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CASE REPORT

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Diffuse pleural metastasis from atypical meningioma

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Abstract

Meningioma is the most common benign primary brain tumour and does not usually metastasise. We report the case of a 69-year-old male patient with a history of meningioma who presented respiratory symptoms. He was found to have diffuse pleural metastasis from meningioma, which occurred 10 years after surgical management of recurrent meningioma. This case study provides insights into the clinical profile, workup and management of metastatic meningioma.

KEYWORDS
imatinib, meningioma, pleural metastasis

INTRODUCTION

Meningiomas are the most common primary neoplasms of the central nervous system. In the most current update of the WHO Classification of Central Nervous Tumours in 2021, meningiomas are categorized into grades I–III based on a combination of genetic features, such as homozygous deletions of CDKN2A/2B or telomerase reverse transcriptase (TERT) promoter mutations, *NF2* mutation and histopathological features, such as the number of mitotic figures, invasive growth pattern and anaplastic features. Grade I is the most common grade, and it typically has a benign course. Grade II is atypical, and grade III anaplastic meningiomas are types of high-grade meningiomas.[1] Less than 1 in 1000 meningioma patients develop metastatic meningiomas, with metastases occurring in less than 0.1% of individuals. When they do occur, they do so primarily in the lungs, liver, lymph nodes and bones.[2] Pleural metastasis from meningioma is rare.[3,4] This study reports the case of a 69-year-old male patient with diffuse pleural metastasis from recurrent intracranial meningioma managed with imatinib.

CASE REPORT

In 2008, a 54-year-old male was diagnosed with left frontal meningioma, underwent surgery and was subsequently followed up with. In April 2013, he suffered from headaches and seizures, and a computed tomography (CT) scan showed a well-defined contrast-enhancing left frontal parasagittal lesion (3.9 × 3 × 2 cm), suggesting recurrence. The patient underwent left frontal craniotomy and excision of the lesion. On the second postoperative day, the patient developed right-sided limb weakness. A repeat CT scan showed the total excision of the lesion with oedema and haematoma in the left frontoparietal region, and the patient's condition improved with medical management. However, a histopathological examination suggested atypical meningioma. The patient was advised to undergo local radiotherapy but was lost during the follow-up period.

In June 2023, 10 years after the second surgery, the patient reported exertional breathlessness, diffuse chest pain, intermittent coughing and left exudative pleural effusion. Anti-tuberculosis medication was initiated because the results of pleural fluid cytology, thoracoscopy and biopsy

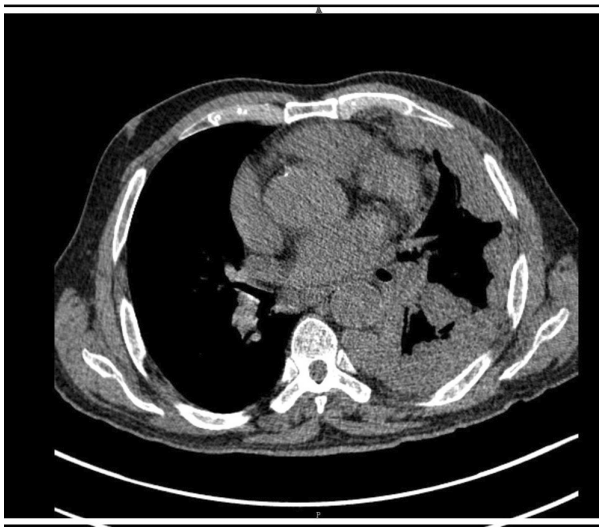

FIGURE 1 Chest computed tomography showing left lower lobe collapse and multiple pleural-based nodules, along with a few subcarinal and right paratracheal nodes.

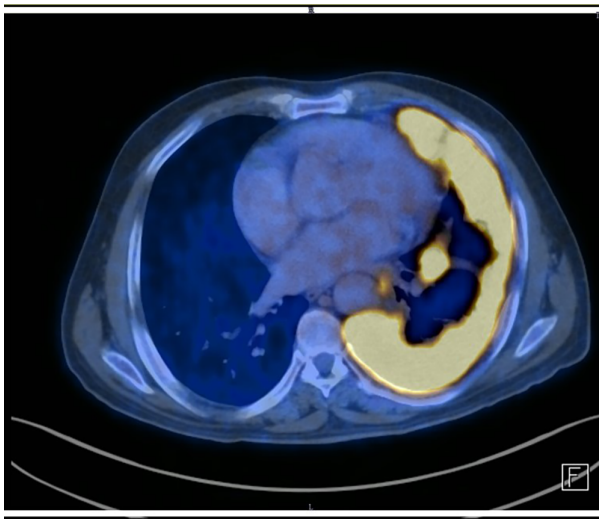

FIGURE 2 FGD PET scan showing metabolically active nodular thickening in left costal, diaphragmatic, peri-fissural and mediastinal pleura.

were inconclusive. However, no improvements were observed. Chest CT was performed in September 2023 and revealed left-sided pleural effusion, left lower lobe collapse and multiple pleural-based nodules, along with a few subcarinal and right paratracheal nodes (Figure 1).

A whole-body FDG (flurodeoxy glucose)PET(positron emission tomography)/CT scan showed metabolically active nodular thickening in the left costal, diaphragmatic, perifissural and mediastinal pleura and pericardial infiltration, indicating primary pleural malignancy (Figure 2).

Repeat pleural fluid cytology yielded inconclusive outcomes, and a thoracoscopic pleural biopsy was performed. Thyroid transcription factor (TTF1) and calretinin were

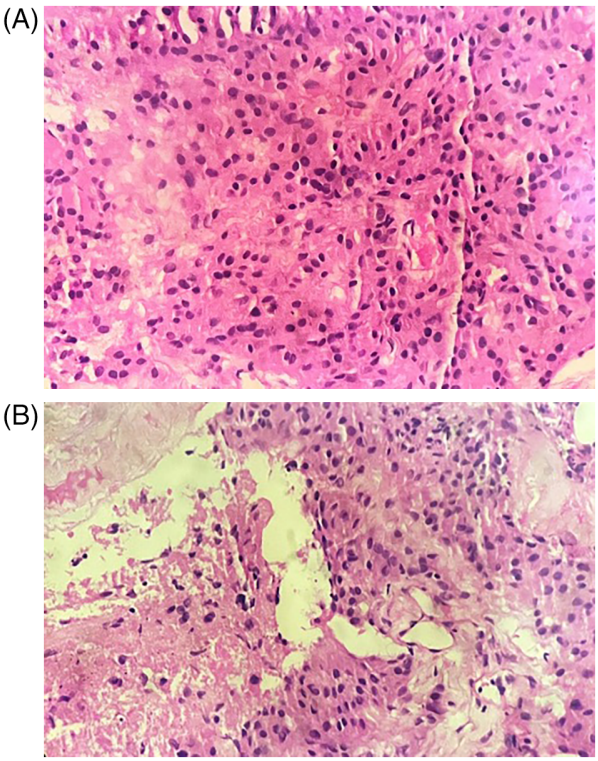

FIGURE 3 (A) Diffuse arrangement of cells having indistinct cell borders, eosinophilic cytoplasm, ovoid nuclei and dense chromatin (H&E, 400×). (B) Tumour with necrosis areas (H&E, 400×).

negative, excluding primary lung carcinoma and mesothelioma, with a Ki 67 labelling index of 7%. Epithelial membrane antigen (EMA) and progesterone receptor (PR) was positive. These findings were suggestive of metastases from meningioma (Figures 3 and 4). Next-generation sequencing involving a 590-gene panel revealed a TERT mutation. After discussing various treatment options, the patient was initiated on imatinib and has tolerated it well. He was doing well during the last 3 months of follow-up.

DISCUSSION

Meningiomas are slow-growing primary brain tumours with a growth rate of less than 1 cm/year. Most meningiomas are benign with a five-year recurrence rate of 3%. Less than 0.1% of patients may develop metastatic disease, with the lungs, liver, lymph nodes and bones being the most prevalent sites.[5] Meningiomas originate from arachnoid cells and are likely to spread to the lungs via microembolisation. However, the exact mechanisms of pleural metastasis remain unclear, as very few cases have been reported.[6] Large cerebral tumours are often linked to metastases, while atypical and anaplastic meningiomas can have a 5%–30% chance of metastases.[7–9]

Demographic factors such as old age, male sex and non-Hispanic white race are linked to worse prognosis in metastatic meningiomas.[10] Studies have also shown a link

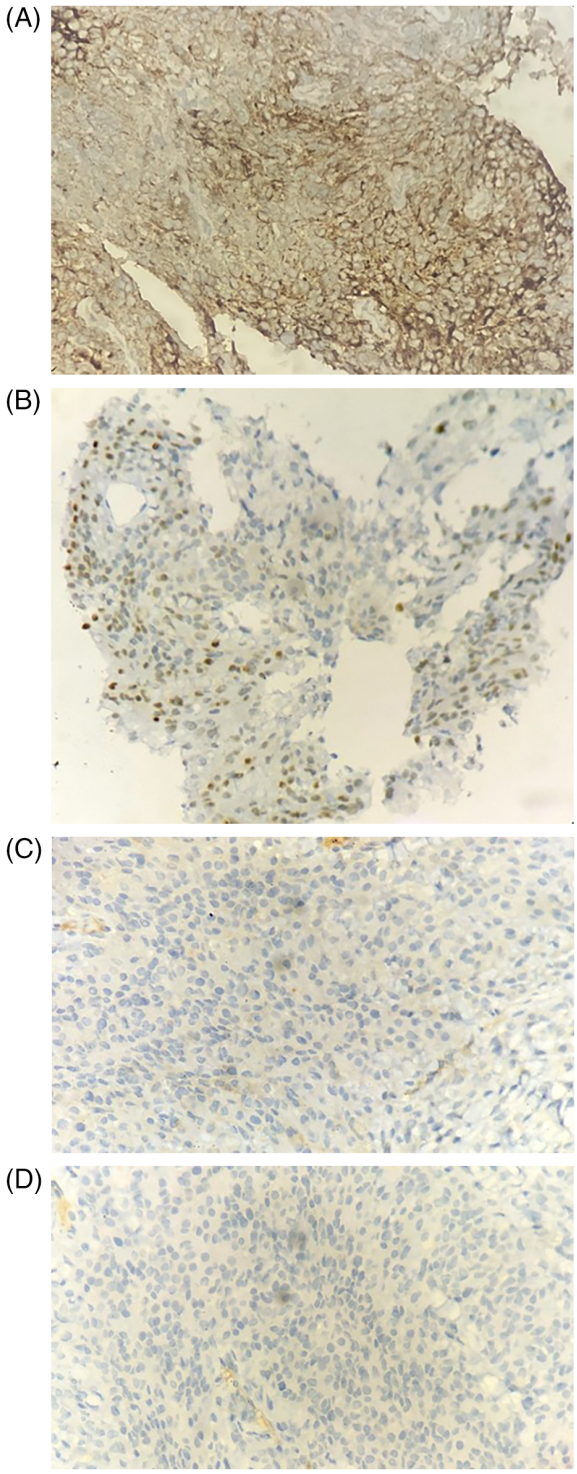

FIGURE 4 (A) Immunohistochemistry for epithelial membrane antigen (EMA) showing membranous positivity in tumour cells, positivity 400×. (B) Immunohistochemistry for progesterone receptor (PR) showing focal nuclear positivity in tumour cells, 400×. (C) Immunohistochemistry for calretinin, which was negative in tumour cells, 400×. (D) Immunohistochemistry for TTF1, which was negative in tumour cells, 400×.

between the tumour site and metastasis; however, lung metastasis from intracranial meningioma is rare. In 1938, Cushing et al. reported a case of lung metastasis from recurrent meningioma.[11] Meanwhile, Enam et al. found that the lung (60%) is the most common extracranial location for intracranial meningioma metastasis,[9,12] whereas Rhim J et al. found these to be rare in Asian populations.[13]

The present study reports a rare case of meningioma with lymph node and pleural metastases, confirmed by histopathological examination and immunohistochemical findings (EMA and PR positive).[14] A TERT promoter mutation was identified, which is relatively uncommon in meningiomas, with a frequency of 6.4%.[15] TERT promoter mutation positivity upgrades the tumour to WHO grade III and could predict the disease's prognosis and the likelihood of recurrence.[16–18]

The management options of recurrent meningiomas after radiation therapy and surgery is limited. The role of systemic treatment for meningiomas is also very limited, and the use of chemotherapeutic drugs has been unsuccessful.[1] Pleural metastatic meningiomas are rare, and there are no specific treatment guidelines for treating them. Surgical resection of pleural metastases from meningiomas has been reported in only a few cases,[19] and few patients have undergone surgery followed by adjuvant radiation and chemotherapy.[3,20] Meningiomas express high levels of hormone receptors, but antiestrogen and progesterone drugs are ineffective in hormonal therapy. Some patients respond to hydroxyurea and recombinant interferon-alpha2b.[17]

Tyrosine kinase inhibitors and monoclonal antibodies targeting angiogenic signalling have shown promising antitumour activity in phase II trials. Novel insights into the (epi-) genetic alterations in meningioma have led to the identification of potential therapeutic targets that are currently under investigation. These include phosphoinositide-3-kinase, focal adhesion kinase, cyclin-dependent kinases, inhibitors of the mammalian target of rapamycin, sonic hedgehog signalling and histone deacetylases.[1] Moreover, imatinib, a tyrosine kinase inhibitor, showed good disease stabilization in a retrospective analysis of the treatment of recurrent meningiomas.[21] However, a phase II study by the North American Brain Tumour Consortium showed that it had low effectiveness.[18]

In conclusion, this case study highlights the rare occurrence of pleural metastasis from meningioma, presenting 10 years of post-surgical management of recurrent meningioma. Although meningiomas are predominantly benign and seldom metastasise, this case emphasizes the importance of conducting long-term follow-ups for patients with a history of meningioma, especially those with a recurrent disease. The presentation of respiratory symptoms in such patients should prompt a thorough investigation into potential metastatic spread. This case also highlights the need for a comprehensive clinical workup and tailored management strategies for metastatic meningioma.

AUTHOR CONTRIBUTIONS

Alma Rose Devasia, Surya Krishnan, S, Swathi Krishna: Study concepts, study design, data acquisition, data analysis and interpretation, manuscript preparation, manuscript editing. **Aravind Perathur and Jyotsna Yesodharan**: Study

concepts, study design, manuscript editing. **Keechilat Pavithran**: Study concepts, study design, data analysis interpretation, manuscript editing, manuscript approval.

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CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY STATEMENT

Not applicable.

ETHICS STATEMENT

The authors declare that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

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