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Case report

Osteolytic clear cell meningioma of the petrous bone occurring 36 years after posterior cranial fossa irradiation: Case report

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ABSTRACT

Objective and importance: While bone invasion and hyperostosis are frequent phenomena in meningiomas, primary intraosseous meningiomas are rare and their occurrence in the skull base is an extraordinary exception. Moreover, radiation-induced meningiomas represent a unique clinical dilemma given the fact that patients with these tumors had often received a prior full course of radiotherapy.

Clinical presentation: A 42-year-old man presented with a 3-month history of progressively worsening facial asymmetry. His medical history was consistent for a posterior cranial fossa irradiation at the age of 6 years for a non-confirmed brain stem tumor. On admission his Karnofsky performance status was graded as 50% and his neurological examination showed a complete right facial nerve paralysis and hearing impairment. Computed tomography and magnetic resonance imaging demonstrated an osteolytic tumor invading the whole right petrous bone without intracranial involvement.

Intervention: As the tumor reached the external auditory canal, a tissue sample was obtained locally. Pathological examination of the lesion identified a grade II clear cell meningioma and the patient was consequently addressed for an intensity modulated radiation therapy. His condition remained unchanged till the most recent follow-up examination, 8 months later.

Conclusions: To the best of our knowledge, a radiation induced osteolytic clear cell meningioma of the petrous bone has not been previously reported. As little literature exists regarding the use of adjuvant therapies for these tumors, intensity modulated radiation therapy remains an attractive treatment option in case of pervious irradiation and general status alteration.

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Abbreviations: CECT, contrast enhanced computed tomography; MRI, magnetic resonance imaging; CCM(s), clear cell meningioma(s); IMRT, intensity modulated radiation therapy; SR, stereotactic radiosurgery; FSR, fractionated stereotactic radiotherapy.

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1. Introduction

Primary interosseous meningiomas are a subtype of primary extradural meningiomas. With only 24 reported cases to date, their osteolytic form is most uncommon.

To the best of our knowledge, a radiation induced osteolytic clear cell meningioma of the petrous bone has not been reported so far. The case presented highlights the possible occurrence of a purely interosseous and aggressive meningioma 36 years after conventional irradiation and searches the relevant literature regarding the possible role of adjuvant therapies in such exceptional situations.

2. Case report

This 43-year-old male was first admitted to the neurosurgery section in June 1979 with a progressively aggravating right bulbar syndrome. A ventriculography by opaque injection was first realized and showed a moderate dilatation of the whole ventricular system. Further investigation by a head computed tomography showed a hypodensity in the right bulbar area (Fig. 1). Although the imaging study was not affirmative, the patient was considered as having a brainstem tumor. Surgery for such lesions was not feasible at that time and the decision was to administer a full dose of radiation therapy without the need of a pathological specimen. Consequently the patient received 40 Gy over his posterior cranial fossa and was discharged home few days later. His condition progressively improved and he became symptom free within 4 months but was lost to view since the mid-80s.

In January 2015, he presented once again for a 1 month history of heaviness, impaired hearing in the right ear, vertigo and a progressively worsening right facial asymmetry.

On examination, his general status was altered with a Karnofsky performance scale graded as 50%. His higher mental functions were normal and his cranial nerves examination was remarkable for a complete right facial nerve paralysis (House–Brackmann grade VI). Moreover, his Rinnie's test was negative and Weber's test lateralized to the right side.

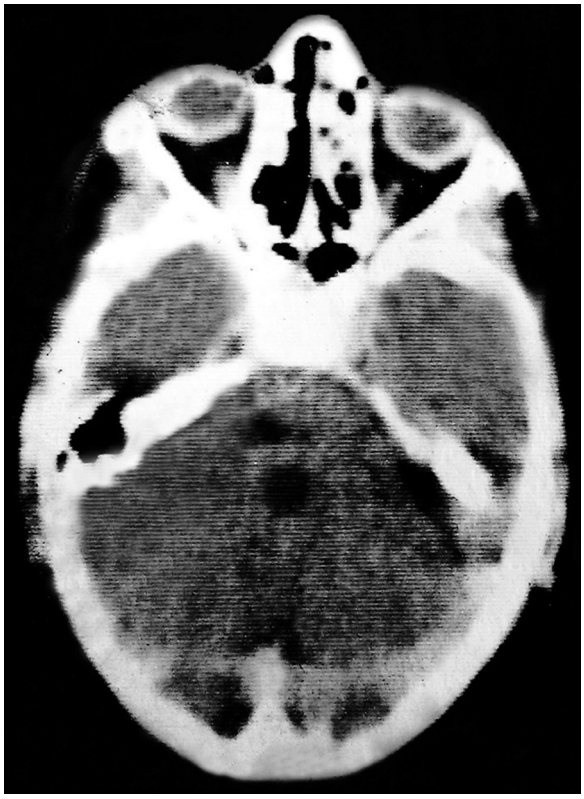

Fig. 1 – Head CT performed in June 1979 showing a right bulbar hypodensity.

Hematological and biochemistry profiles were normal. Contrast enhanced computed tomography of the head (Brilliance 64-multislice CT scanner, Philips Medical System, MA) revealed a heterogeneously enhancing osteolytic mass of the right petrous bone. The tumor reached the right external

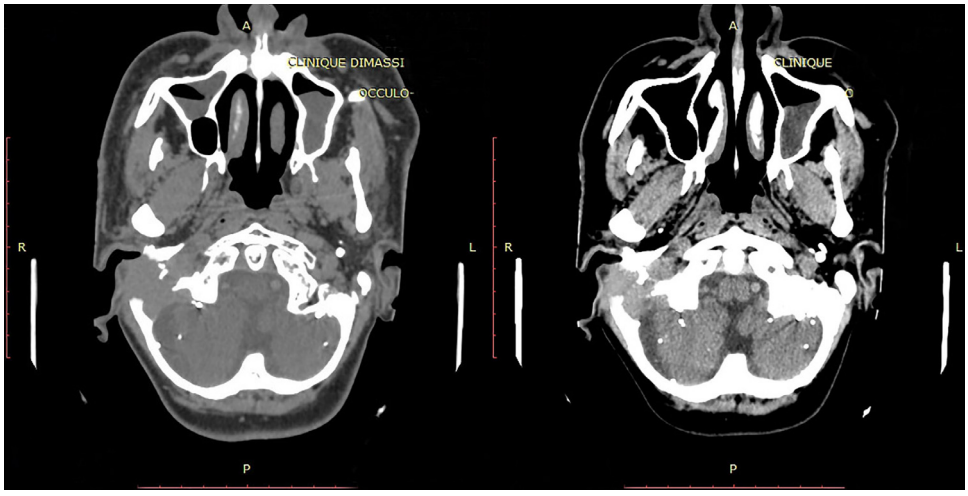

Fig. 2 – Axial CT images of the petrous temporal bones demonstrate a large lytic lesion on the right side with extensive destruction of the mastoid process and lateral petrous region. The external auditory meatus and middle ear cavity are also involved.

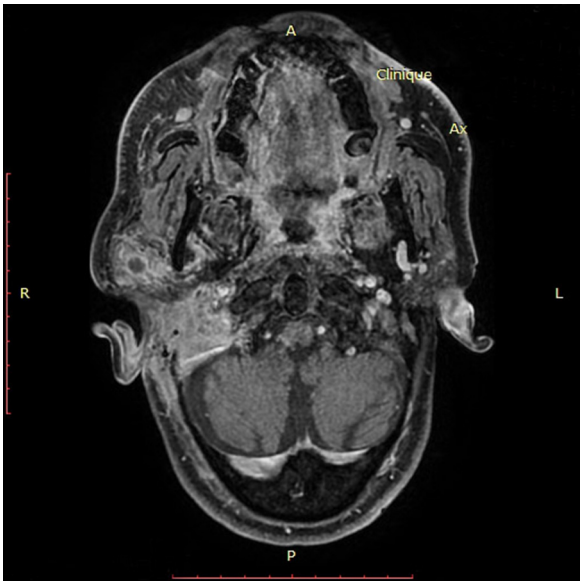

Fig. 3 – Axial T1-weighted MRI with contrast enhancement demonstrates a right-sided tumor of the petrous bone without intracranial involvement.

auditory canal while the underlying dura matter and brain parenchyma seemed to be intact (Fig. 2).

Magnetic resonance imaging of the brain (Ingenia 3T MR scanner, Philips Medical System, MA; with and without contrast) showed a T1 isointense to hyper intense, T2 mixed signal intensity, destructive lesion of the petrous bone encompassing the ipsilateral facial nerve and internal carotid artery without any intracranial extension (Fig. 3).

A gray-whitish tumor specimen was obtained from the external auditory canal. On histopathological examination, the tumor was composed of round to polygonal cells arranged in whorls, showing clear cytoplasm and round to oval nuclei with dispersed chromatin and inconspicuous nucleoli. There was perivascular and interstitial deposition of a collagenous material in a block manner. Tumor cells tested positive for PAS and epithelial membrane antigen and the final histological diagnosis was a WHO grade II clear cell meningioma. Ki-67 labeling index was 7.5% (Fig. 4).

No surgical intervention was decided and we judged preferable to address the patient directly to an intensity modulated radiation therapy. His clinical status remained unchanged till the most recent follow-up examination, 8 months later.

3. Discussion

Meningiomas are the most common benign intracranial neoplasm and typically arise from meningocytes or ''arachnoid cap cells'' located within the arachnoid layer of the meninges. Meningiomas without contact with the surface of the arachnoid membrane are labeled ''ectopic meningiomas'' [1,2] and were first described by Winkler in 1904 [3]. While bone invasion and hyperostosis are frequent phenomena in such cases, primary intraosseous meningiomas without any additional soft tissue component are rare and almost all of them are of osteoblastic subtype [4,5]. With only 24 reported cases to date, the osteolytic subtype is most uncommon (Table 1) and worth noted, only three localized in the skull base [1,11,18]; especially the petrous bone region.

This case is significant not only because it satisfied the criteria of a radiation-induced tumor defined by Cahan in 1948 [25], making it the first radiation induced meningioma of bone; but also an intraosseous clear cell meningioma (CCM) has never been previously reported.

CCM constitutes represents a rare variant of grade II meningiomas accounting for only 0.2% of all meningiomas and is distinct from more typical forms for being more locally aggressive, associated to a recurrence rate as high as 61% and a possible metastatic potential [26,27]. These tumors, moreover, have no sex predilection and typically affect young individuals in their mid to late twenties. They also differ from typical forms in their site of occurrence. In fact, the majority of cases of CCM were intradural spinal lesion (50%). Other possible sites of occurrence include the supratentorium (21%), the cerebellopontine angle (21%) and the foramen magnum and skull base (7%) [26].

From a clinical standpoint, diagnosing an intraosseous meningioma preoperatively is somehow difficult to clinicians even if the patient's symptoms include a gradually expanding mass [5]. Imaging techniques are comparable to those used for skull metastases, and appearance on MRI and CT is also

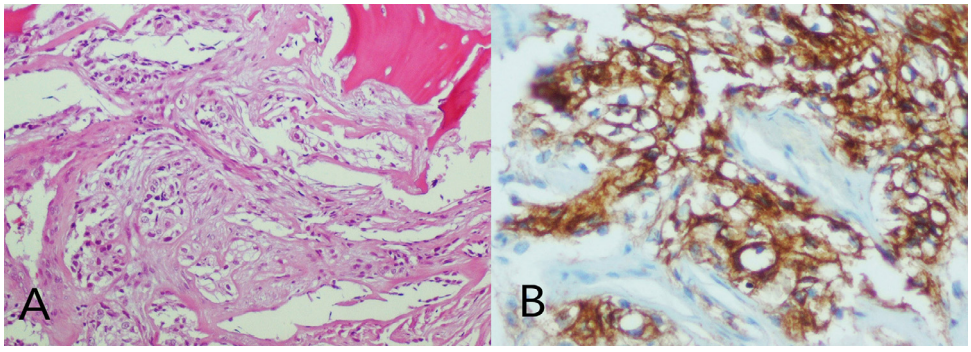

Fig. 4 – Photomicrographs of the tumor specimens showing: (A) Tumor cells having round nuclei with clear cytoplasm. (H&E, original magnification, ×100.) (B) Diffuse membranous positivity for epithelial membrane antigen. (Epithelial membrane antigen, ×40.)

Table 1 – Literature review of intraosseous osteolytic meningiomas.

Author, year	Age	Sex	Location
Pearl et al., 1979 [6]	44	W	Calvaria
Young, 1983 [7]	n.p.	n.p.	Calvaria
Ammirati et al., 1990 [1]	21	M	Skull base
Koga et al., 1993 [8]	63	M	Calvaria
Ghobashy and Tobler, 1994 [9]	65	W	Calvaria
Levin et al., 1995 [10]	n.p.	n.p.	Calvaria
Ayadi et al., 1997 [11]	36	W	Skull base
Changhong et al., 1997 [12]	n.p.	n.p.	Calvaria
Muthukumar, 1997 [13]	55	M	Calvaria
	50	M	Calvaria
	65	M	Calvaria
Lee et al., 1992 [14]	61	M	Calvaria
Kaneko et al., 1988 [15]	71	W	Calvaria
Qasho and Celli, 1998 [16]	46	W	Calvaria
Okamoto et al., 2000 [17]	78	W	Calvaria
Rosahl et al., 2004 [18]	38	M	Skull base
Tokgoz et al., 2005 [19]	44	M	Calvaria
Agrawal et al., 2007 [20]	70	W	Calvaria
Sheikhrezaie et al., 2009 [21]	62	M	Calvaria
Yener et al., 2009 [22]	78	M	Calvaria
Kim et al., 2012 [5]	68	M	Calvaria
	74	W	Calvaria
Bujok and Bienioszek, 2014 [23]	59	W	Calvaria
Tang et al., 2014 [24]	82	W	Calvaria

consistent. Osteolytic tumors of the skull base should include chondroma, chondrosarcoma, dermoid, epidermoid tumor, brown tumor, multiple myeloma, plasmacytoma, giant cell tumor, aneurysmal bone cyst, eosinophilic granuloma, or metastatic cancer [20,28]. But, regard of its distinct histological features, clear cell meningioma needs to be differentiated from other clear-cell neoplasms including metastatic renal-cell carcinoma, pleomorphic xanthroastrocytoma, oligodendroglioma, hemangioblastoma, germinoma, lipid-rich glioblastoma, and clear-cell ependymoma outlining the major role of immunohistochemistry in assessing the differential diagnosis.

It has been already established that Meningiomas are the most common radiation-induced neoplasms of the central nervous system [29,30] and that the risk for development of secondary meningiomas after high-dose cranial irradiation increases with the duration of follow-up [29], reaching a cumulative risk of 8.18% after 25 years [31]. Several authors have also emphasized the relation between the tumor histology and the latency period: a more pronounced proliferative activity, results in a shorter latency and is commonly associated with atypical/anaplastic variants [29]. But these reports are tempered by ones like ours in which a locally aggressive tumor appeared almost 36 years after initial irradiation.

Independently of the presumed radiation induced etiology of our patient's tumor, understanding how a meningioma can strictly develop in the intraosseous compartment is still unclear and several explanations have been put forward to explain the ectopic origin of primary intraosseous meningiomas: arachnoid cells may accompany cranial nerves during their course through skull foramina [32] or localize in the arterial sheath of vessels supplying the periosteum or piercing the skull [3] and may develop into meningioma cells at a later stage [33]. Alternatively, the mesenchymal origin of the meninges can explain the pathogenesis of primary intraosseous meningiomas since multipotential mesenchymal cells have the ability to differentiate into different tissue types, particularly of meningeal subtype. Which is undoubtedly supported by the fact that these tissues have been already found as metaplasia in meningiomas [34]. In the present case, an aggressive meningioma localized within the petrous bone. In this location, we believe it reasonable to assume that arachnoidal cell clusters found regularly at the level of the internal auditory meatus, jugular foramen, at the geniculate ganglion, the Eustachian tube or in association with the greater and lesser superficial petrosal nerves in autopsy specimens of patients without meningioma [34], may probably represent the cells of origin of this meningioma.

Even under the current therapeutic armamentarium, intraosseous meningiomas still represent a real challenge especially when located within the skull base. In addition, the increasing number of survivals of patients with childhood malignancies implies that the prevalence of radiation induced intraosseous meningiomas is likely to increase in the future. The mainstay of treatment remains complete surgical excision since this has been shown to be associated with a better long-term outcome compared with subtotal excision [35]; but an extensive surgical excision is not always feasible like in our case. Moreover, some patients already received the maximum tolerable dose of radiation and conventional radiotherapy is not an option: under these considerations, clinicians may consider patients with such lesions as stronger candidates for adjuvant therapies, depending on the clinical circumstances [5] and the previous irradiation dose. Stereotactic radiosurgery (SR) or fractionated stereotactic radiotherapy (FSR) may be appropriate adjuncts to surgery or may be the alternative to surgery in some high-risk patient independently of the radiation-related relation of these tumors. The seize of the tumor must also be considered in the management strategy and facing a large tumor nearly invading the whole petrous bone, IMRT can be of great help since it allows dose escalation. Selected volumes can in fact be spared, but only at the expense of higher dose to other areas.

Finally as current therapies are starting to integrate molecular factors in the treatment of radiation induced meningiomas, the role of medical therapies targeting aberrant molecular pathways can be discussed. To date, several agents such as hydroxyurea have been attempted with variable success rates [36]. Interestingly, Bevacizumab, a monoclonal antibody targeting VEGF, has recently been utilized in the management of secondary meningiomas in isolation or following SRS for the prevention of recurrences with a reasonable success [36,37], but its possible future use in strictly intraosseous variants like ours still needs to be assessed.

4. Conclusion

Clear cell meningioma may present as a purely intraosseous osteolytic tumor 36 years after high dose cranial irradiation. Immunohistochemistry plays a major role in the definitive diagnosis to exclude other neoplasms with clear-cell features and a multimodal management protocol taking benefit from the expansion of the available therapeutic armamentarium

can be of great adjunct in such challenging cases. Finally, as the prognosis depends on the time at diagnosis, a close follow up extending over a long period of time should be indicated in all previously irradiated patients.

Consent

Although, written informed consent is not needed in this paper as illustrations do not permit the recognition of the patient, we have obtained such consent for the publication of this article and the accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of the journal.

Conflict of interest

None declared.

Acknowledgement and financial support

None declared.

Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; Uniform Requirements for manuscripts submitted to Biomedical journals.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.pjnns.2016.04.003.

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