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Unusual case of intraosseous primary intracranial malignant melanoma

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Accepted 4 January 2024

SUMMARY

Primary intracranial malignant melanoma (PIMM) represents 0.07% of central nervous system tumours; clinical behaviour and prognosis are not well documented. Preoperative diagnosis of PIMM is complex and it could be easily misdiagnosed, especially with malignant meningioma.

We are reporting a case of a man with a history of rapidly arising motor slowing associated with urinary incontinence, presenting with mild convergent strabismus caused by paralysis in abduction in the right eye. A brain CT showed a lesion compatible with malignant spheno-orbital meningioma, and the patient underwent gross total resection. Intraoperatively, the blackish lesion infiltrated and eroded the bone; it was placed externally on the dura mater with a mild reaction and without attachment. Histological examination confirmed PIMM. Intraosseous localisation of PIMM has been observed in the basic bone structure of the oral cavity. We report the first intraosseous spheno-orbital PIMM case and present an embryological theory about how this unusual tumour can develop.

BACKGROUND

Primary intracranial malignant melanoma (PIMM) is a very rare tumour; clinical behaviour and prognosis are not well documented. Preoperative diagnosis is often complex, and PIMM could be misdiagnosed over other disease entities, such as metastasis, malignant or benign brain tumours.[1] The standard treatment of PIMM has not been established, and the overall prognosis is extremely poor.[1 2]

Intraosseous localisation of PIMM has been observed in the basic bone structure of the oral cavity[3 4]; to the best of our knowledge, no case of intraosseous neurocranial placement has been reported. We present the first intraosseous spheno-orbital PIMM case involving the anterior and middle cranial fossa bone and orbital cavity.

CASE PRESENTATION

A man in his 50s, with a history of rapidly arising motor slowing associated with urinary incontinence, presented with mild convergent strabismus caused by paralysis in abduction in the right eye; he denied diplopia and visual field disturbance. An urgent non-contrast brain CT showed a right extra-axial frontal lesion characterised by a heterogeneous appearance in the anterior and middle right cranial fossa, infiltrating the roof of the orbit and extending along the lateral wall of the orbital cavity (dimensions 4.3×3.8×3.8 cm), without hyperostosis and associated with internal bleeding, extensive perifocal oedema and mass effect (midline shift of 11 mm) (figure 1). Brain MRI cannot be performed safely because the patient had non-MR-compatible pacemaker.

The lesion appeared suspicious for meningioma, and the patient underwent gross total resection.

On close intraoperative observation, the tumour appeared blackish and vascularised; it originated from the spongiosa of the bone, growing from the deep layers outwards, eroding and destroying the cortical layer, with a mild dural reaction and no attachment (figure 2). No other definite site of origin was identified.

Considering the consistency of the tumour, its location in the deep layers of the bone with erosion and destruction of the cortical layer and its high level of adhesiveness, it was impossible to remove the entire tumour en bloc. Almost the entire extraosseous lesion was excised en bloc; the intraosseous part was aspirated with a cavitron ultrasonic surgical aspirator (CUSA) with a bone tip, resulting in a macroscopically complete excision. According to literature data, the risk of leptomeningeal carcinomatosis (LMS) incidence after resection must be evaluated on the variable proximity of the metastatic lesions to the cerebrospinal fluid (CSF) pathways, in addition to known factors such as a piecemeal resection modality and a location in the posterior fossa. For resection of brain metastasis only in contact with the parenchyma, neither

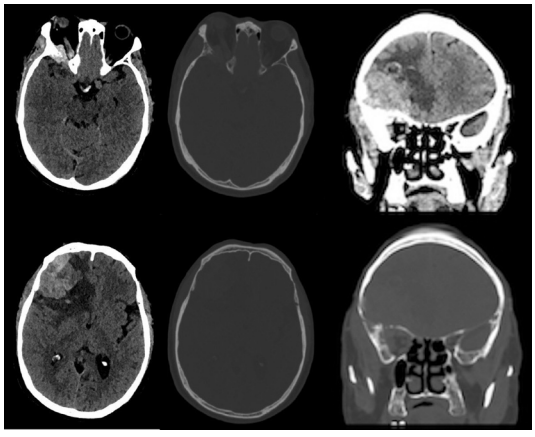

Figure 1 Right extra-axial frontal lesion characterised by the heterogeneous appearance with evidence of an aggressive lesion in the anterior and middle right cranial fossa infiltrating the roof of the orbit and extending along the lateral wall of the orbital cavity, without hyperostosis and associated with internal bleeding, extensive perifocal oedema and mass effect.

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To cite: Guarrera B, Coati I, Giarletta M. *BMJ Case Rep* 2024;**17**:e256623. doi:10.1136/bcr-2023-256623

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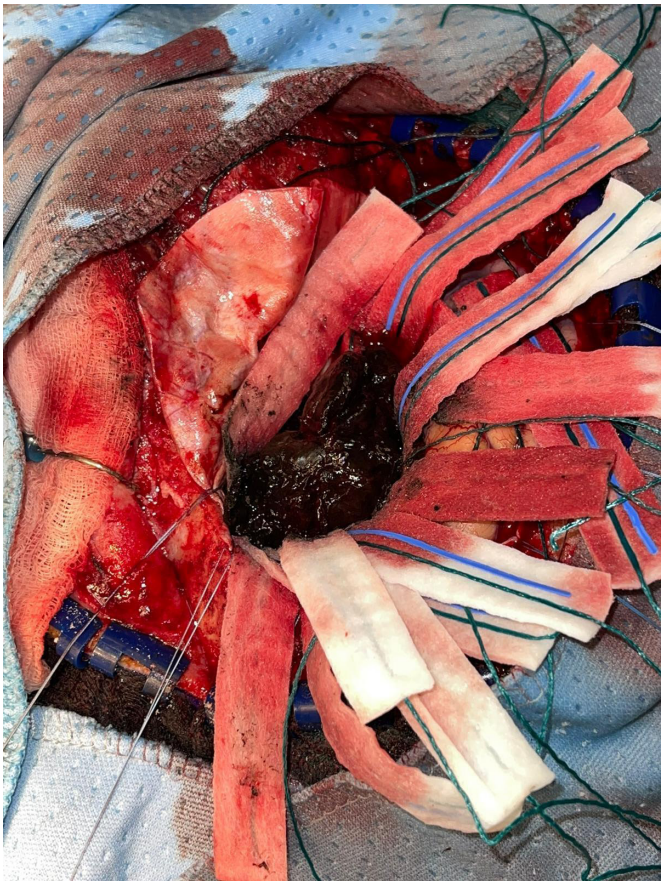

Figure 2 Intraoperative aspect of the lesion appearing blackish, vascular and placed externally to the dura mater.

piecemeal resection nor the spread of tumour cells through the CUSA increased the incidence of LMS, whereas attention should be paid to the possibility of iatrogenic LMS when using the CUSA for resection of metastatic lesions close to the CSF pathways.[5]

Considering the possibility of macroscopic mechanical dissemination, the lesion was gently isolated from the brain parenchyma using a dissector and cotton patties; the afferent vessels were coagulated and then cut.

Histological examination showed spindle-cell epithelioid morphic neoplasia arranged in bundles, organised in fibroadipose tissue, striated muscle and bone lamellae with massive neoplastic infiltration. The cells with intense melanic pigment showed severe cytological atypia and areas of necrosis (figure 3). Immunohistochemistry demonstrated the absence of PD-L1 gene SP263, S100 positivity (clone 4C4.9), melan A positivity (clone A103), HMB45 positivity (clone HMB45), SOX-10 positivity (SP267) and BAP1 positivity (clone C-4). Neoplastic cells conserved nuclear expression, with mitosis up to 5–6/mm^2 (figure 3). Molecular mutational analysis (exon 15) on a sample area containing 95% tumour cells did not reveal detectable mutations in the BRAF gene. Morphological and immunophenotypical features are compatible with malignant melanoma.

Clinical and radiological examinations exclude any other localisation of melanoma.

After neurosurgical treatment, the patient did not report any new neurological deficits and the strabismus appeared unchanged.

After 6 months, despite three cycles of ipilimumab plus fotemustine associated with radiotherapy, a new CT of the brain contrast shows a recurrence of the tumour associated with meningeal carcinomatosis.

He passed away 9 months after the surgical procedure because he developed post-surgical hydrocephalus.

INVESTIGATIONS

A preoperative CT cerebral angiography showed a left posterior communicating artery aneurysm with a wide base of implantation on the carotid siphon (8 mm), and a thin basilar artery about to the presence of an incomplete fetal type of posterior cerebral arteries, associated with a left carotid web. The next angiographic study confirmed these results.

A postoperative contrast CT scan of the brain confirmed the tumour gross total resection and excluded postoperative complications (figure 4).

Ocular examination, CT of the whole body, gastroscopy, colonoscopy, positron emission tomography-CT with 18F-FDG and whole-body skin check excluded any other localisation of the melanoma.

DIFFERENTIAL DIAGNOSIS

PIMM must be differentiated from meningioma, schwannoma, choroid plexus papilloma, astrocytoma, solitary fibrous tumour and high-grade glioma.[1 6]

In our case, the tumour was preoperative, regarded as suspicious for spheno-orbital meningioma, considering neuroradiological features and clinical signs. This diagnosis was intraoperatively denied taking into account the marked blackish colour, intraosseous placement, absence of implantation base on the dura mater and extemporaneous histopathological examination.

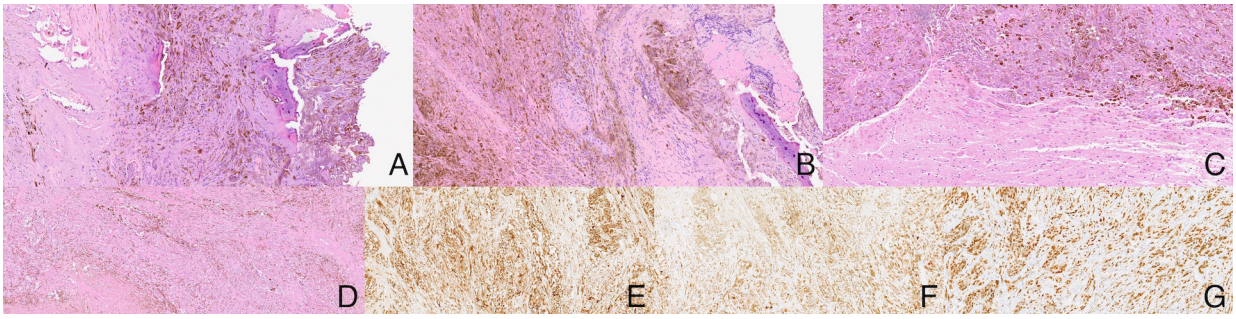

Figure 3 (A) Detail of melanoma infiltrating bone tissue (10×). (B) Detail of melanoma infiltrating muscle and bone tissue (10×). (C) Detail of melanoma infiltrating cerebral parenchyma (10×). (D) Epithelioid neoplasia with abundant melanic, cytoplasmic pigment (4×). (E) The neoplasia is HMB45 positive (10×). (F) The neoplasia is melan A positive (10×). (G) The neoplasia is SOX-10 positive (10×).

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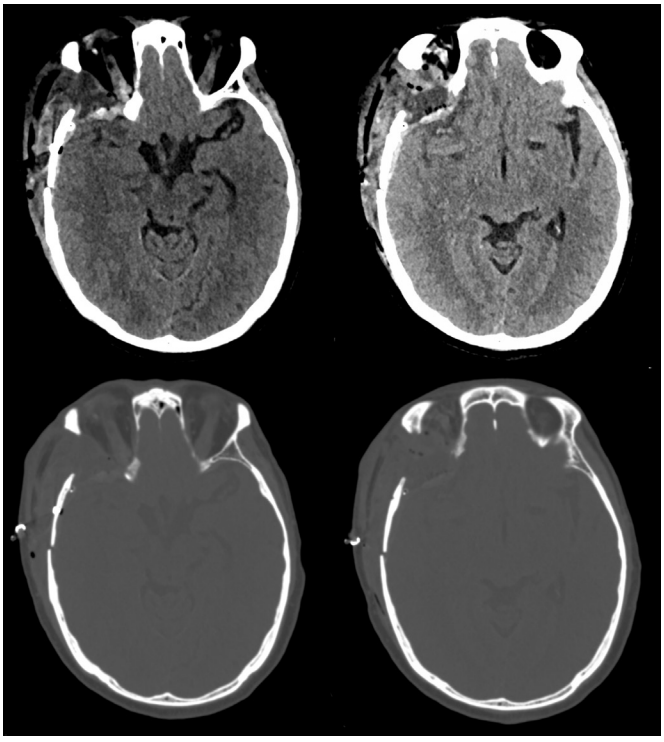

Figure 4 Postoperative CT confirmed gross total resection.

TREATMENT

After gross total resection, the patient underwent chemotherapy based on three cycles of ipilimumab plus fotemustine, associated with radiotherapy. He was waiting for endovascular treatment of the left posterior communicating artery aneurysm.

OUTCOME AND FOLLOW-UP

Three months after surgery, a new CT scan of the brain was performed, and after 6 months, a second one followed: the last neuroimaging showed a tiny recurrence of the disease placed in the surgical cave associated with meningeal carcinomatosis. 11 months after the surgical treatment, the patient expired.

DISCUSSION

PIMM is a very rare tumour accounting for approximately 1% of all melanomas and represents 0.07% of central nervous system (CNS) tumours.[1]

PIMM is classified into two types considering the pathological behaviour: the diffuse type presents an infiltrating spread of the tumour and is predominant among children with neurocutaneous melanosis complex or phakomas[7]; while the solitary type appears as a nodular mass.[8]

PIMM originates from a malignant transformation of precursor melanocytes, which are derived from the neural crest and migrate actively to peripheral sites such as the skin, mucous membranes, parenchyma and uvea.[9] Three different theories explain the localisation of melanocytes in the CNS: (1) the mesoderm gives rise to pigment cells which reach the brain or spinal cord via the pial blood vessels; (2) CNS melanomas derived from aberrant embryonic ectodermal cells; (3) in the neurogenic theory, pigment cells originate from the neural crest.[1 4 10] To the best of our knowledge, any association between molecular profile and theory of the origin has not been defined, and there are no clear clinical outcomes in response to molecular therapy between the three groups.[7 8]

Clinical PIMM presentation is variable, as it causes frequently an increase in intracranial pressure, cranial nerve palsies and meningism,[11] or rarely, pituitary dysfunction.[12]

PIMM is diagnosed when other sites of possible primary melanoma are excluded with a clinical and radiological examination, and differential diagnosis based on neuroimaging test is difficult.

It is known that the MRI findings of most melanoma are complex and variable, showing different signals. When the tumour is rich in melanin, it presents high and low signals on T1-weighted imaging (T1WI) and T2-weighted imaging (T2WI), respectively. Blood vessels at the periphery of the tumour may cause haemorrhage, but the haemoglobin signal usually masks the paramagnetic effect of melanin.[13] Diffusion-weighted imaging combined with perfusion-weighted imaging examination typically shows high tumour perfusion, with a great advantage in terms of clarity and accuracy, providing some value in the diagnosis of melanoma. MRI can divide the presentation of melanoma into four types. The first one is the melanin type, with T1WI and T2WI at high and low signals; the second one is the non-pigmented type, where T1WI and T2WI show equally low and equally high signals. The third type is a mixed type with mixed signals; and the fourth type is the haematic type, in which only haemorrhage occurs.[14 15]

Hayward[16] proposed the following factors to differentiate PIMM from secondary melanoma: (1) no malignant melanoma outside the CNS, (2) leptomeningeal involvement, (3) intramedullary spinal lesions, (4) hydrocephalus, (5) tumour location in the pituitary or pineal gland, and (6) a single intracerebral lesion.

Standard treatment of PIMM has not been established: total resection or biopsy is considered taking into account dimension, site and neuroradiological features. Adjuvant treatment includes stereotactic radiosurgery, whole-brain radiotherapy (higher dose can be considered), chemotherapy based on dimethyl-triazeno-imidazole-carboxamide, and/or immunotherapy.[11]

The outcome for patients with PIMM is better than in those with metastatic melanoma, and it depends on the degree of mitosis, leptomeningeal dissemination, extent of surgical excision and location of the tumour; it is on average 9–24 months.[17]

Our patient was admitted to neurosurgery for suspected spheno-orbital malignant meningioma based on clinical and neuroimaging, but intraoperative tumour features were not compatible: a dural reaction appeared without invasion, and the blackish intraosseous lesion infiltrated and eroded the bone (figures 1 and 2). The review of the literature showed that intraosseous localisation of PIMM in bones contributing to the framework of the oral cavity, with natural and macroscopic features like our case, was observed.[3 4] In modern jawed vertebrates, the viscerocranium and rostral parts of the neurocranium are derived from neural crest cells[10]; based on the neurogenic theory, it is possible to explain the maxillary and mandibular alveolus as the frontal and sphenoidal intraosseous site.

Patient's perspective

We were thoroughly informed by the neurosurgeons about the severity of the pathology and the difficulty of neurosurgical procedure. After the surgery, when I woke up in the ICU [intensive care unit], I was afraid that I had lost the eye function, but this did not happen. The hospitalization was pleasant, but I wanted to go home as soon as possible.

I and my family are grateful for the professionalism of the neurosurgical team.

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Learning points

- Primary intracranial malignant melanoma (PIMM) is a very rare tumour; preoperative diagnosis is often complex and it could be misdiagnosed with other disease entities, such as other malignant brain tumours, metastatic brain tumours and even benign tumours. The standard treatment of PIMM has not been established, and the overall prognosis is extremely poor.
- Intraosseous localisation of PIMM has been observed in the bone structure of the oral cavity, and no case of intraosseous neurocranial placement of PIMM has been reported.
- Based on the neurogenic theory, it is possible to explain the maxillary alveolus and mandibular as the frontal and sphenoidal intraosseous site.
- In a patient presenting with neuroradiological features of malignant meningiomas or aggressive intraosseous lesion, we suggest considering PIMM in the differential diagnosis with other tumours.

To the best of our knowledge, we reported the first case of intraosseous neurocranial localisation of PIMM. In a patient presenting with neuroradiological features of malignant meningiomas or aggressive intraosseous lesion, we suggest considering PIMM in the differential diagnosis with other tumours.

Contributors The following authors were responsible for drafting of the text, sourcing and editing of clinical images, investigation results, drawing original diagrams and algorithms, and critical revision for important intellectual content—BG, IC and MG. The following author gave final approval of the manuscript—BG.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Parental/guardian consent obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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