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ONCOLOGY

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Primary mucosal melanoma of the eustachian tube

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Abstract Melanomas of the upper airway tract constitute around 1% of the total melanomas of the head and neck. They are usually more advanced in depth of invasion or size at the time of diagnosis than melanomas of the skin. The case of a 74-year-old Caucasian female with primary malignant melanoma of the left eustachian tube and bilateral neck metastasis is presented. The procedure from the diagnosis of neck metastasis to the location of the primary melanoma is described. The management of the malignant melanoma neck metastasis should also involve endoscopic examination of the upper aerodigestive tract, since the primary lesion can occur there.

Keywords Mucosal melanoma · Head and neck · Eustachian tube

Introduction

Malignant melanoma is a disease known since ancient times, as witnessed by findings on mummies of pre-Columbian Incas in Peru dating back 2,400 years. However, up until now melanoma has remained a poorly understood disease characterized by unpredictable behavior. The tumor primarily affects the skin, and much less frequently the mucosa [1]. Melanoma of the upper aerodigestive tract mucosa accounts for 1% of all head and neck melanoma cases [2].

In most cases, symptoms occur late in the course of the disease, which generally implies a poorer prognosis for these patients [3]. Although patients with malignant melanoma of the upper aerodigestive tract mucosa rarely present with neck metastases as the initial symptom of the disease [4], we present a 74-year-old female patient in whom the diagnosis of primary melanoma of the eustachian tube was made on the basis of examinations performed for the neck lymph node enlargement. To our knowledge, only one such case has been described in the literature to date [5].

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Case report

A 74-year-old Caucasian woman was referred to an ENT specialist for probatory biopsy of enlarged lymph nodes of the neck bilaterally. Previous examinations including ultrasonography (US) and computed tomography (CT) of the neck and cytologic biopsy of the neck lymph nodes raised suspicion of a malignant melanoma metastasis. The patient's history revealed that bilateral painless lymphadenopathy had developed 6 months before, following a viral infection of the upper airways with residual partial hearing loss of the left ear.

US of the neck showed a hypoechoic zone of 45×34×22 mm (height × length × width) subangularly on the right, and a hypoechoic zone of 40×41×26 mm in the upper third of the neck on the left. CT of the neck revealed an oval expansive growth of 38×35 mm on the right side and another one of 60×33 mm on the left side of the neck, with pronounced marginal annular imbibition upon contrast medium injection. The expansive growths overtly pushed the vascular structures medially and ventrally, extending from the base of the skull to the subglottic region.

Fine-needle aspiration of the tumorous growths of the neck showed mostly uniform cells with occasional anisocytosis. The cells were rounded or oval in shape, with central nuclei of granular chromatin and pronounced nucleoli. In the cytoplasm, dark-green to dark-brown granules were observed. The finding indicated dissemination of a malignant melanoma.

Upon admission, a bundle of lymph nodes, 4×5 cm in dimension, insensitive on palpation, attached to the base and mobile along the skin, was found on inspection of the neck bilaterally. The biopsy of the neck nodes on the left side suggested a malignant melanoma metastasis. As there was no skin lesion indicative of malignant melanoma by its clinical features, and because of the metastasis localization on the neck, a complete ENT examination

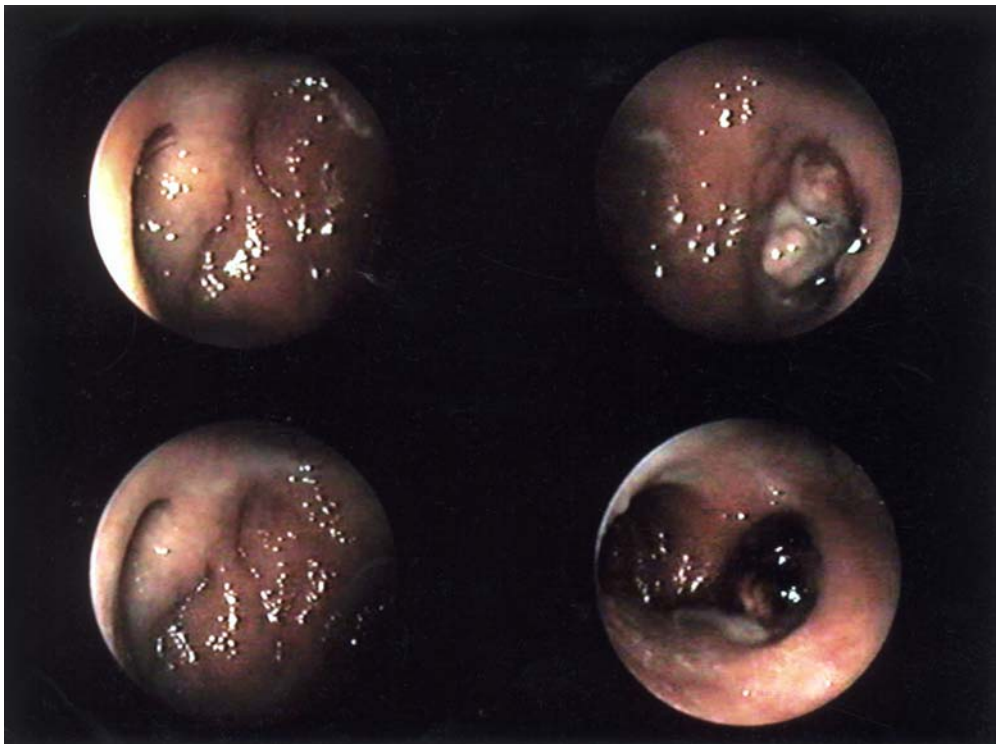

Fig. 1 Rhinoscopy showed *dark colored* tumor in the left eustacian tube pharyngeal ostium before and after incisional biopsy in comparison with the right eustacian tube pharyngeal ostium

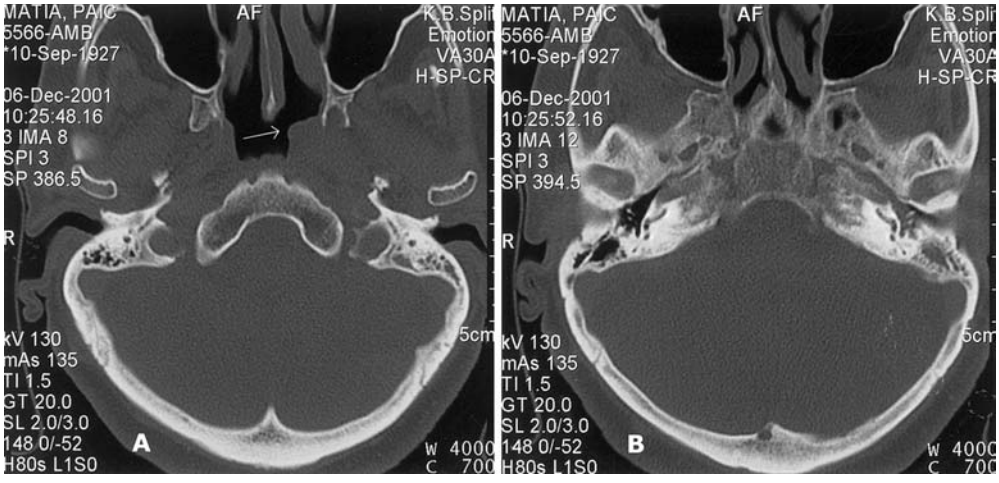

Fig. 2 **A** Nasopharyngeal and temporal bone CT scan showing an expansive tumor of the lateral left nasopharyngeal wall, **B** tumor's progression to the left middle ear

was performed in search of the primary tumor on some of the upper aerodigestive tract mucosa. A tumor growth of about 2 cm in diameter, round in shape and dark in color, protruding from the ostium of the left eustachian tube into the epipharynx was detected by a fiberscope (Fig. 1). On otoscopy, the left eardrum was turbid, and the cavity was filled with effusion content. A tympanometry curve showed type B recording on the left, whereas a tonal audiogram indicated conductive hearing loss of the left ear at a level of 40 dB.

CT with axial 2-mm scans of the nasopharynx showed a soft tissue prominence of the left lateral wall with asymmetry of the epipharyngeal air bands at a level of 1.2 cm, corresponding to the expansive growth. The lesion extended to the eustachian tube and middle ear region, with the auditory ossicles preserved. No signs of bone destruction were observed. I.v. contrast was not used because of the patient's iodine sensitivity (Fig. 2A and B).

Incision biopsy was performed for suspicion of malignant melanoma of the left eustachian tube. On routine histological hemalaun-eosin stained sections, microscopy revealed that the tumor cells varied in shape and size (Fig. 3A). Some cells were giant and epitheloid, with abundant eosinophilic cytoplasm containing visible melanin pigment. The nuclei had prominent nucleoli and occasional nuclear pseudoinclusions. There were numerous multinuclear tumor cells and bizarre mitoses. On immunohistochemistry, tumor cells were positive for S-100 and melanoma antibody HMB-45 (Fig. 3B).

CT of the chest and lungs, performed to assess the extent of the disease dissemination, revealed a finely granular consolidate of 0.6 cm in size, corresponding to a metastasis, in the left lung parenchyma at the base of the superior lobe. CT of the abdomen and scintigraphy of the skeleton did not point to further dissemination of the disease.

Because of the patient's advanced age and extent of the disease dissemination, the oncology team consisting of an oncologist, radiotherapist, oncologist chemotherapist, ENT specialist and dermatologist made a decision to treat the patient with chemotherapy including tamoxifen and demethyl triazene imidazole carboxamide (DTIC). At the time of this report, the patient is receiving this therapy.

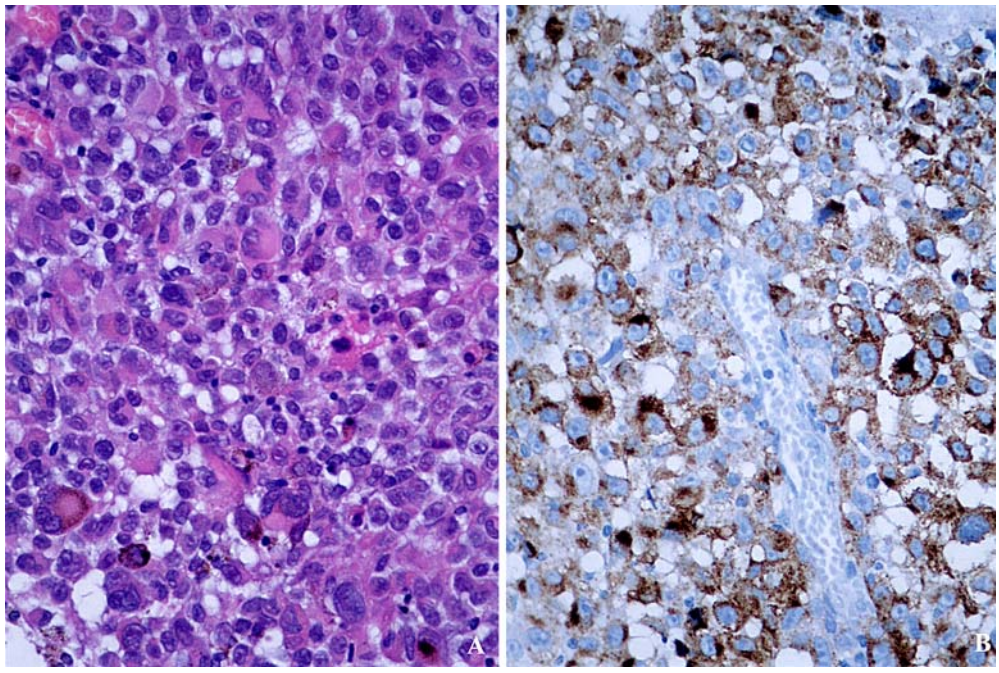

Fig. 3 **A** Microphotograph showing melanoma tumor cells of various sizes and shapes. Some of the cells are large and epitheloid and have ample eosinophilic cytoplasm with visible melanin pigment. Nuclei have prominent nucleolus and occasional nuclear pseudoinclusion. Multinucleated tumor cells and bizarre mitotic figures are common (×400). **B** Immunohistochemical staining where the tumor cells exhibit rather strong positivity for HMB-45 (×400)

Discussion

Malignant melanoma develops because of the neoplastic proliferation of melanocytes found in the basal layer of the epidermis, mucosa and retina. The etiology of mucosal melanoma is unknown [4]. Its prognosis is poorer than that of skin melanoma because of the advanced stage of the disease at the time of diagnosis, the rich vascular and lymphatic perfusion of the mucosa it arises from and the absence of clinical suspicion of tumor because of its low incidence at these localizations [6].

Mucosal melanomas of the head and neck mostly occur at the age of 40–70 years, with a slight male predominance, equally involving the sinonasal or oral mucosa [4, 7]. To the best of our knowledge, only one case of primary melanoma of the eustachian tube has been reported in the literature [5].

Malignant melanoma of the nasal cavity may manifest with epistaxis, nasal obstruction, rhinorrhea, ulceration, pressure and facial or nasal edema. In the pharyngeal cavity, it may also cause hemorrhage, voice modification, hearing and deglutition impairment and difficult breathing. All these symptoms are indicative of an advanced stage of the disease [8].

The biopsy followed by histological analysis is the only reliable method to make an accurate diagnosis. All other diagnostic methods such as US, CT, nuclear magnetic resonance and skeleton scintigraphy are used to assess the grade of local and systemic spread of the disease. The concept of excision biopsy has generally been adopted for skin melanoma, as incision biopsy is considered to be associated with a certain risk of iatrogenic dissemination. In case of mucosal melanomas, however, the concept of incision biopsy is used, because due to their localization, an appropriately performed excision would mostly imply a mutilating operative procedure without previous verification of the diagnosis. It is of utmost importance to inform the pathologist of the type of tumor suspected, thus allowing for additional target immunohistochemistry tests to be performed; these are required because of the frequently confusing and masking microscopic pattern of the melanoma.

Macroscopically, melanomas of the upper aerodigestive tract mucosa are mostly polypoid. They may vary in color from dark blue and black to pink. On cross-section, they show no capsule or sharp delineation from the surrounding tissue.

Microscopically, the tumor exhibits invasive growth. Tumor cells may have a sarcomatoid appearance with eosinophilic cytoplasm, or may be spindle-shaped, clustering in the form of small nests or ducts, imitating the picture of adenocarcinoma. It is just this varied and confusing microscopic picture that necessitates additional examinations, including immunohistochemistry testing for vimentin, S-100 protein or Fontana's silver stain to demonstrate melanin. Clark's classification of skin melanomas cannot be applied to mucosal melanomas because of the histological differences, i.e., the absence of proper dermis and subcutis in the mucosal membranes. Therefore, the measurement of tumor thickness (classification according to Breslow) has a much greater prognostic value [4].

If the disease is localized, the treatment of choice is surgical procedure including cryosurgery [9]. As compared with skin melanomas, surgical treatment of mucosal melanomas is more complex [8]. In the management of nasal and paranasal sinus melanomas, one should be aware of the fact that a radical operation usually cannot be performed because of the specific anatomic relationships in the region. Generally, the practice is to surgically remove as much of the tumor as possible, followed by radiother-

apy, which has a poor primary effect on melanomas because of their relative radioresistance [4]. However, there were no statistical differences in local control or survival between patients receiving surgery alone and those receiving surgery and radiotherapy [10]. In case of disease dissemination, chemotherapy (DTIC) is recommended, unfortunately, with quite disappointing results. Interferon may be used as an adjuvant therapy. Irrespective of the mode of treatment, however, the prognosis of malignant melanoma of the head and neck mucosa is considerably poorer than in cases of cutaneous melanomas. The reasons for this are: late onset of symptoms, delayed diagnosis and inadequate operative procedure radicalness due to the anatomic properties of the primary tumor localization [4, 11].

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