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LETTER TO THE EDITORS

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Extraocular sebaceous carcinoma in Muirr Torre Syndrome with unfavorable prognosis

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Sebaceous carcinoma (SC) is a rare malignant tumor derived from the adnexal epithelium of sebaceous glands. It has been traditionally classified into two variants on the basis of its location, extraocular and ocular sebaceous carcinoma. Extraocular sebaceous carcinoma is rare (25% of reported cases [1, 2]) and occurs most commonly on the face and scalp, but they have been reported to occur almost anywhere on the body. It can exhibit such a different variety of histologic patterns and clinical presentations, and the diagnosis is often delayed for months to years.

These carcinomas are commonly associated with Muirr Torre Syndrome (MTS). The MTS consists of a rare autosomal dominant condition characterized by the association of cutaneous sebaceous neoplasms (sebaceous adenoma, sebaceous epithelioma, or sebaceous carcinoma, basal cell carcinoma with sebaceous differentiation, with or without keratoacanthomas) and the presence of at least one internal malignancy [3–8]. The biologic behavior of SC depends on the site, but particularly debated whether there is a different aggressiveness of origin. Most of the literature reports that ocular tumors are highly malignant neoplasms with frequent locoregional and/or distant metastasis and intracanial extension [9–13]; extraocular sebaceous carcinoma on the other hand are considered as slow growing tumors of low malignant potential [9, 10, 14, 15]. In fact 15–30% of the patients affected by ocular SC developed metastasis to the lymphnodes; widespread metastatic disease secondary to extraocular SC is very uncommon. Classically it has been considered that when metastases occur, only regional lymphnodes were involved [16, 17].

Many authors consider the presence of histologic and immunohistochemistry indices prognostically unfavorable (small differentiation, presence of vascular or lymphocytic invasion and presence of a pattern of pagetoid cells) [9, 18–20]. The discussion on the biologic aggressiveness of the neoplasia is still open. To support the opinion that the behavior of extraocular SC is not significantly different from those arising in the ocular region, this report describes a highly aggressive scalp SC in an MTS case.

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Case report

A 42-year-old Italian woman presented with a 2-week history of an asymptomatic subcutaneous nodule in her scalp which enlarged rapidly within 1 month. Macroscopically it presented as a hard nodule measuring about 1 cm in diameter. There was no pre-existing lesion and the patient denied any other symptoms. Past medical history was insignificant. She had a significant family history of autosomal dominant colon cancer, but no genetic studies were performed. The patient was provisionally diagnosed for an inflammatory cyst and was treated with a wide local excision with 0.3 cm margins down to the galea under local anesthesia (Fig. 1a, b).

Formaldehyde-fixed, paraffin-embedded tissue of the nodules was sectioned and stained with hematoxyline and eosin. Step sections were studied under a conventional microscope. The nodule histopathologically showed that the neoplasm was located in the middle to deep dermis without any connection to epidermis. Histologically it consisted of well-circumscribed lobules of neoplastic cells with eosinophil cytoplasm and severe atypia, nuclear pleomorphism, frequent mitosis. An inflammatory infiltrate in the surrounding connective tissue was associated with the neoplasia which was diagnosed as SC.

The gastrointestinal endoscopy was normal, the total body CT scan control showed an abnormal mass between the intrahepatic cava vein and aorta 4.5 cm in diameter.

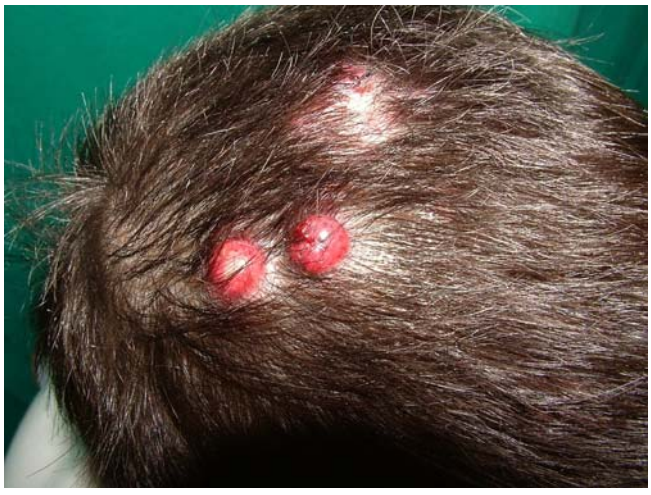

Fig. 1 Sebaceous carcinoma recurrence

While we evaluated the opportunity to treat by surgery this mass, 1 month after the first diagnosis, her skin lesion on the scalp recurred and new lesions appeared. Ten SCs with intact surgical borders were histopathologically reported. After 20 days (50 days after the first diagnosis), she developed asthenia and dyspnoea. In her chest X-ray, a pleural effusion was noted. Cytologic examination showed neoplastic cells (nuclear atypia, scanty eosinophilic, cytoplasm, cells with large clear or foamy cytoplasm), and microscopic examination of pleural biopsy showed neoplasm with lobules of tumor cells. The nuclei of neoplastic cells, like that of cutaneous lesions, were monomorphous, small, and basophilic. Two months later her primary skin lesion appeared, six courses of chemotherapy with cisplatin (80 mg/m^2) and gemcitabin (1,250 mg/m^2) was given in 21 days interval. After chemotherapy innumerable skin lesions recurred and numerous malignancies were discovered at total body CT scan control (liver, bone). We started five courses of new chemotherapy with Taxotene (25 mg/m^2), weekly in association with 5FU 200 mg/m^2 daily by continuous infusion. After courses of chemotherapy there was no response. Her total body CT taken 10 days after the end of the last course showed innumerable hypodense lesions in brain, liver, kidney, lung suggesting metastatic disease, and a big mass of 6 cm in diameter (which was earlier 4.5 cm) between vena cava and aorta. She died 11 months after the first diagnosis during a quiescent night. No autopsy was done. Her genetic status remains unknown as she refused investigations.

Discussion

Sebaceous carcinoma is the adnexal tumor of skin. Many authors found sebaceous neoplasms in patients with MTS with a variety of histologic patterns [7, 21–24]. Often SC appears before the diagnosis of initial visceral malignancy (is performed in 30% of patients with MTS) [5, 7]. The most frequent site for SC related to MTS is the ocular area, and risk for internal malignancy from SC in these patients seems to be lower than in extraocular SC. Extraocular SC has been traditionally considered as a locally invasive malignant neoplasm that only rarely metastasises. [1, 16, 25–29], and statistically the number of reported cases is insignificant.

Histopathologic differential diagnosis of extraocular SC includes other primary cutaneous neoplasms and cutaneous metastases, mostly composed of clear cells (squamous cell carcinoma, clear cell hidradenocarcinoma, clear cell syringoid carcinoma, clear cell porocarcinoma). Metastases to the skin from malignant neoplasms composed of clear cells, namely renal bladder breast and prostatic carcinoma or melanoma, may also mimic SC [16]. This report describes an aggressive scalp SC. The patient developed skin, lung, and subcutaneous metastases shortly after the excision of the primary neoplasm, and continues to recur after chemotherapy in many organs. In this patient there was a family history of hereditary colon cancer, so a diagnosis of MTS was ruled out. The skin scalp tumor recurred in the same area a month later and other lesions reappeared after the patient received chemotherapy. We believe that extraocular SC also has the capability to metastasise widely [7, 30]. In this case, the brain and skin scalp lesions represent metastases from scalp primary SC rather than synchronous primary tumors (all histologic features are identical). Maybe the abdominal mass was another primary tumor that gave at first pleuric lung metastases after visceral one. Furthermore, only one case of primary bronchial SC was reported in literature and no typical squamous differentiation existed in clear cells of pleural effusion and pleural biopsy [31].

Sebaceous histopathologic characteristic was remarkable not only in the primary scalp lesions but also in all the other metastases. Due to the rarity of extraorbital SC, calculating survival rate is difficult; visceral metastases anyway support poor outcome. The authors believe that some of the sebaceous neoplasm in MTS may have a high potential of malignancies. Currently wide surgical excision of lesions is the accepted treatment for SC. Therefore following it up with screening for local recurrence and for distant malignancies should be scheduled, and further studies are warranted to evaluate the efficacy of different chemotherapies on extraorbital SC.

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