A RARE CONJUNCTIVAL SPITZ NEVUS: A CASE REPORT AND LITERATURE REVIEW

VERVAET N., VAN GINDERDEUREN R.*, VAN DEN OORD J.J.**, FOETS B.**

ABSTRACT

A conjunctival Spitz nevus is a very rare, benign melanocytic lesion, which can be mistaken for a malignant melanoma. We present a case of a 28-year old man, who suffered from a rapidly growing, non-pigmented mass in the left caruncular area, extending to the nasal conjunctiva. The lesion was excised and pathologic examination showed nests of large, polygonal, non-pigmented epithelioid cells, located in the stroma. The overlying epithelium showed focal erosions. At the base, there was a lymphocytic infiltrate.

Immunohistochemical techniques, with stainings for S-100 protein, HMB-45 and MIB-1, were used for further investigation and showed the melanocytic origin of the lesion (S-100 staining) as well as many cells in cell cycle (MIB-1 staining). However, no mitoses were seen.

The clinical image, combined with pathologic and immunohistochemical findings, provided the diagnosis of a Spitz nevus localised in the conjunctiva. Although the cutaneous location of Spitz nevi is well known, conjunctival Spitz nevi are very rare and because of their mucosal origin, some of the histological features are different.

SAMENVATTING

De Spitz nevus van de conjunctiva is een zeldzaam, goedaardig melanocytair letsel dat kan leiden tot differentieel diagnostische problemen met het maligne melanoom. Wij stellen een casus voor van een 28-jarige man, die zich presenteerde met een snel groeiende, niet gepigmenteerde massa ter hoogte van de caruncula van het linkeroog, uitbreidend naar de nasale conjunctiva. Het letsel werd verwijderd en pathologisch onderzoek toonde nesten van grote, polygonale, niet gepigmenteerde, epithelioide cellen. Deze nesten waren gelokaliseerd in het stroma. Het bekledend epitheel toonde focale erosies. Er was een lymfocytair infiltraat aanwezig aan de basis van het letsel.

Immunohistochemische technieken, met kleuringen voor S-100 proteïne, HMB-45 en MIB-1, werden toegepast voor verdere investigatie en toonden de melanocytaire oorsprong van het letsel (S-100 kleuring) alsook vele cellen in celcyclus (MIB-1 kleuring). Er werden echter geen cellen in mitose aangetroffen.

De combinatie van het klinisch beeld met de pathologische en immunohistochemische bevindingen, heeft geleid tot de diagnose van een Spitz nevus, gelokaliseerd in de conjunctiva.

In tegenstelling tot op de huid gelokaliseerde Spitz nevi, die goed gekend en vaak beschreven zijn, is de conjunctivale Spitz nevus zeer zeldzaam. Omwille van de mucosale origine, zijn sommige histologische kenmerken verschillend.

RÉSUMÉ

Le naevus de Spitz conjonctival est une lésion rare, mais bénigne, d'origine mélanocytaire, difficile à distinguer du mélanome malin. Nous présentons le cas d'un homme âgé de 28 ans, qui s'est présenté avec une masse, non-pigmentée, de croissance rapide. La masse était localisée près de la caroncule de l'œil gauche, étendante vers la conjonctive nasale. La lésion a été excisée, et l'examen pathologique a démontré des nids de cellules grandes, polygonales, non-pigmentées et de forme épithélioïde, localisées dans le stroma. L'épithélium montrait des érosions. Une infiltration de lymphocytes était présente à la base de la lésion. Des techniques immuno-histochimiques, avec recherches de S-100, HMB-45 et MIB-1, ont été appliquées pour l'investigation profonde et ont démontré l'origine mélanocytaire de la lésion

** Department of Ophthalmology, UZ Leuven, Leuven, Belgium*
*** Department of Pathology, UZ Leuven, Leuven, Belgium*

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(coloration de S-100) ainsi que plusieurs cellules au cycle cellulaire (coloration de MIB-1). Cependant, aucune mitose a été montrée. L'image clinique, combinée avec les résultats des recherches pathologiques et immuno-histochimiques a abouti au diagnostic d'un naevus de Spitz, localisé au niveau de la conjonctive. Contrairement au naevus de Spitz de la peau, bien connu et souvent décrit, la présentation conjonctivale est très rare. A cause de l'origine mucosale, les caractéristiques sont différentes.

KEY WORDS

Conjunctiva, Malignant Melanoma, Nevus and Spitz.

MOTS-CLES

Conjonctive, Mélanome Malin, Naevus et Spitz.

INTRODUCTION

The conjunctiva of the eye can be the seat of different types of benign and malignant lesions. Generally, these tumours are classified as melanocytic or nonmelanocytic, based on the clinical evidence of intrinsic pigment and on the histopathologic evidence of origin from melanocytes (9). Examples of nonmelanocytic conjunctival lesions are vascular, fibrous, epithelial, lymphoid and metastatic tumours. Most of the melanocytic lesions can be classified as nevi (52%) , whereas melanoma and primary acquired melanosis are examples of malignant or atypical pigmented lesions (9).
The most common location of these nevi is the bulbar conjunctiva (juxtalimbal or epibulbar), followed by the plica, the caruncle and the eyelid margin (5).
The conjunctival Spitz nevus is a very rare lesion of melanocytic origin. Literature review revealed that only a very small number of this kind of lesion has been described to date (6). It is characterized by its predominant appearance in children and young adults and its rapid growth, which may raise suspicion about malignant melanoma. This is also the most important differential diagnosis (5, 6, 8).

CASE REPORT

A 28-year old man presented at our consultation with a non-pigmented lesion of the nasal conjunctiva of the left eye, extending from the caruncle. He had first noticed this lesion eight months earlier, and since then its volume increased steadily. Visual acuity, anterior and posterior segment evaluation revealed no abnormalities. On inspection a non-pigmented mass with a diameter of 9 millimetres, localized near the caruncle and immobile, was visible (Fig. 1). Because of the unclear nature of the lesion and its rapid growth, it was excised. Pathologic examination showed a symmetric lesion composed of nests of large, polygonal, non-pigmented epithelioid cells, located in the stroma, which tended to confluence (Fig. 2: smaller magnification and Fig. 3: larger magnification). The overlying epithelium was focally eroded. The cells were characterized by abundant cytoplasm and the nuclei showed prominent nucleoli. In the depth of the lesion, the cells

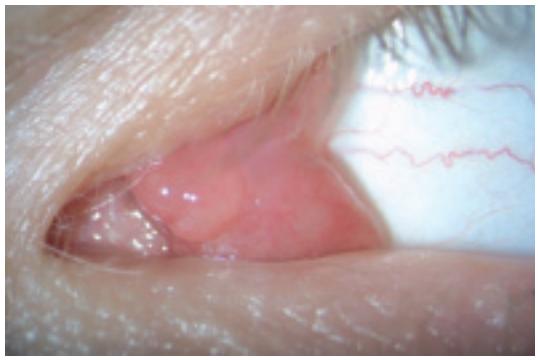

Fig. 1: : Elevated, unpigmented lesion of the left eye, localized near the caruncle, extending to the nasal conjunctiva.

showed maturation towards smaller, single cells. At the base, there was a lymphocytic infiltrate showing lymphoid follicles (Fig 2). Several cords and islands of normal epithelium with goblet cells extended into the stroma.
Immunohistochemistry showed immunoreactivity for S-100 protein and for tyrosinase-associated protein. S100 protein typically stains melanocytes, as well as nerve cells. Tyrosinase-associated protein is very specific for melanocytes. HMB-45 immunoreactivity was present in the superficial, junctional nests, but disappeared in the depth of the lesion (Fig. 4). HMB-45 is known as a typical antibody against melanoma cells, although it is not specific, because it can also be positive in active growing nevus cells. Staining for MIB-1, an antibody identifying cells in cycle, was positive in several nuclei of cells in the superficial layers. The

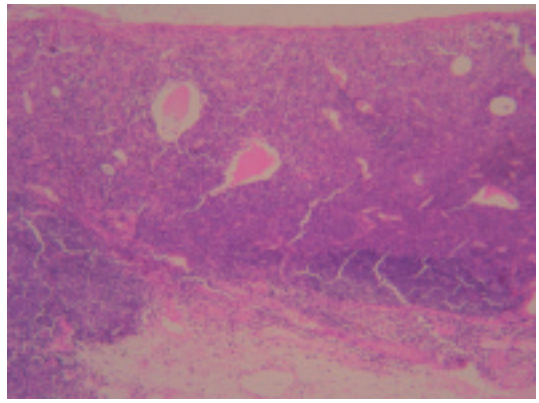

Fig. 2: Pathology shows nests of epithelioid cells. Cords of normal epithelium extend into the stroma. A lymphocytic infiltrate is present at the base.

cell cycle is the process by which eukaryotic cells divide. This means that the cell doubles its genome during a synthesis phase, and later, during mitosis, halves that genome and divides the chromosomes between two daughter cells. The MIB-1 test shows cells which are in the phase before which you can see the mitosis figure, a phase which can take relatively more time. In the current specimen, no actual mitoses were seen. In conclusion, this lesion showed the features of a Spitz nevus composed of predominantly epithelioid cells. However, the confluence of junctional nests and the presence of several cells in cell cycle, gave this lesion some of the features of an atypical Spitz nevus, as described in literature. After exci-

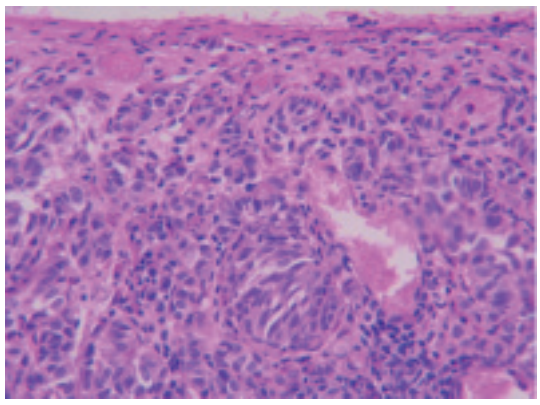

Fig. 3: Large, polygonal epithelioid cells, characterized by abundant cytoplasm and prominent nuclei.

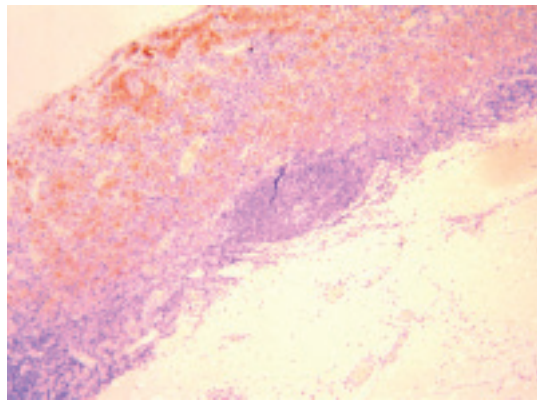

Fig. 4: HMB-45 positivity most prominent in the superficial layers of the lesion, disappearing towards the depth. The lymphocytic infiltrate is present at the base.

sion, no recurrence was detected after 24 months of follow-up.

DISCUSSION.

Literature review made clear that a conjunctival Spitz nevus is a very rare melanocytic lesion, of which only a few cases have been described before (6).

Conjunctival nevi in general are relatively common, benign lesions. A typical conjunctival nevus is a benign proliferation of nevus cells that form nests along the junction of the epithelial and subepithelial tissue. They can be divided in junctional, compound and subepithelial lesions, the latter located in the substantia propria. These three types are not so much distinctive entities as they are stages in the evolution of melanocytic proliferation (5). Their most frequent location is in the juxtalimbal area, followed by the plica and caruncle (5). They present as sharply demarcated lesions, which are usually located intra-epithelially and can be moved freely over the scleral surface. In a retrospective study by Shields et al. of 1643 melanocytic and nonmelanocytic conjunctival tumours, 52 % of melanocytic lesions were diagnosed as nevus (9). Their colour ranged from darkly pigmented, through lightly pigmented to completely non-pigmented. Around puberty, some nevi may grow and become more pigmented. Usually, an acquired conjunctival nevus undergoes progressive maturation and only exceptionally gives rise to conjunctival melanoma (5). However, there can be considerable confusion concerning these benign, melanocytic lesions of the conjunctiva. In some cases they are histologically indistinguishable from primary acquired melanosis (PAM) with atypia, which can evolve into melanoma. Next to these common acquired conjunctival nevi, a variety of unusual nevi, including balloon-cell nevi, Spitz nevi, blue nevi and dysplastic nevi, can be identified in the conjunctiva (5).

Looking at the Spitz nevus in particular, this nevus was named after Sophie Spitz, a pathologist who, in 1948, described a series of patients with 'juvenile benign melanoma'(10). It concerned skin lesions, particularly in young children, which were histologically diagnosed as malignant, but which didn't show malignant behaviour, although rapid growth was possible. Sophie Spitz pointed out that cytological atypia and architectural chaos are not always equivalent to malignancy. However, she recognized that the lesions were not unequivocally benign, because one of thirteen cases she described resulted in fatal metastasis.

Ever since the first description of a lesion as a Spitz nevus, the diagnosis still is a major challenge for most pathologists (1,2).

Most cutaneous Spitz nevi present on the skin of children and adolescents, although the lesion has also been described in adults more than once. They usually present as non-pigmented, pink or orange-red papules or nodules on the skin of face or legs. This difference in incidence in children and adolescents comes from the fact that nevus cells tend to proliferate under the influence of hormonal changes (5). Conjunctival Spitz nevi have been encountered almost exclusively in children and adolescents, and compared with the skin, this location is exceptionally rare (5).

Architectural and cytological features specific for cutaneous Spitz nevus are (1-4): left-right symmetry, lack of pigmentation, lack of extension of junctional nevus cells beyond subepithelial nevus cells, increased numbers of blood vessels and scattered inflammatory cells. The cells in Spitz nevi are spindle and/or epithelioid and are organized in nests and bundles, with also some single cells. The pigment cells contain abundant cytoplasm, a vesicular nucleus and often a prominent nucleolus.

In some occasions, the characteristics of a Spitz nevus may raise suspicion about a malignant melanoma. Histological arguments which are in favour of the diagnosis of Spitz nevus against malignant melanoma are sharp lateral borders, lack of mitotic figures and maturation of cells (3,4).

Apart from these clinical and pathological findings, immunohistochemical techniques can be used to differentiate between Spitz nevi and malignant melanoma (2, 7). In particular, the expression of HMB-45 in the deep parts of the lesion, and abundant MIB-1 immunoreactivity are strong arguments in favour of malignant melanoma (2).

Considering clinical, pathological and immunohistochemical results, the above described case showed the characteristics of a Spitz ne-

vus, including symmetry, sharp borders, cell maturation towards the depth and lack of mitoses. Also, the ingrowth of epithelial islands in the stroma and the absence of any sign of recurrence or malignant transformation, favours the diagnosis of a benign lesion, although the presence of some atypical features cannot be neglected.

CONCLUSION.

Although cutaneous Spitz nevi are quite well known and have often been described, conjunctival Spitz nevi seem to be exceptionally rare. One should consider it when confronted with a more or less pigmented, rapidly growing mass on the conjunctiva of a child or young adult. It is recommended to excise the lesion, to make further histological examination possible. Histological arguments pro and contra Spitz nevus should be evaluated and further immunohistochemical investigations can be done. It is very important to make the differential diagnosis with malignant melanoma, because the latter, although rare, can also exist in children and young adults.
This will still be a big challenge in the future, for clinicians as well as pathologists.

REFERENCES

(1) BARNHILL R.L. – The Spitzoid lesion: rethinking Spitz tumours, atypical variants, 'Spitzoid melanoma' and risk assessment. Modern Pathology 2006; 19: 21-33

(2) CROTTY K.A., SCOLYER R.A., LAWRENCE LI L.X., PALMER A.A., WANG L., McCARTHY S.W. – Spitz naevus versus Spitzoid melanoma: when and how can they be distinguished? Pathology 2002; 34: 6-12.

(3) EDWARDS S.L., BLESSING K. – Problematic pigmented lesions: approach to diagnosis. J Clin Pathol 2000; 53: 409-418.

(4) FERRARA G., ARGENZIANO G., SOYER H.P., CHIMENTI S., DI BLASI A., PELLACANI G., PERIS K., PICCOLO D., RUBEGNI P., SEIDENARI S., STAIBANO S., ZALAUDEK I., DE ROSA G. – The spectrum of Spitz nevi. A clinicopathologic study of 83 cases. Arch Dermatol 2005; 141: 1381-1387.

(5) FOLBERG R., JACOBIEC F.A., BERNARDINO V.B., IWAMOTO T. – Benign conjunctival melanocytic lesions: Clinicopathologic features. Ophthalmology 1989; 96: 436-459.

(6) KANTELIP B., BOCCARD R., NORES J.M., BACIN F. – A case of conjunctival Spitz nevus: Review of Literature and Comparison with cutaneous locations. Ann Ophthalmol 1989; 21: 176-179.

(7) RIBE A., McNUTT N.S. – S100A6 protein expression is different in Spitz nevi and melanomas. Mod Pathol 2003; 16: 505-511.

(8) SEREGARD S. – Pigmented spindle cell naevus of Reed presenting in the conjunctiva. Acta Ophthalmol. Scand. 2000; 78: 104-106.

(9) SHIELDS C.L., DEMIRCI H. KARATZA E., SHIELDS J.A. – Clinical survey of 1643 melanocytic and nonmelanocytic conjunctival tumors. Ophthalmology 2004; 111: 1747 - 1754

(10) SPITZ S. – Melanoma of childhood. Am J Pathol 1948; 24: 591-609.

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Correspondence and reprints:

Dr. N. VERVAET
Dept. of Ophthalmology
University Hospitals K.U. Leuven
Kapucijnenvoer 33
B-3000 LEUVEN
Email: nathalievervaet@hotmail.com