

A case of metastatic melanoma of IACs with a rapidly decay of auditory and vestibular function

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ABSTRACT

Melanoma is one of the tumours whose incidence has increased the most in recent decades.

Metastasis of the inner ear and cerebellopontine angle from melanoma are rare and only few cases of melanoma metastases with simultaneous bilateral involvement of the inner ear have been reported.

We report the case of DM, a 52 years old man, who was admitted to our department for a rapidly worsening sensorineural hearing loss with bilateral tinnitus and postural instability. Seven years before, the patient was diagnosed with a stage III-B melanoma of the trunk treated with surgical excision and axillary lymph-nodes dissection. The following oncological follow-up resulted negative. Vestibular evaluation excluded vestibular neuritis, revealing instead an horizontal nystagmus on the left side, alteration of the right orbicularis oculi muscle with minimal lagophthalmos and gait anomalies. The CT-scan excluded a stroke. The MRI showed bilateral enhancing lesions at IACs, thickened appearance at the right VIII cranial nerve level with hyperintensity of the signal and a similar lesion at D1 spine level. A debulking surgery and biopsy with translabyrinthine access were planned.

The histological report showed a BRAF mutated melanoma and for that reason the patient was referred to the oncology department to start immunotherapy treatment.

1. Introduction

Melanoma, along with breast cancer, is one of the tumours whose incidence has increased the most in recent decades. In the United States Melanoma is now regarded as the fifth most common cancer in men and the sixth most common cancer in women with an incidence of 21.8/100.000 [1]. In Europe it has a variable incidence of 10–25/100000 new cases per year [2]. Until a few years ago the only therapeutic strategy to affect the mortality rate of this tumour was its early detection and surgical removal. Nowadays more therapeutic options are available thanks to the advent of the latest immunotherapeutic drugs and target therapy, although the early diagnosis, even in the case of advanced and/or metastatic melanoma, is essential [3].

This implies that the recognition of the signs and symptoms of any metastases is essential. We report the case of a patient with bilateral simultaneous metastases of inner ear from skin melanoma who underwent surgery for the molecular characterization of the tumour.

2. Case report

A 52-year-old male was admitted to our Otorhinolaryngology department with rapidly worsening sensorineural hearing loss and bilateral tinnitus associated with postural instability. Seven years before, the patient was diagnosed with a stage III-B melanoma of the trunk with 1mm Breslow's index treated with surgical excision with 1cm of surgical margin of safety and axillary lymph-nodes dissection. Histologic examination of the excised lymph nodes was negative. The patient thus began an oncological follow-up.

Two months before our observation, the patient complained of a sudden onset of dizziness and nausea and he was examined by a local otolaryngologist who did not find any signs of vestibular asymmetry.

The following month the patient complained progressive hearing loss and bilateral tinnitus. Audiometry revealed the presence of moderate sensorineural left-sided hearing loss at 6 and 8kHz and a severe right-sided hearing loss at 250Hz and from 4000 to 8000Hz. In the following days the symptoms worsened and, for this reason, the patient was admitted to the Siena Emergency ENT Department.

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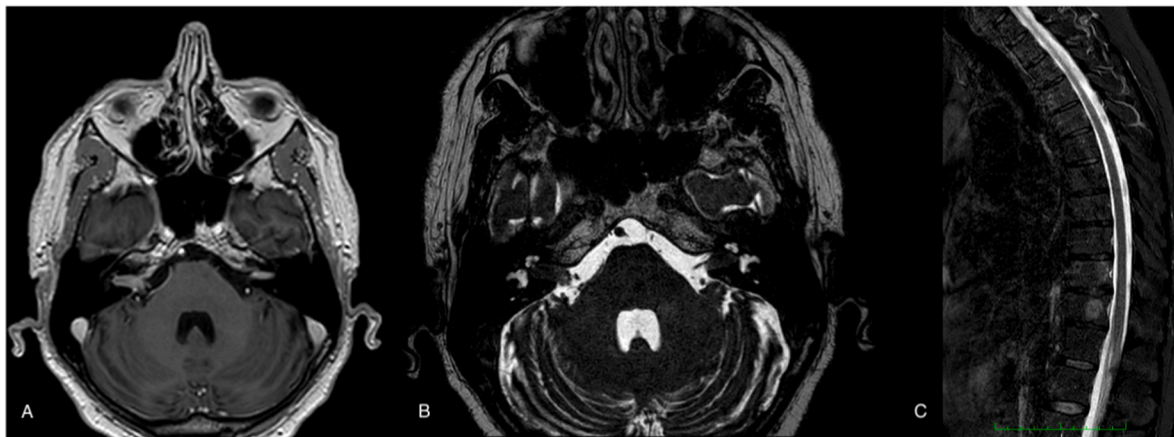


Fig. 1. A-B IACs lesion at MRI. C-D1 level spine lesion at MRI.

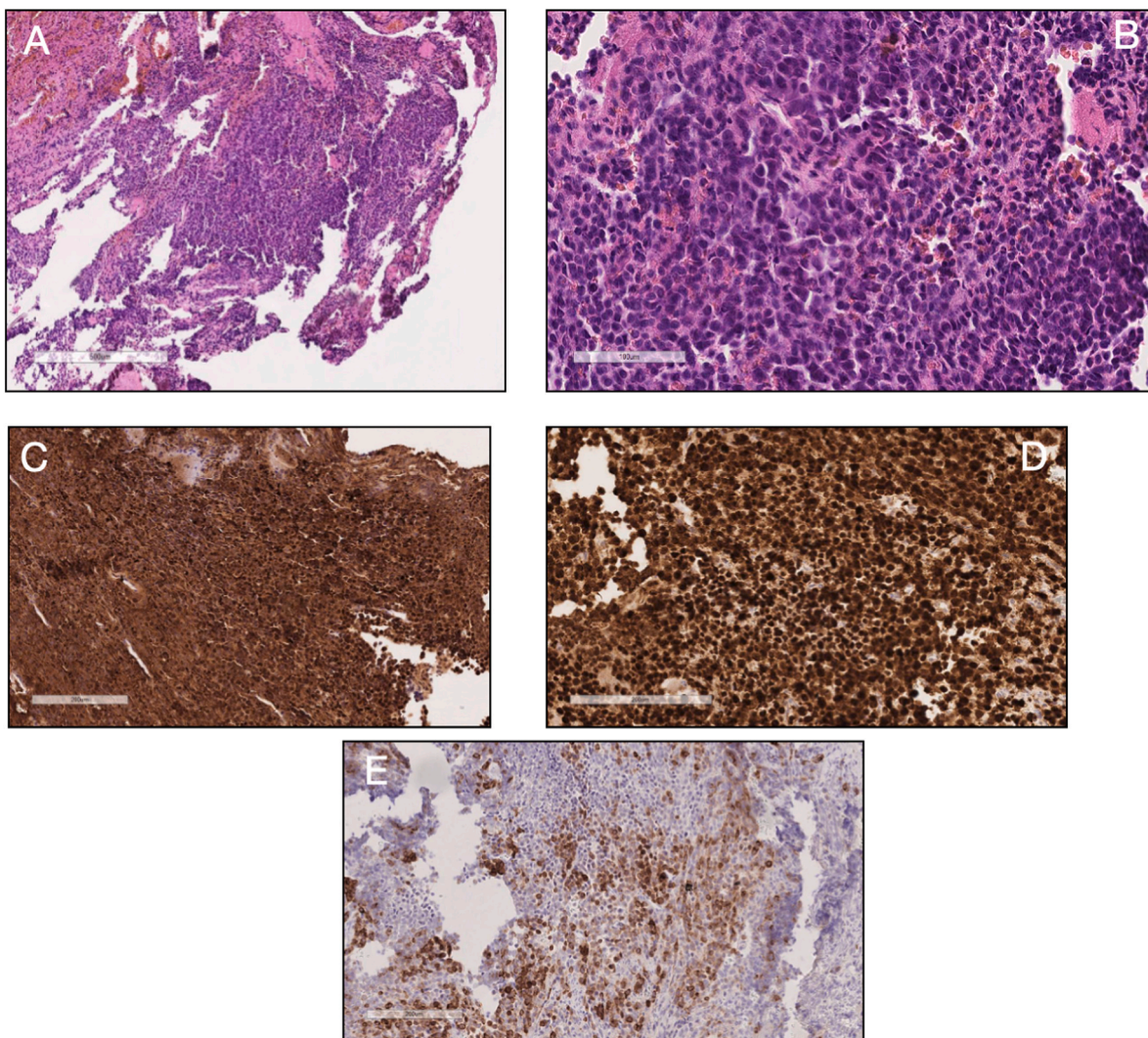


Fig. 2. Histological analysis of the specimen. A-Dense aggregate of epithelioid cells that infiltrates fragments of fibrous tissue with numerous vascular structures. B-At higher magnification a proliferation of rounded cells with little cytoplasm, hyperchromatic nuclei and some prominent nucleoli are seen. Only few cells appear to contain focal pigment deposits. C-All the cells demonstrate a strong and diffuse cytoplasmic and nuclear positivity for S-110 Immunostaining. D-Strong nuclear immunoreaction for SOX10 in all the neoplastic cells. E-Over half of the neoplastic cells showed cytoplasmic positivity for HMB45 immunostaining.

Pure tone audiometry (PTA) showed an almost complete right-sided hearing loss and severe left-sided hearing deterioration which evolved into a complete bilateral hearing loss in the following 2 weeks.

Vestibular evaluation excluded vestibular neuritis, as well as the neurological evaluation revealed horizontal nystagmus on the left side, slight functional alteration of the right orbicularis oculi muscle with

minimal lagophthalmos as well as gait anomalies. A CT-scan was performed on suspicion of a stroke but it did not recognize any alterations of the cerebral parenchyma.

The Magnetic resonance imaging (MRI) of the skull, brain and spine showed bilateral enhancing lesions at the internal auditory canals (IACs) in T2-dependent sequences, thickened appearance at the right VIII cranial nerve level with hyperintensity of the signal and a similar lesion at D1 spine level. (Fig. 1).

Due to the radiological findings, the suspect of multiple metastatic lesions from melanoma arose and for that reason a debulking surgery and biopsy for molecular characterization of the tumour were planned. Prior to a right complete mastoidectomy, an extended posterior exposure of the sigmoid sinus with access to the posterior fossa dura and exposure of the cerebellopontine angle was performed. Debulking surgery of the metastatic lesion was performed. The immediate histological evaluation was positive for neoplastic tissue while the definitive histological report showed a BRAF mutated melanoma (mutation 600 c.1799T > A - c1799-1800 TG > AA) (Fig. 2).

After histological confirmation of the diagnosis of melanoma metastases, the patient was referred to the oncology department to start immunotherapy treatment.

3. Discussion

As regards metastases of cutaneous melanoma, the most frequently affected organs, excluding the skin and lymph nodes, are lungs (10–40 %), liver (15–20 %), brain (5–20 %), skeleton (5–20 %), adrenal gland (1–10 %), gastrointestinal tract (1–10 %), pleura (<5 %) and pancreas (<5 %) [1].

Cerebellopontine-angle tumours account for approximately 6–10 % of all intracranial tumours but a large majority of these entities are benign with a favourable prognosis. Metastatic tumours in the internal auditory canal and pontocerebellum angle are uncommon, with an estimated rate of incidence of only 0.3–0.7 % [4].

Reviewing the literature metastasis of the inner ear and pontocerebellum angle from melanoma are rare and only few cases of melanoma metastases with simultaneous bilateral involvement of the inner ear have been reported [4–12].

The diagnosis of metastatic tumours in the internal auditory canals mainly depends on clinical symptoms rather than imaging features.

If a patient has a previous history of malignancy and develops rapidly progressive neurologic deficits of cranial nerve VII or VIII, hearing loss, facial palsy, vertigo, tinnitus, and imbalance, a potential diagnosis of metastatic tumour in the internal auditory canal should be considered. Early examinations, biopsy, or surgery should be highlighted, which may facilitate the pathologic diagnosis as well as accurate treatment and thus improve the individual's prognosis. In these cases, palliative surgery is also of fundamental importance, especially to typify the neoplasm in order to evaluate the best target therapy to choose (BRAF and PD-L1 inhibitors).

Given the three lesions observed at MRI, an histological diagnosis was mandatory to understand the best therapeutic strategy for the patient. Since he had an important hearing loss associated with vestibular deafferentation, the translabyrinthine approach to the lesions in the IAC was the most suitable. It represents the safest option and it is advisable in the case of hearing deterioration, allowing a good exposure of the IAC with very low risk of leakage. If the patient would have had a normal hearing or vestibular function, the retrosigmoid approach had to be considered, even if the exposure of IAC would have been more difficult [13]. Furthermore, a biopsy on the lesion on D1 was at great risk for the spine safety. Due to a negative promontory stimulation test it was impossible to rehabilitate the hearing of the patient with a cochlear implant.

A differential diagnosis with Neurofibromatosis type 2 was required, given the presence of bilateral IAC lesions. Histological findings were crucial: they showed a strong and diffuse positivity for S100 and SOX10

antibodies and a cytoplasmic immunoreaction for HMB45, confirming the diagnosis of metastatic melanoma. On the other hand, meningioma is strongly positive for S100 and SOX10 antibodies, schwannoma shows only S100 immunostaining, but both are consistently negative for HMB45 antibodies [14].

Metastatic melanoma of the IAC might benefit from different therapeutic, surgical or radiosurgical strategies. Considering that the patient also had D1 spine metastasis, the best solution would have been immunotherapy [3,15].

4. Conclusions

It is known that cutaneous melanoma can metastasize even after many years from the onset and the early recognition of signs and symptoms characterising even a rare localization is of fundamental importance for palliative reasons and to undertake a targeted and early surgical and immunotherapeutic therapy.

Ethical statement

The case report we present a rare case of bilateral IACs metastasis from melanoma. For this reason the Institutional Review Board was not consulted.

The patient was asked a written informed consent prior to the surgery we performed.

The patient anonymity has been preserved in the case report we present.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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