Unusual association of diseases/symptoms

An elusive cause of pleural effusion

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Summary

A 32-year-old man was admitted with cerebrospinal fluid leakage from a right scalp surgical wound after a resection of recurrent meningioma and reconstruction of skull with muscle flap 3 weeks earlier. On day 4 of admission, he was found to be tachycardic and decreased breath sounds on the right side. Chest x-ray revealed a large right pleural effusion which was found to be exudative after thoracentesis. Infectious work-up and cytology was negative. CT showed both parietal and visceral pleural masses, which was consistent with meningioma on ultrasound-guided biopsy. He underwent right-side decortication and pleurodesis for recurrent pleural effusion. He declined further treatment and opted for hospice care and expired a month later.

BACKGROUND

Meningiomas are usually benign but sometimes atypical meningioma has a metastatic potential. Exudative pleural effusion as a manifestation of metastatic intracranial meningioma is rare.

CASE PRESENTATION

A 32-year-old man was admitted with cerebrospinal fluid (CSF) leakage from a right scalp surgical wound after a resection of recurrent meningioma and reconstruction of skull with muscle flap 3 weeks earlier. His medical history was significant for acute lymphoblastic lymphoma at age 3 for which he underwent cranial radiation. He was diagnosed with meningioma, 6 years prior to this presentation. He has had multiple resections, cyberknife therapies and various chemotherapy treatments for recurrences of intracranial meningioma. Medicine consultation was requested for tachycardia on day 4 since admission.

The patient had no chest pain, cough, fever or shortness of breath. His blood pressure was 110/50 mm Hg, pulse of 110/min, regular, with oxygen saturation of 93% on room air. Physical examination revealed decreased breath sounds on the right side. There was no evidence of peripheral oedema or calves tenderness.

INVESTIGATIONS

Initial haemogram and serum chemistry were normal. ECG revealed sinus tachycardia, while chest x-ray was notable for a large right pleural effusion (figure 1). Ultrasound duplex of lower extremities was normal. The pleural effusion was new and was not evident on a previous chest x-ray performed 3 weeks earlier. A litre of straw colour fluid was drained through a thoracentesis. Pleural fluid was remarkable for 319 nucleated cells/ μ l with 63% polymorphonuclear leucocytes, lactate dehydrogenase of 2530 μ /l and total protein of 3.4 g/dl suggestive of an exudative effusion. Pleural fluid gram stain and cultures were non-revealing and cytology was negative for malignant cells. A CT of the chest was done for further evaluation of rapidly reaccumulating pleural effusion. In

addition to a large right pleural effusion with atelectasis, a confluent mass involving both parietal and visceral pleura was seen (figure 2). There were no lung masses other than an indeterminate (2.8 $\times$ 5 mm) left upper lobe nodule. Ultrasound-guided biopsy of the pleural mass was consistent with meningioma with 5–15 mitoses/10 high-power field (hpf) (WHO grade 2; figures 3 and 4).

TREATMENT

Incidentally found meningiomas that are asymptomatic and small can usually be followed up clinically and with serial imaging studies. Alternatively, symptomatic or enlarging meningiomas warrant surgical resection if feasible. When complete resection is achievable and histology is consistent with WHO grade 1, adjuvant radiation therapy (RT) is not indicated. RT is indicated when a complete resection cannot be performed without causing significant neurological deficits due to its location.¹ Atypical meningiomas (WHO grades 2 and 3) have a higher chance of recurrence even after complete surgical

Figure 1 Chest x-ray showing large right pleural effusion.

Figure 2 CT of chest showing parietal (lower arrowhead) and visceral (upper arrowhead) pleural soft tissue mass.

resection and therefore adjuvant RT may be indicated.^{2 3} When tumours are located close to important neurological structures and surgery may result in significant neurological deficits then stereotactic radiosurgery and stereotactic radiotherapy may be helpful.

Atypical meningiomas may recur even after surgical resection and adjuvant radiotherapy. In this subset of patients, additional chemotherapy may be tried although there is no consensus on the regimen. Inhibitor of growth factors, angiogenesis and hormonal influences are being studied using different regimen in separate clinical trials. Imatinib (inhibitor of platelet-derived growth factor), bevacizumab (inhibitor of vascular endothelial growth factor and therefore angiogenesis), somatostatin analogues are being studied.¹ Travitzky *et al*⁴ described a case where they had success with doxil (pegylated liposomal form of doxorubicin) in the treatment of pleuropulmonary metastases from a cranial meningioma.

Figure 3 Histology of pleural mass showing mitoses.

Figure 4 Histology of pleural mass showing necrosis.

OUTCOME AND FOLLOW-UP

Since the initial diagnosis of intracranial meningioma, the patient had failed multiple chemotherapy regimens including temozolomide, sorafenib, for his recurrent aggressive tumour. During this admission, the patient's hospital course was however complicated by acute renal failure, secondary to non-steroidal anti-inflammatory drugs, requiring haemodialysis. Due to renal insufficiency and recent surgical scalp wound, the patient was not felt to be a candidate for further chemotherapy treatment with monoclonal antibody such as bevacizumab, an inhibitor of vascular endothelial growth factor. Given the rapid reaccumulation of his pleural effusion, patient underwent decortication of his lung and talc pleurodesis. The patient had declined further chemotherapy and opted for hospice care and expired a month later.

DISCUSSION

Meningiomas are tumours arising from arachnoid cells, usually benign, and mainly located in the central nervous system. They are typically slow-growing tumours and are thus 'perceived' as benign. Metastatic meningiomas have been reported as low as 0.1%.⁵ The most common site of metastatic spread is lung followed by abdominal viscera, lymph node and bones.^{5 6} Exudative pleural effusion as a primary manifestation of metastatic intracranial meningioma has rarely been reported.^{7 8}

Intracranial radiation has been associated with a four-fold increase in the development of meningioma.⁹ Our patient was diagnosed with symptomatic meningioma at the age of 26 (23 years after been exposed to radiation). Rubinstein *et al*⁹, in their analysis of 201 patients, found that meningiomas arising as a result of exposure to intracranial radiation are usually located in the parafalcine/vertex area rather than at the skull bases similar to our patient. Whether meningiomas related to radiation are associated with higher risk of metastatic spread is unclear. Manipulation of meningiomas (from multiple surgeries for recurrence), venous sinus invasion, WHO grade 2 (atypical) or 3 (anaplastic) histology, have higher predilection for metastatic spread.^{10 11} WHO grade 2 are histologically atypical and have ≥ 4 mitotic cells/10 hpf, whereas WHO grade 3 have ≥ 20 mitotic cells/10 hpf with cytological evidence of malignancy.¹² Meningiomas may

metastasise through various routes: haematogenous, lymphatic and direct extension. There have also been reports of metastatic spread via CSF pathways.¹³ In patients with aggressive meningiomas, manipulation of tumour during surgery and invasion of venous sinuses, haematogenous spread is common.

Although primary pulmonary meningiomas arising from ectopic arachnoid cells in the lung have been reported, our patient's atypical features on histology coupled with the aggressive nature of his meningioma requiring numerous surgical interventions probably led to the haematogenous metastatic spread to the pleural cavity.^{14 15}

Given our patient's history of atypical (WHO grade 2) intracranial meningioma and unexplained exudative pleural effusion, cytology on pleural fluid was analysed twice with no yield. CT of chest showed predominant extensive pleural (visceral>parietal) masses. Despite this widespread pleural involvement, pleural fluid cytology was unrevealing. Ultrasound-guided biopsy of the pleural masses was consistent with metastatic meningioma (WHO grade 2).

Learning points

- Although uncommon, physicians should be aware of the metastatic potential of intracranial meningioma, especially in the setting of recurrent meningioma or WHO grade 2 or 3 histology.

Competing interests None.

Patient consent Obtained.

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