuloma, osteochondroma, amelanotic subungual melanoma and glomus tumour. Misdiagnosis and total onychodystrophy frequently occur as a result of late treatment or inadequate treatment strategy. Dermoscopy could be a useful technique, involved in the diagnostic process, although X-ray examination and histopathology are mandatory for the diagnosis.

CASE REPORT: We report a rare case of subungual exostosis of the great toe associated with repeated trauma of the nail bed. The lack of radiographic and histopathological examination could lead to misdiagnosis and inadequate treatment. Although completely benign, subungual exostosis should be considered in differential diagnosis of nail bed tumors in young adults, in order to avoid associated complications and unneeded aggressive surgical interventions.

CONCLUSION: Complete excision of the lesion and delicate separation from the underlying nail bed structures results in total resolve of the problem, by providing the lowest risk of recurrences.

Introduction

Subungual exostosis (SE) is a relatively uncommon, benign osteocartilaginous tumor of the distal phalanx of the toes or fingers, considered as a rare variant of osteochondroma [1][2].

First described by Dupuytren in 1847, SE is the most common nail tumor of young adults, representing a benign bony proliferation of the distal phalanx with unknown etiology [2][3].

The proposed possible triggering factors include constant irritation of the bone, previous trauma and longstanding infection [1]. Two inherited conditions could be manifested as subungual exostosis, namely multiple exostoses syndrome and multiple exostoses-mental retardation syndromes [3]. Although completely benign, SE must be differentiated between a number of other subungual tumors, both benign and malignant [4]. There are increasing evidences of histological differences between subungual exostosis and subungual osteochrondroma. Histologically, subungual exostosis has a fibrocartilaginous cap whereas osteochondroma has distinctive hyaline cartilage [5]. When the

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Case Report

Subungual Squamous Cell Carcinoma Associated with Long Standing Onychomycosis: Aggressive Surgical Approach with a Favourable Outcome

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Keywords: Subungual squamous cell carcinoma; nail neoplasms; HPV; viral wart; surgery; onychomycosis.

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Abstract

BACKGROUND: Tumours of the nail bed are rare. Squamous cell carcinoma is the most frequent among them. Chronic infection, chemical or physical trauma/microtrauma, genetic disorders such as congenital ectodermal dysplasia, radiation, tar, arsenic or exposure to minerals, sun exposure, immunosuppression, and previous HPV infection have all been discussed as etiologic factors. The diagnosis is often delayed because of the variety of clinical manifestations, often resembling benign or common infectious processes. Rapidly growing ulcerative lesions should also be considered as potential malignancy. Furthermore, a lack of antifungal or antibacterial treatment response is the most indicative symptom, always requiring subungual biopsy. Early diagnosis is of great importance for therapeutic effectiveness.

CASE PRESENTATION: We present a case of subungual squamous cell carcinoma, associated with long-lasting onychomycosis in a 76-year-old female patient, treated with amputation of the distal phalanx and the distal part of the proximal phalanx.

CONCLUSION: Although there are no available data in the literature to confirm or reject the contribution of the chronic nail infection to the malignant process, we emphasise the importance of this co-existence regarding the possible disguising of the malignant process. An early biopsy of a chronic persistent nail lesion may be preventive and beneficial regarding avoiding more aggressive treatments and achieving a favourable prognosis.

Introduction

Subungual squamous cell carcinoma (SSCC) is a rare malignancy, with few reported cases affecting the toe reported in the medical literature [1]. The aetiology of these lesions is poorly understood, and although this location is associated with low risk for metastasis, cases with inguinal lymph node metastasis after amputation of the affected toe have also been described [1]. The diagnosis is often delayed because of the variety of clinical manifestations, often resembling benign or common infectious processes [2]. For that reason, the real incidence of this tumour is difficult to determine [2, 3]. Although a standardised therapeutic approach does not currently exist, early diagnosis is essential for treatment effectiveness [3].

Case report

We present a 76-year-old Caucasian female patient who presented to the dermatology unit with a 3-year history of chronic, persistent ulceration on the left great toenail (Figure 1a). The diagnosis of onychomycosis was made three years ago, based on the clinical manifestation of yellowish discoloration of the nail, dystrophy of the nail, confirmed by direct

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Antioxidant response and biocompatibility of curcumin-loaded triblock copolymeric micelles

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RESEARCH ARTICLE

Antioxidant response and biocompatibility of curcumin-loaded triblock copolymeric micelles

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ABSTRACT

To evaluate the safety profile of cationic micelles, based on triblock copolymer poly(dimethylaminoethyl methacrylate)–poly(e-caprolactone)–poly(dimethylaminoethyl methacrylate) ($PDMAEMA_9$–PCL_{70}–$PDMAEMA_9$), the effects of empty (PM) and curcumin loaded micelles (PM-Curc) on nonenzyme induced lipid peroxidation (LPO) *in vitro*, hemolytic activity and morphological changes in some organs after repeated intraperitoneal administration *in vivo* were studied. To induce LPO, rat liver microsomes were incubated with a solution of iron sulfate and ascorbinic acid (Fe^{2+}/AA). The effect of empty PM (40 and 100 μg/ml), PM-Curc and free curcumin (both at 3.48 and 8.7 μg curcumin/ml) was assessed at 20 min incubation time. In the non-enzyme induced LPO model, the investigated substances at all concentrations significantly decreased the formation of malondialdehyde (MDA), compared to the Fe^{2+}/AA induced LPO group. According to the results it can be concluded that curcumin alone and loaded in PM, exert significant antioxidant activity. In the biocompatibility safety studies, the mean hemolytic index for polymeric carrier was less than 2%, indicating it was non-hemolytic. The general appearance of the organ tissues from *Wistar* rats, treated *in vivo* with curcumin loaded PM was similar to that of controls, thus showing no apparent toxicity after repeated 14-days treatment.

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Antioxidant activity; lipid peroxidation; hemolysis; curcumin; polymeric micelles

Introduction

Curcumin is a natural polyphenol with numerous beneficial effects for human health, which include antioxidant, anti-inflammatory, neuroprotective, chemopreventive and chemotherapeutic properties (Chuengsamarn et al., 2012; Huang et al., 2013; Kusuma et al., 2014; O'Sullivan-Coyne et al., 2009; Thakare et al., 2013). Several mechanisms have been proposed for curcumin antioxidant effects, including inhibition of superoxide anion production and lipid peroxidation (LPO) (Dutta et al., 2005). Curcumin prevented mitochondrial reactive oxygen species (ROS) generation, reduction of membrane fluidity and the reduction of antioxidant enzyme levels (superoxide dismutase, catalase) and reduced glutathione in hepatic tissues, indicating hepatoprotective effect in a model of diethylnitrosamine induced hepatocellular carcinoma in rat (Ghosh et al., 2012). Despite its favorable pharmacological properties, there are some limitations for the development of curcumin as a potential therapeutic drug formulation. Curcumin is unstable in aqueous solution at physiological pH and undergoes rapid biotransformation (Lin et al., 2000). A fast metabolic elimination by reduction and low bioavailability *in vivo* were also reported (Anand et al., 2007; Pan et al., 1999). The curcumin plasma or tissue concentrations were reported to be either negligible or only low after its oral administration (Cheng et al., 2001; Dhillon et al., 2008; Sharma et al., 2004).

Considering the important health effects of curcumin, different approaches have been evaluated in order to overcome the limitations described above. Oral administration of curcumin loaded in nanoemulsion showed enhanced absorption in mice compared with curcumin suspension in methylcellulose (Zhongfa et al., 2012). Another study reported an improved stability of encapsulated curcumin against hydrolysis and biotransformation in phosphate buffer saline (Mohanty & Sahoo, 2010). Polymeric micelles are appropriate system for improving the problems in drug delivery. They are composed of amphiphilic block copolymers which spontaneously form micelles having hydrophobic core and hydrophilic shell. Thus, highly hydrophobic drugs could be loaded in the hydrophobic core, therefore polymeric micelles have been extensively used for solubilization and targeted delivery of drugs. Different curcumin loaded polymeric micelles were described, including amphiphilic methoxy poly(ethylene glycol)-b-poly (ε-caprolactone-co-p-dioxanone) (Song et al., 2011), poly(D,L-lactide-coglycolide)-b-poly(ethylene glycol)-b-poly(D,L-lactide-co-glycolide) (PLGAePEGePLGA) (Zhao et al., 2012)

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Case Report

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A Patient with Multiple Keratinocytic Cancers (MKC): Uncommon Presentation in a Bulgarian Patient

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Keywords: skin cancer; surgery; island flap; basal cell carcinoma; squamous cell carcinoma

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Abstract

Keratinocyte skin cancers, including basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), are the most common cancer occurring in people with fair skin, worldwide. Despite all known triggers, several suggested contributors are still investigated. We will focus our attention on the personal history of previous cancers and radiation exposure as occupational risk factors, as in the presented case. We report a patient, with multiple BCCs, and subsequent occurrence of a SCC on photo-exposed area of the face, as we want to emphasize the importance of strict following up of these patients, regarding the risk for developing new tumors in short periods of time, no matter if the triggering exposure factor is known from the history, or not. Although keratinocytes tumours are associated with the low mortality rate, we focus the attention on the fact, that the history of non-melanoma skin cancer is associated with increased mortality.

Introduction

Keratinocyte skin cancers, including basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), are the most common cancer occurring in people with fair skin, worldwide [1]. The highest incidence has been reported in Australia, because of the higher cumulative UV-exposure, with higher prevalence among man after 60 years of age, with the higher domination of BCC, than SCC [1][2]. Exposure to UV radiation is the primary triggering factor for malignant transformation in both-melanoma and non-melanoma cancers, although the pattern of exposure that gives rise to different types of tumours appears to vary [2]. Other risk factors, playing role in the cancer genesis of these kinds of tumors include: patient's phenotype (light-coloured skin, eyes and hair), personal and family history of skin cancer, exposure to ionizing radiation, arsenic, and certain petroleum products, previous PUVA therapy, xeroderma pigmentosum, Basal cell nevus syndrome, immunosuppression and variety of precancerous skin conditions [3]. Most of the cases are the result of the simultaneous contribution of many risk factors [3].

Книга
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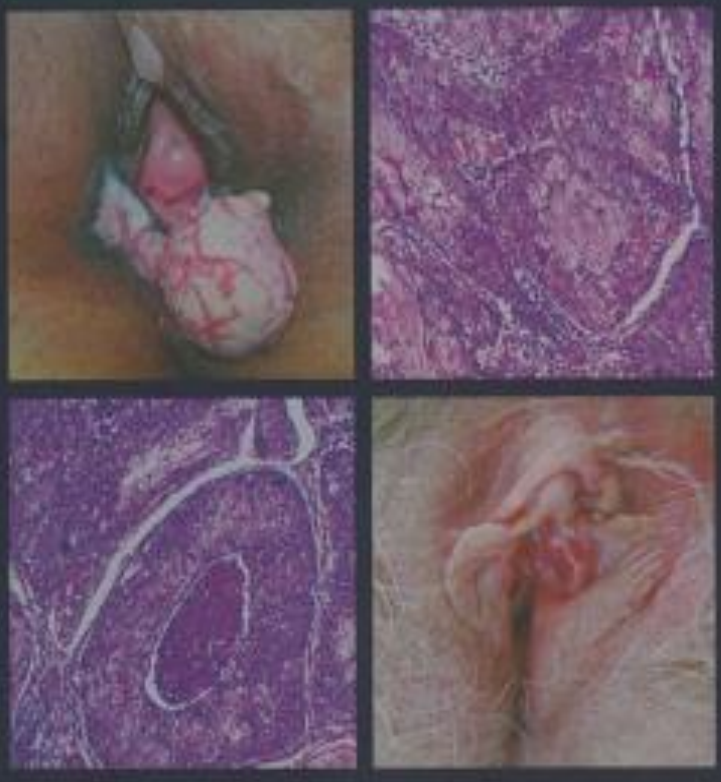
Лакс Бук
Пловдив
2015

Г. Чернев
А. Чокоева
У. Волина

ЗЛОКАЧЕСТВЕНИ ТУМОРИ НА ВУЛВАТА

Георги Чернев
Анастасия Чокоева
Уве Волина

ЗЛОКАЧЕСТВЕНИ ТУМОРИ НА ВУЛВАТА



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Най-често срещананият кожен тумор – базалноклетъчният карцином (БКК) – се локализира по-рядко в областта на женските гениталии, като тази локализация представлява около 1% от всички случаи на БКК. Появата му в тази област съставлява около 1-4 % от всички неоплазми. Клиничната му изява е характерна за по-напредналата възраст, между 40-90 години (средно 68), като много по-често се засягат жените от бялата раса.

Епидемиология

За разлика от кожната му форма, ултравиолетовата радиация и слънчевата експозиция не са пряко свързани рискови фактори при тази локализация на БКК. Хронични възпаления или lichen sclerosus et atrophicans са предразполагащите фактори с по-голямо значение за появата му в областта на вулвата. Syphilis, хронични възпаления и раздранения, както и предхождаща радиотерапия, също оказват влияние върху канцерогенезата. Предшестващи

НЕВРОЕНДОКРИННИ ТУМОРИ НА ВУЛВАТА

Анастасия Чокоева,
Георги Чернев,
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Невроендокринните тумори са редки малигнени тумори, които се локализират в гениталния тракт в около 2% от случаите, като засягат цервикс, яйчници, вагина и вулва. Свързани са с лоша прогноза, поради агресивното си поведение, висок метастатичен потенциал и чести рецидиви.

Вулварен карцином на Меркел
(Merkel Cell Carcinoma)

Карциномът на Меркел (първичен невроендокринноклетъчен карцином), наричан още трабекуларен карцином, е рядък тумор, с невроендокринен произход, локализиран в 60% от случаите по кожата на фотоекспонираните участъци на тялото – глава, шия, торс.

АДЕНОКАРЦИНОМИ НА ВУЛВАТА

Георги Чернев,
Анастасия Чокоева,
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Първичните аденокарциноми се срещат изключително рядко в областта на вулвата, като съставляват около 2% от всички неоплазми с такава локализация. Засягат предимно жени след менопаузална възраст, средно около 50 годишни.

Класификацията им е разнородна и включва широк спектър неоплазми като екстрамамарна болест на Пейджет, карцином на потните жлези, breast-like аденокарцином, аденокарцином на апокринните жлези, аденокарцином на Бартолиновите жлези, както и някои редки форми, които показват сходни клинични и хистопатологични характеристики.

Аденокарциномите на вулвата имат агресивно протичане с висока склонност към рецидивиране и метастазиране. Прогнозата е неблагоприятна при авансирали процеси и налични метастази в белите дробове или костите. Смъртността е сравнително висока, като 5-годишната преживяемост се изчислява средно на около 60%.

РЕДКИ ВАРИАНТИ НА АДЕНОКАРЦИНОМ НА ВУЛВАТА

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Аденоидният кистозен карцином на вулварните потни жлези, наричан още hydradenoid carcinoma, е изключително рядко заболяване, с агресивно протичане и висока склонност към рецидивиране.

„Чревният тип" муцинозен аденокарцином е изключително рядък вариант на аденокарцином, с лоша прогноза, висок метастатичен потенциал и висока смъртност. Названието на този вид тумор произлиза от тясната връзка и установена висока асоциация между коморбидната му изява, паралелно с тумори на гастроинтестиналния тракт.

Освен радикална вулвектомия с лимфаденектомия, провеждането на гастроскопия и колоноскопия е задължителна, с оглед високата асоциация на този вид рак с карциноми на гастроинтестиналния тракт, най-вече на дебелото черво.

Първичен аденокарцином на млечни жлези, произлязъл

РЕДКИ МЕКОТЪКАННИ САРКОМИ НА ВУЛВАТА

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Уве Волина

Малигнен фиброзен хистиоцитом на вулвата

Malignant fibrous histiocytoma (MFH)

MFH е агресивен тумор с екстремно рядка локализация в областта на вулвата. Описан е за първи път от O'Brien и Stout през 1964, като най-често срещаният мекотъканен сарком в зрялата възраст, който съставлява около 20-24% от всички саркоми. Понастоящем, са описани по-малко от 10 случая при жени в млада и средна възраст, средно 30-40-годишни.

Обикновено се локализира по големите лабии и се представя клинично като бавно растяща болезнена туморна маса с размери около 3-6 см в диаметър.

Канцерогенезата на този вид неоплазми не е съвсем