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CASE REPORT

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Benign extracranial meningioma with pulmonary metastasis: a case report and review of literature

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Abstract

Background Meningiomas are common central nervous system tumors, predominantly intracranial, they rarely develop extracranially. Moreover, benign meningiomas seldom metastasize.

Case presentation This article presents a case report of a 55-year-old Chinese male patient with a primary World Health Organization grade 1 meningioma originating from the petrous apex of the temporal bone, accompanied by pulmonary metastasis. Following two incomplete resections of the primary tumor, the patient underwent radiotherapy and has since maintained a stable condition.

Conclusion The case report highlights the rare occurrence of pulmonary metastasis in a benign World Health Organization grade 1 meningioma originating from an extracranial site. It also illustrates the important role of radiotherapy in treating patients with meningioma. Additionally, a review of related literature is provided to gain insights for the diagnosis and treatment of the disease.

Keywords Benign meningioma, Pulmonary metastasis, Radiotherapy

Introduction

Meningiomas are the most frequently reported central nervous system tumor, accounting for 36.4% of tumors overall. The majority of meningiomas are benign [World health Organization (WHO) grade 1] [1]. Metastasis of meningiomas is rare, with an incidence of less than 0.1% [2]. Metastasis can occur through cerebrospinal fluid dissemination, hematogenous spread, or lymphatic transmission, with the majority of metastatic cases arising from aggressive WHO grade 2 or 3 meningiomas. Metastasis from grade 1 meningiomas is extremely rare. Meningiomas primarily occur intracranially, with extracranial meningiomas accounting for less than 2% of cases [3]. Herein, we report a rare case of a patient with a WHO grade 1 meningioma located at the petrous apex of the temporal bone extracranially, accompanied by pulmonary metastatic lesions. Following surgical resection of the primary lesion, the patient experienced tumor recurrence and underwent a second surgical excision. Postoperative radiotherapy was administered to the residual lesions and the tumor bed area. Subsequent regular follow-ups indicated that the primary lesion remained stable, while the pulmonary metastases showed slow progression.

Case report

A 55-year-old Chinese male patient presented with a 2-month history of decreased hearing in the right ear, accompanied by otalgia, otorrhea, and vertigo. Physical

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examination shows that the patient's taste disappeared and there was numbness on the right side of the tongue. On 17 September 2019, an enhanced magnetic resonance image (MRI) of the head (Fig. 1) revealed an irregularly enhancing lesion in the region of the right petrous bone and jugular foramen, measuring approximately 19×35×26 mm, with a linear enhancement within the right internal auditory canal. The patient had a history of hypertension and diabetes, with no relevant family medical history. On 27 September 2019, the patient underwent a mastoidectomy approach for the excision of a mass in the jugular foramen area. The tumor was located in the jugular foramen area, invading and eroding the middle ear cavity, and was tightly adherent to the lower cranial nerves, making separation difficult and resulting in residual tumor tissue. The postoperative pathological examination revealed proliferative tumor cells with mild to moderate pleomorphism and occasional mitotic figures. Immunohistochemistry showed the following results: CD34 (−), CD68 (−), S-100 (−), Vimentin (+), EMA (+), ER (−), PR (partially+), SSTR2a (partially+), CK (+), STAT6 (−), CD163 (+), Desmin (−), GFAP (−), Olig-2 (−), E-Cadherin (+), INI-1 (+), Ki-67 (partially positive at 5–8%), P53 (a few weakly positive), H3K27Me3 (+), Bcl-2 (−), and EGFR (+). The diagnosis was meningothelial meningioma, WHO grade 1. During the patient's evaluation, pulmonary nodules were detected. A chest computed tomography (CT) scan revealed a nodule in the lateral segment of the right middle lobe and multiple tiny nodules under the right pleura, which were not treated.

At 8 months following the initial presentation (May 2020), the patient experienced a recurrence of right-sided otalgia and otorrhea with minor bleeding, accompanied by a sensation of ear fullness and dizziness. Otoscopic examination revealed a mass in the right external auditory canal. An enhanced head MRI performed in May 2020 demonstrated an irregular nodular lesion measuring approximately 13 mm×7 mm, following the course of the internal auditory canal. The lesion exhibited isointense signals on T2-weighted imaging (T2WI) and showed significant uniform enhancement post-contrast, suggestive of tumor recurrence (Fig. 2a). There was an increase in both size and number of pulmonary nodules (Fig. 2b). A biopsy was performed, and the pathological findings were as follows: the pulmonary nodules consisted of densely packed oval or short spindle-shaped tumor cells with mild pleomorphism. There were three mitotic figures per ten high-power fields (HPF), along with thin-walled blood vessels and collagen septa. Immunohistochemistry results: AE1/AE3(+), EMA(focally positive), Vimentin(+), CD34(−), Bcl-2(−), Stat6(−), CD99 (partially positive), S-100(−), SSTR2(−), PR(−), Desmin(−), SMA(−), CK19(−), CK7(−), P53(8%+), and Ki-67 (15%+). These findings are consistent with metastatic meningioma.

On 18 May 2020, the patient underwent surgical resection of a tumor in the jugular foramen region. During the procedure, extensive bleeding occurred while separating the tumor tissue up to the jugular bulb, leading to the cessation of separation and the removal of the tumor tissue. The tumor was subtotally excised. Postoperative pathology revealed proliferative fibrous tissue with tumor cells arranged in nests and sheets. The cells were oval to short spindle-shaped with mild atypia, and no definitive mitotic figures were observed. Compression deformation was significant in some tissues. Immunohistochemistry results: AE1/AE3(+), EMA (focal positive), Vimentin (focal positive), SSTR2(−), PR(−), S-100(−), and Ki-67 (10%+). The results lead to a diagnosis of meningioma. Programmed cell death 1 ligand 1 (PD-L1) Tumor Proportion Score (TPS)was 1%. PD-L1 Combined Positive

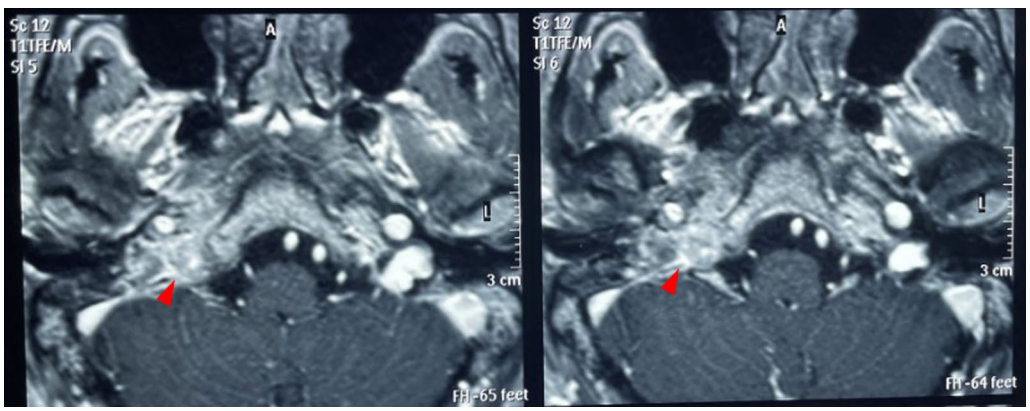

Fig. 1 Magnetic resonance imaging demonstrates patchy, heterogeneous enhancement in the region of the right petrous bone and jugular foramen

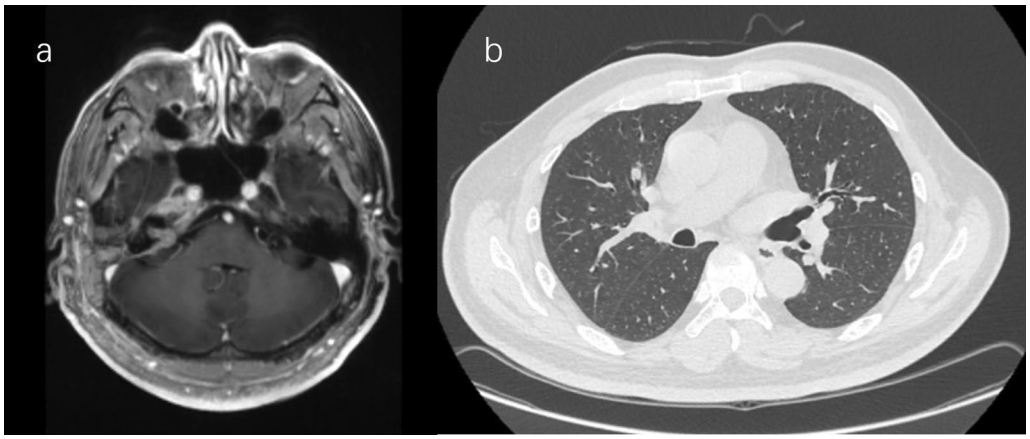

Fig. 2 Magnetic resonance imaging suggests tumor recurrence, with nodular shadows along the internal auditory canal showing uniform enhancement post-contrast (**a**); thoracic computed tomography reveals multiple nodules in both lungs (**b**)

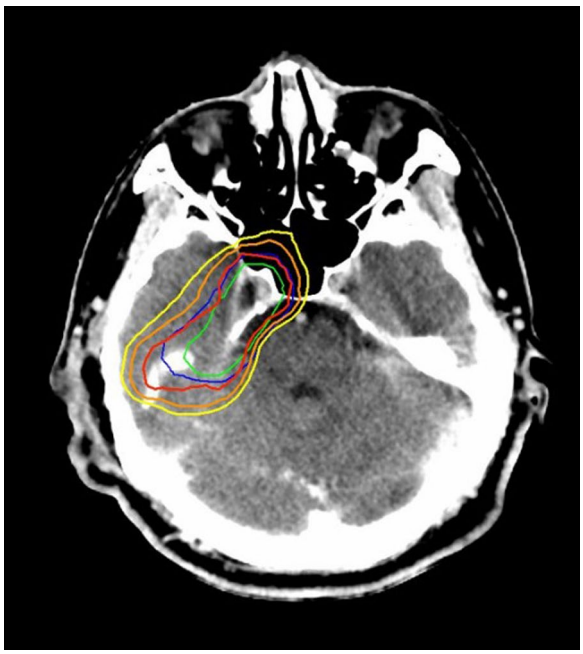

Fig. 3 Radiotherapy plan

Score (CPS) was 5. And genetic testing indicated a mutation in *breast cancer-associated protein 1* (*BAP1*), while no mutations were detected in *TERT*, *CDKN2A*, or *CDKN2B*.

From 13 July 2020, to 21 August 2020, the patient received postoperative radiotherapy. The clinical target volume (CTV) included the postoperative tumor bed and residual tumor lesions. Considering setup and other systematic errors, a 3 mm margin was added to form the planning target volume (PTV), as shown in Fig. 3. The patient was treated with 6MV X-ray irradiation using volumetric modulated arc therapy (VMAT) technology, with a radiation dose to the PTV of 60 Gy in 30 fractions. No significant adverse reactions occurred during the radiotherapy process. In addition, no treatment was given for the pulmonary metastatic lesions.

Follow-up examinations of the patient were routinely conducted until September 2023, during which the meningioma lesion at the apex of the petrous part of the temporal bone remained stable (Fig. 4a). The nodules in both lungs exhibited a slow enlargement (Fig. 4b). The patient continued to undergo regular monitoring without any specific intervention.

Discussion

Meningiomas are common primary tumors of the central nervous system, accounting for approximately 36.4% of cases, with the majority being benign [1]. Meningiomas originate from arachnoidal cap cells located on the inner surface of the dura mater and can occur within the cranium or on the surface of the spinal dura mater, occasionally presenting in the ventricles or extracranial organs. Risk factors for the development of meningiomas include cranial irradiation, while other less defined factors encompass sex, hormones, smoking, diabetes, hypertension, and mobile phone usage [4].

The WHO currently classifies 15 subtypes of meningiomas into three grades of malignancy: grade 1, grade 2 (atypical), and grade 3 (anaplastic). Between 2004 and 2010, the proportions of WHO grade 1, 2, and 3 meningiomas were 94.6%, 4.2%, and 1.2%, respectively [5]. Among these, WHO Grade 1 meningiomas are benign and include nine pathological types: meningothelial, fibrous, transitional, psammomatous, angiomatous, microcystic, secretory, lymphoplasmacyte-rich, and metaplastic meningiomas. WHO grade 2 meningiomas are atypical,

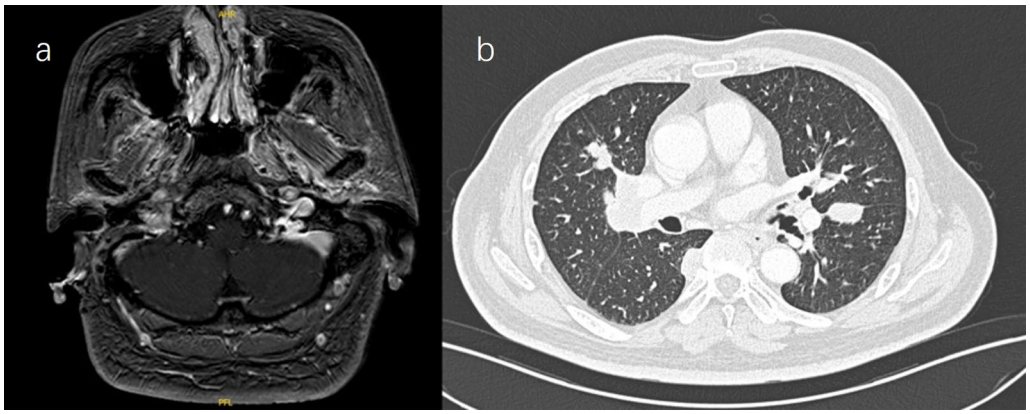

Fig. 4 Magnetic resonance imaging reveals stable lesions at the apex of the petrous part of the temporal bone (**a**); thoracic computed tomography imaging indicates multiple bilateral pulmonary nodules with increased size (**b**)

chordoid, or clear cell, and WHO grade 3 meningiomas are anaplastic [6]. The criteria defining atypical or anaplastic (i.e., grade 2 and 3) meningioma should be applied regardless of the underlying subtype. In the 2021 5th edition of the WHO Classification of Tumors of the Central Nervous System, the diagnostic criteria for WHO grade 2 meningiomas are as follows (meeting any one of the criteria is sufficient for diagnosis): (1) 4–19 mitotic figures in ten consecutive HPF of each 0.16 mm^2, (2) unequivocal brain invasion (not only perivascular spread or indentation of brain without pial breach), (3) specific morphological subtype (chordoid or clear cell), (4) at least three of the following: increased cellularity, small cells with high N:C ratio, prominent nucleoli, sheeting, foci of spontaneous necrosis. The diagnostic criteria for WHO grade 3 meningiomas include (meeting any one of the criteria is sufficient for diagnosis): (1) 20 or more mitotic figures per ten HPF, (2) pronounced anaplastic features (sarcomatous, carcinomatous, or melanotic appearances), (3) *TERT* promoter mutation, (4) homozygous deletion of *CDKN2A* and/or *CDKN2B* [7]. WHO grade 2 and 3 meningiomas exhibit a certain degree of invasiveness, with a propensity for recurrence and progression. The 5-year recurrence rates for grade 2 and 3 meningiomas are approximately 50% and 90%, respectively, with overall 10-year survival rates of 53% for grade 2 and 0% for grade 3 [8].

Meningiomas primarily occur intracranially, with a rare subset manifesting extracranially, accounting for less than 2% of cases. The symptoms are predominantly related to the affected area. Among these, the scalp is the most common site, with an incidence of 40.4%, followed by the ear and temporal bone at 26%, and the nasal cavity at 24%. Histologically, the majority of meningiomas are of the meningothelial type (77.4%), followed by atypical (7.5%), psammomatous (4.1%), and transitional (2.7%) variants. Notably, nearly all (95%) meningiomas of the ear and temporal bone are meningothelial in nature [3]. In the case presented, the meningioma was located at the right petrous apex and jugular foramen, which is an uncommon site for occurrence. The pathology confirmed a meningothelial meningioma, aligning with the common type found in the ear and temporal bone region.

Meningiomas rarely metastasize, with an incidence of less than 0.1% [2]. The majority of cases with metastasis are classified as WHO grade 2 or 3 meningiomas, and the pathways of metastasis include cerebrospinal fluid dissemination, hematogenous spread, or lymphatic migration. Grade 1 meningiomas seldom exhibit metastasis, with only a few individual cases reported. Daniel [9] documented a case of a patient with a WHO grade 1 meningioma who developed synchronous pulmonary metastasis, while Asioli [10] reported a patient with psammomatous meningioma who, 12 years post-resection of the primary intracranial lesion, presented with multiple pulmonary metastases. Other metastatic sites include the liver, lymph nodes, and bones, with less frequent occurrences in the kidneys, thyroid, and adrenal glands. Delgado-Lopez [11] described a case of transitional meningioma with bone metastasis occurring 8 years after intracranial surgery, and Cerda-Nicolas [12] reported a case of fibrous meningioma with multiple metastases to the lungs, liver, spleen, and kidneys. The aforementioned cases represent instances of benign meningiomas that metastasized, a rare occurrence. This paper discusses a case of pulmonary metastasis from a WHO grade 1 meningioma, which is also quite uncommon. In this case, the benign meningioma exhibited malignant behavior. We analyzed the patient's pathological results and genetic sequencing, identifying several adverse prognostic factors. The Ki-67 labeling index, indicative of proliferating cells and associated with the risk of recurrence

in neurotumors, was found to be 10% and 15% in different sampled tissues from the patient. Research conducted by Miriam *et al*. has demonstrated that each additional percentage point increase in Ki-67 is associated with a 12% heightened risk of recurrence. The critical threshold for Ki-67 is established at 4%; patients with meningiomas exhibiting Ki-67 levels below 4% have a median recurrence time of 4.8 years, whereas those with higher Ki-67 levels experience recurrence within a shorter interval of 0.60–0.75 years [13]. The presence of *BAP1* mutations, pertaining to the breast cancer-associated protein 1-a tumor suppressor gene-indicates inactivation through extensive genomic aberrations, including deletions spanning entire exons or larger genomic regions, and is commonly associated with tumor metastasis and poor prognosis. *BAP1* gene mutations are frequently observed in clear cell renal carcinoma, liver cancer, and melanoma. Recent findings have also identified *BAP1* mutations in patients with rhabdoid and papillary meningiomas. This paper represents the first report of *BAP1* gene mutations in benign meningiomas [14, 15]. In summary, the presence of *BAP1* mutations and elevated Ki-67 levels in the patient suggest an unfavorable prognosis. However, whether these factors are associated with metastasis remains inconclusive.

Incidentally discovered asymptomatic meningiomas may be subject to follow-up observation. For patients with tumor progression or symptomatic presentation, surgical resection remains the standard treatment approach. The risk of recurrence following complete resection of WHO grade 1 meningiomas is low, and postoperative radiotherapy is generally not required; however, if recurrence occurs postoperatively or if the resection is incomplete, radiotherapy is necessary. Regardless of the completeness of resection, postoperative radiotherapy is recommended for grade 2 and 3 meningiomas [6]. Postoperative radiotherapy is an effective treatment modality for controlling residual tumors. Condra *et al*. reported that the 15-year local control rate for patients with benign meningiomas who underwent subtotal resection and did not receive radiotherapy was 30%, compared with 87% for those who received postoperative radiotherapy ($P=0.0001$). The disease-specific survival rate was 57% for the non-radiotherapy group and 86% for the radiotherapy group. After complete resection of meningiomas, the 15-year local control rate was 76%, with a disease-specific survival rate of 88% [16]. Gudjonsson reported 19 patients with skull base WHO grade 1 meningiomas involving neurovascular structures deemed inoperable, who underwent stereotactic body radiotherapy (SBRT) with a dose of 24 Gy in 4 fractions. With a minimum follow-up of 36 months, no tumor progression was observed [17]. Proton therapy is also a viable treatment option for meningiomas; in a study of 16 patients with untreated, recurrent, or residual meningiomas, the 3-year progression-free survival rate exceeded 90% following proton therapy, indicating a safe and effective treatment [18]. For this patient in the report, the initial surgery did not achieve complete resection, and no postoperative radiotherapy was administered, leading to tumor recurrence 6 months postsurgery. Given the complexity of the tumor's location, adjacent to the external auditory canal and blood vessels, the second surgery resulted in a subtotal resection. Postoperative precision radiotherapy was administered, and to date, the tumor has remained stable without any signs of recurrence.

Meningiomas lack effective pharmacological treatments, and chemotherapy has limited efficacy, with no recommended systemic therapy currently endorsed. In recent years, checkpoint inhibitors and other forms of immunotherapy have emerged as potential treatment options. The expression of PD-L1(Programmed cell death-ligand 1) may indicate the potential efficacy of immune checkpoint inhibitor therapy. Nidamanuri [19] conducted a retrospective analysis of eight patients with grade 2 and 3 meningiomas treated with anti-PD-1 therapy, reporting a median progression-free survival (PFS) of 7 months and a median overall survival (OS) of 1.75 years. Notably, patients with positive PD-1/PD-L1 expression had a median PFS of 2 years and a median OS of 3 years. Current clinical trials are exploring immunotherapy in patients with high-grade meningiomas. A single-arm, open-label, phase II trial (NCT03279692) reported outcomes for 25 patients with recurrent or progressive grade 2 and 3 meningiomas treated with the PD-1 inhibitor pembrolizumab, showing a 6-month progression-free survival rate of 48% and a median PFS of 7.6 months [20]. Another phase II clinical trial using nivolumab in patients with recurrent grade 2 and 3 meningiomas postsurgery and radiotherapy found a 6-month progression-free survival rate of 42.4% and a median survival of 30.9 months [21]. In the present case, the patient exhibited an increasing trend in pulmonary metastatic lesions and positive PD-L1 expression, suggesting that targeted or immunotherapy could be considered to control disease progression on the basis of the patient's condition.

Conclusion

In this case report, the patient presented with a WHO grade 1 meningioma originating at the petrous apex of the temporal bone, a rare extracranial manifestation. The meningioma was classified as benign; however, it displayed pulmonary metastasis, which is an exceptionally rare occurrence. Pathological examination of the patient showed low mitotic figures, which did not meet the criteria

for diagnosing high-grade gliomas. Nonetheless, the elevated Ki-67 proliferation index and the presence of a *BAP1* gene mutation may suggest a possible association with tumor recurrence and metastasis. The treatment course indicates that post-subtotal resection radiotherapy can reduce the risk of meningioma recurrence. For pulmonary metastatic lesions, regular follow-up is recommended, and local radiotherapy may be considered when necessary. Targeted therapy and immunotherapy also represent potential treatment options for the patient in the future. Through the reporting of this case a review of the relevant literature, we aim to contribute to the diagnostic and therapeutic understanding of this disease, potentially helping in the management of similar conditions.

Abbreviations

WHO	World Health Organization
HPF	High-power fields
CTV	Clinical target volume
PTV	Planning target volume
VMAT	Volumetric Modulated Arc Therapy
BAP1	Breast cancer-associated protein 1
PD-L1	Programmed cell death-ligand 1
PFS	Progression-free survival
OS	Overall survival

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Declarations

Ethical approval and consent to participate
Individual case reports do not require approval from the institutional review board. The patient provided informed consent for the publication of this case report and accompanying figures.

Consent for publication
Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests
The authors declare no competing interests.

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