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Case Report

SEBACEOUS CARCINOMA OF THE EYELID AND MUIR-TORRE SYNDROME

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SUMMARY – Muir-Torre syndrome is a rare form of hereditary nonpolyposis colorectal cancer syndrome; simplified, it is an association of at least one sebaceous skin tumor and at least one visceral malignancy. It follows an autosomal dominant pattern of inheritance. We present a case of a recurrent sebaceous carcinoma of the eyelid in a patient previously operated on for colorectal carcinoma. During his treatments, he was examined by experts in different medical fields. After genetic counseling, he also underwent genetic testing.

Key words: *Eyelid; Sebaceous carcinoma; Skin; Genetics; Gastrointestinal tumor; Muir–Torre syndrome; Lynch syndrome*

Introduction

Muir-Torre syndrome (MTS) is a rare, autosomal dominant condition. It is a form of Lynch syndrome. While in Lynch syndrome, gastrointestinal or genitourinary malignancies are most common, sebaceous skin tumors predominate in MTS[1,2]. The most common malignancy in MTS is colorectal cancer, usually localized in the right colon[1]. Breast cancer, lymphoma, leukemia, salivary gland tumors, respiratory tract tumors, and chondrosarcoma can also be part of MTS[1]. Other benign tumors that appear in MTS are ovarian granulosa cell tumor, hepatic angioma, benign schwannoma of the small bowel, and uterine leiomyomas[1]. Sebaceous carcinomas typically occur on the upper eyelids in older women with a weak immune system, and those who underwent head and neck radiation treatments[2,3]. They arise from the meibomian glands and the glands of Zeiss[3]. They are rare eyelid tumors, 0.2%-0.7% of all eyelid tumors[4], but highly malignant. Sebaceous carcinoma may also occur almost anywhere in the skin, on the ears, feet, penis, or labia[5]. On the eyelids, it appears as a firm, yellow nodule with a tendency to ulcerate. They are often mistaken for chalazia, chronic blepharoconjunctivitis or carbuncles[6]. Eyelid sebaceous carcinoma can invade the orbit, metastasize and have a lethal outcome. Local recurrence reports vary from 9% to 36% of patients, and distant metastasis occurs in 3% to 25%[7,8]. It can disseminate to the parotid gland, liver, lungs and bones[7,8]. Lesion architecture defines the differential diagnosis of sebaceous carcinoma, adenoma or epithelioma. It can be infiltrative, which implies carcinoma or circumscribed adenoma. However, some lesions may have circumscribed borders that show cytologic atypia.

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On pathology, sebaceous carcinoma is a malignant neoplasm with pathophysiologically prominent cellular pleomorphism that tends to have a pagetoid extension of atypical sebaceous cells in the conjunctiva or the epidermis[9,10]. Occasionally, the tumor invades the orbit adipose tissue and, in case of invasion to subcutaneous tissue, favors a diagnosis of carcinoma over benign tumor.

Case Report

A 68-year-old man came to the ophthalmology emergency department with a rounded nodule less than 5 mm in diameter on the right upper eyelid three years before (Fig. 1). He had a history of an athero-

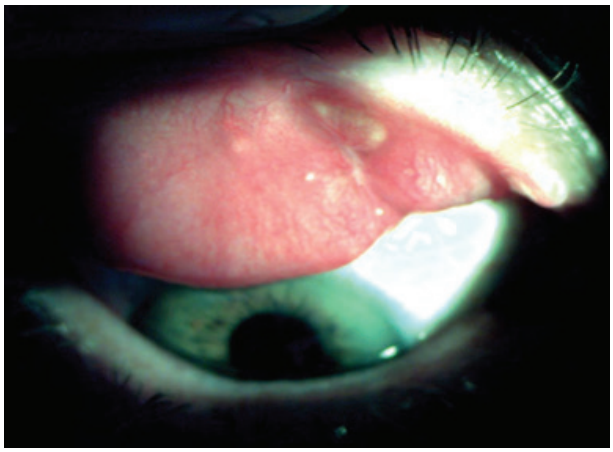

Fig. 1. Rounded nodule of tarsal plate on the right upper eyelid in the 68-year-old patient (with the patient's permission).

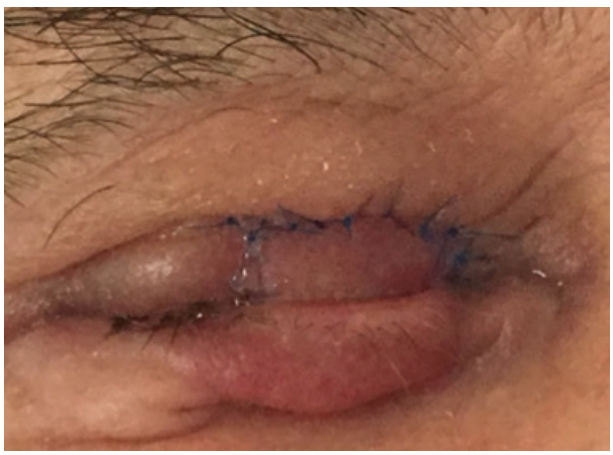

Fig. 2. Right upper eyelid after excision and lid reconstruction using the Cutler-Beard technique (with the patient's permission).

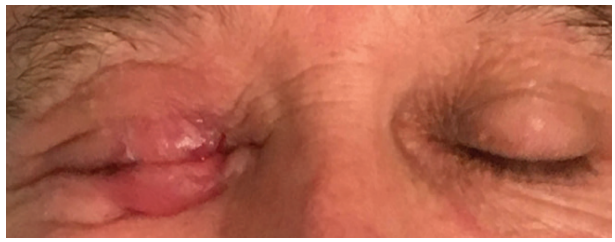

Fig. 3. Right upper eyelid after excision and lid reconstruction using the Cutler-Beard technique – postoperative day 7 (with the patient's permission).

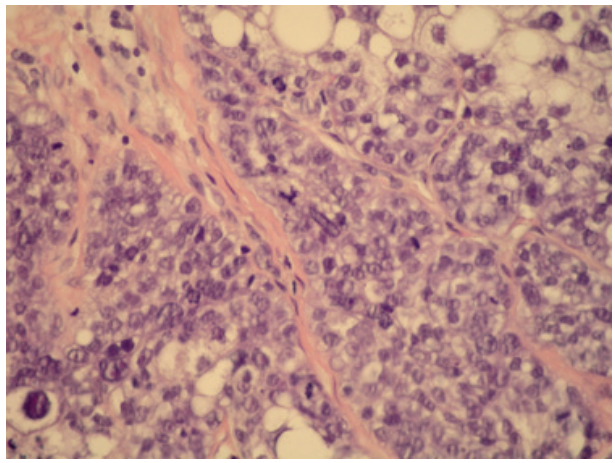

Fig. 4. Histopathologic analysis reveals atypical epithelial cells with signs of sebaceous differentiation, i.e., cytologic atypia and mitotic figures.

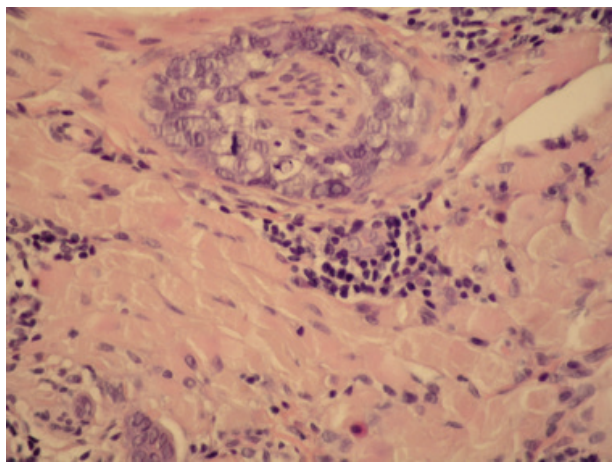

Fig. 5. Mitotically active, moderately differentiated atypical epithelial cells confirmed the diagnosis of sebaceous carcinoma.

ma-like nodule of the same localization operated at another institution seven years before and reoperated two years before, without follow-up. Histopathology in both interventions showed sebaceous carcinoma.

The tumor was excised and the lid reconstructed using the Cutler-Beard technique (Figs. 2 and 3). Histopathology documented atypical epithelial cells with signs of sebaceous differentiation, i.e., cytologic atypia and mitotic figures (Figs. 4 and 5). Infiltrative sheets and cords of mitotically active, moderately differentiated atypical epithelial cells confirmed the diagnosis of sebaceous carcinoma. Additional workup included dermatology examination (no other skin lesions), neck ultrasound (showed one enlarged lymph node of not more than 1 cm), computed tomography of the brain and orbits (which was normal), and oncologist consultation. MTS was suspected based on the patient's history. Sixteen years earlier, the patient had surgery and received chemotherapy for adenocarcinoma of the ascending colon. He also regularly visited a nephrologist because of benign kidney tumors. However, when genetic counseling confirmed the possibility of MTS, we did not confirm it with tests that included immunohistochemical staining of DNA mismatch repair proteins mutL homolog 1 (MLH1) and mutS homolog 2 (MSH2), which did not show any pathogenetic variant in our patient, no deletion or duplication.

During subsequent follow-up at our hospital, a 2-mm nodule was found at the same lid of the patient a year after. Fortunately, histopathology showed inflammation without malignancy. Currently, the patient is well and recurrence-free.

Discussion

As mentioned above, MTS is associated with gastrointestinal tumors, primarily hereditary nonpolyposis colorectal cancer (HNPCC). Skin lesions may develop before or after the diagnosis of visceral malignancy. Sebaceous carcinoma is an aggressive skin neoplasm. It can recur locally even after complete excision, and it can also have local and distant metastasis[2]. Local recurrences usually develop in the first five years after excision. Recurrence rates are around 30%[2].

Gene mutations usually cause MTS in MLH1 on chromosome 3, or MSH2 on chromosome 2[11]. It is associated with an inherited defect in one copy of a DNA mismatch repair gene, which leads to microsatellite instability[11]. Approximately 70% of tumors associated with MTS have this microsatellite instability[11]. Since our patient had a history of matching MTS, he may have been in the other 30%.

While defects in the *hMLH1* and *hMSH2* genes are evenly distributed in HNPCC, abnormalities of *hMSH2* are seen in more than 90% of MTS patients. Other genes involved in MTS are *MSH-6, MLH-3,* and *PMS-2*. Loss of two retinoid receptors, RXR-beta and RXR-gamma, can also be expressed in sebaceous carcinoma[12]. In either of these genes, a mutation gives an increased lifetime risk of developing the skin changes and types of cancer associated with the condition.

Although MTS is a rare disorder, families with MTS are probably more common than reported. MTS occurs in both sexes, with a male to female ratio of 3:2[6]. Patient age at MTS presentation ranges from young adulthood to elderly patients, with a median age of 50 years[6].

Diagnostic criteria usually used for MTS are the Amsterdam criteria[13]. Our case had a colorectal carcinoma diagnosed under the age of 50 and no family history, but recurrent sebaceous carcinoma of the eyelid. Nevertheless, MTS should be considered in such patients with sebaceous carcinomas and visceral malignancy. Even when MTS is not confirmed, patients with a suggestive clinical history data or immunohistochemical staining pattern should receive long-term oncologic surveillance as our patient.

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Sažetak

SEBACEALNI KARCINOM VJEĐE I MUIR-TORREOV SINDROM

K. Ranđelović, R. Iveković, O. Zrinšćak, H. Čupić, S. Ramić, Z. Vatavuk i *I. Petric Vicković*

Muir-Torreov sindrom je rijedak oblik nasljednog sindroma nepolipoznog kolorektalnog karcinoma koji zapravo objedinjuje barem jedan sebacealni karcinom kože i jedan visceralni zloćudni tumor. Nasljeđuje se autosomno dominantno. Prikazujemo slučaj bolesnika s recidivirajućim sebacealnim karcinomom vjeđe prethodno operiranog zbog kolorektalnog karcinoma. Tijekom liječenja bolesnika je obradio oftalmolog koji ga upućuje na širu obradu i konačno na genetsko savjetovanje kada je odlučeno da se bolesnik podvrgne genetičkom testiranju.

Ključne riječi: *Vjeđa; Sebacealni karcinom; Koža; Genetika; Gastrointestinalni tumor; Muir–Torreov sindrom; Lynchov sindrom*