

## Mesothelioma Metastasising to The Sciatic Nerve

### Dear Editor,

Malignant mesothelioma (MME) is a rare primary neoplasm affecting the serosal membranes.<sup>1</sup> Epidemiological studies have shown that incidence in many Western countries has increased by as much as 50% since the 1970s.<sup>2</sup> MME related to asbestosis was first recognised in the 1870s. A report by Wagner et al<sup>3</sup> found a link between asbestos exposure and MME in a study of workers at a crocidolite mining area in South Africa. Wives of asbestos workers are also known to develop MME after being in contact with contaminated clothing.<sup>3</sup>

MME typically spreads locally and areas of local spread include lung, heart, pericardium, chest wall and vertebrae.<sup>4</sup> Distant metastases are uncommon and documented areas include brain, spleen, bone marrow, prostate, thyroid, orbit, uterus, pelvis, tonsil, tongue and mandibular alveolus.<sup>4</sup>

MME with direct spread to the adjacent nervous system is extremely rare,<sup>5</sup> with several cases of MME spreading along nerve roots and intradurally reported.<sup>5</sup> To the best of our knowledge, there has been no report of mesothelioma metastatic to the sciatic nerve.

### Case report

A 56-year-old Malay female non-smoker who worked in an electronics factory first presented with atypical right chest discomfort and dyspnea in August 2000. Her mother passed away from suspected mesothelioma. Her father was believed to have had occupational exposure to asbestos. Physical examination was normal except for mildly reduced breath sounds over the right lung base. Her chest radiograph and CT (computed tomography) thorax scan revealed a right pleural effusion with no pleural nodularity or mediastinal lymphadenopathy. Pleural fluid cytology and pleural biopsy were non-conclusive for malignancy. The patient subsequently underwent video assisted thoracoscopic (VATS) pleural biopsy and pleurectomy. Histology showed “non-specific inflammation with mesothelial hyperplasia” with recommendation for continued clinical follow-up. She had several follow-up CT thorax scans up to 2005 which repeatedly showed a stable but persistent right pleural effusion.

The patient remained symptom-free for 8 years until she presented again in December 2009 with weight loss of 6 kg over the past year. A contrast enhanced CT thorax scan showed a loculated pleural effusion encasing most of the right hemithorax with medial extension to the azygo-

oesophageal recess (Figs. 1A and 1B). There was resultant volume loss in the right lung. There were nodular, solid, pleural-based components within the right pleural effusion; the largest lesion measuring 20 mm in thickness. The nodular lesions were hypodense and did not show enhancement. The inferior vena cava was displaced anteriorly and the oesophagus to the left by the pleural effusion. There were also several enlarged right hilar nodes with central hypodensity, indicative of necrosis. Background lung changes of fibrosis in the middle and lower lobes and tiny subpleural opacities were also noted. Incidentally, there were several hypodense, lobulated soft tissue masses within the left sciatic nerve extending via the greater sciatic foramen (Figs. 2A and 2B). Our patient did not have any neurological complaints related to the left sciatic nerve.

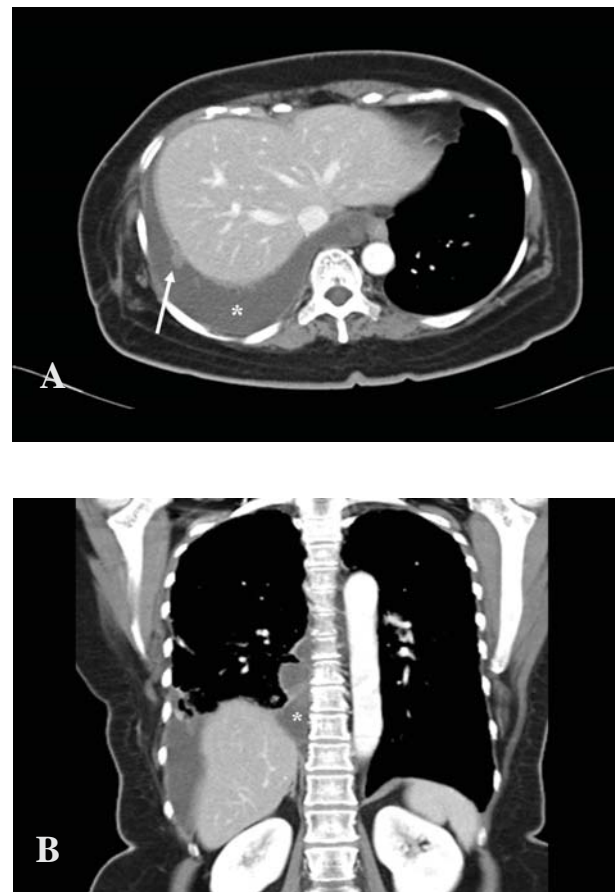


Fig. 1. A 56-year-old woman with malignant mesothelioma. (A) Contrast enhanced axial CT image shows a loculated right pleural effusion (\*) with pleural nodularity (arrow). (B) Contrast enhanced coronal CT image shows a loculated pleural effusion (\*) with encasement of the lower right hemithorax.



Fig. 2. (A) Contrast enhanced axial CT image shows nodular thickening of the left sciatic nerve (arrow). (B) Contrast enhanced coronal CT image shows nodular thickening of the left sciatic nerve, exiting the greater sciatic foramen (arrow).

The patient underwent endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) of the periesophageal cystic collection and a subcarinal lymph node. Papillary groups of atypical mesothelial cells were seen in the pleural fluid (Fig. 3). CT guided biopsy of the left sciatic nerve mass showed a group of atypical mesothelial cells which were similar to those seen in the pleural fluid sample (Fig. 4). These cells showed positive staining with calretinin, WT-1 and CK5/6; consistent with epithelioid malignant mesothelioma.<sup>6,7</sup>

The patient was referred to medical oncology and started receiving chemotherapy since January 2010. She was treated with a combined chemotherapeutic regime consisting of pemetrexed, cisplatin, aprepitant and dexamethasone for 7 months and was started on a new regime of carboplatin, gemcitabine and dexamethasone for the past 1 month. The patient had been receiving the medications on an outpatient basis and did not require any hospitalisation since the initial diagnosis was made.

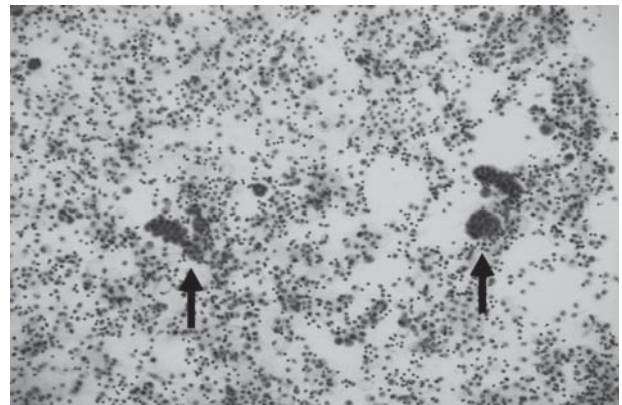


Fig. 3. Pleural fluid obtained via endoscopic ultrasound. Original magnification x 400, Papanicolaou stain. Papillary groups of atypical mesothelial cells are seen (arrowed).

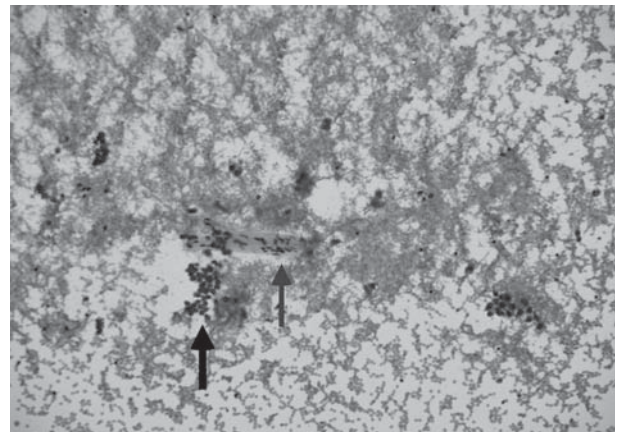


Fig. 4. Fine needle aspiration of left sciatic nerve mass. Original magnification x 400, Papanicolaou stain. The darker (larger) arrow shows a group of atypical mesothelial cells similar to those seen in the pleural fluid sample. The lighter (smaller) arrow shows a small nerve twig, confirming site of sampling.

## Discussion

Malignant mesothelioma (MME) is a rare primary neoplasm. It arises in the parietal or visceral pleura and less commonly in the peritoneum and pericardium. MME usually occurs in individuals who have occupational exposure to asbestos but it is occasionally seen in others who live in close proximity to an asbestos factory or have relatives who work with asbestos.<sup>8</sup> A long latent period of 25 to 40 years after asbestos exposure is often needed before the development of MME. This suggests multiple somatic genetic events are needed for carcinogenesis of mesothelial cells.<sup>8</sup> MME is often preceded by widespread pleural fibrosis and plaque formation.<sup>8</sup> In this case, our patient had developed a pleural effusion 9 years prior to

the histological diagnosis of MME.

MME patients most commonly present with non-pleuritic chest pain and dyspnoea. Other presentations include clubbing, pleural thickening and pleural effusion on screening chest radiographs. Thoracentesis and pleural biopsy are often inadequate to differentiate adenocarcinoma from MME. Video-assisted thoroscopic (VATS) pleural biopsy is currently the recommended diagnostic tool.<sup>3</sup> Routine chest radiographs and CT thorax scans usually show pleural effusions or pleural-based masses, with right-sided lesions being more common.<sup>3</sup> Chest CT is optimal for assessment of disease extent.<sup>3</sup>

MME is difficult to differentiate pathologically from adenocarcinoma and cytology can mimic benign reactive mesothelial cells. Histochemical analysis becomes important in diagnosis.<sup>3</sup> There are 3 histologic types of MME, namely, epithelial, sarcomatous and mixed (biphasic).<sup>1</sup> The epithelial type is the commonest (60%) and the biphasic type is the least common (25%).<sup>6</sup> Immunohistochemical markers are relatively specific for mesothelioma and they include anti-calretinin, anti WT1 and anti-CK 5/6 antibodies which were all seen in our patient.<sup>7</sup>

MME typically spreads locally and distant metastases are very rare.<sup>4</sup> Furthermore, it is extremely unusual for malignant mesothelioma to spread to the nervous system<sup>9-11</sup> and to the best of our knowledge, this is the first reported case of MME metastasising to a distant peripheral nerve. Other sites of MME spread to the nervous system have been reported. The number of histologically proven brain metastases from MME was noted to be 14 by Wrofiski et al<sup>11</sup> in their case report published in 1993. Intradural spinal cord spread of MME was documented by Payer et al<sup>9</sup> in 2007 to be 4 cases after an extensive literature review of English-language journals from 1966 to 2006. All the previously reported cases of intradural spread of MME have occurred in the thoracic spine and they have occurred either via direct extension into the intervertebral foramen or via neurotropic spread along a nerve root into the intradural space. Payer et al<sup>9</sup> made an observation that all 3 patients with MME spread to the intradural spinal cord have a relatively prolonged history of MME before spinal involvement. They have had the disease for 18, 24 and 28 months before the disease was spread to the spinal cord, greater than the reported average survival for MME patients. Although the mechanism of tumour spread is different in the case of our patient, she too had a protracted course of disease. The time lag between her first clinical presentation with symptoms suspicious for MME to the time she was conclusively diagnosed was roughly 8 to 9 years.

Overall, peripheral nerves appear to be relatively resistant to metastatic disease and this has been postulated to be due to structural characteristics of their vasculature.<sup>12</sup>

Primary tumours that have been reported to metastasise to the peripheral nervous system were from breast, pelvic cancers, leukaemias and melanoma.<sup>13</sup> It has also been reported in previous retrospective studies that the prevalence of metastases to the brachial and lumbosacral plexi was 0.43% and 0.71%, respectively.<sup>13</sup>

Since our patient did not have any imaging features of MME spread in the spinal cord or abdomen, we postulate that it was via haematogenous means that the metastasis had reached the sciatic nerve.

There are no prospective trials on treatment of MME metastases to the peripheral nerve or the spinal cord as these cases have been very few. Treatment of intramedullary spinal cord metastases currently depends on expert opinion, case reviews and literature reviews<sup>10</sup> and it follows the treatment pathway for parenchymal brain metastases.<sup>4</sup> In their paper reviewing management of metastatic disease to the peripheral nervous system, Gachiani et al<sup>14</sup> noted that the main symptoms are severe pain and progressive loss of nerve function. They reported that only 46% of patients in one series experienced pain relief after radiotherapy and it was a disappointing outcome.<sup>14</sup> They felt that surgery would be indicated for lesions causing pain, paresthesia, progressive deficit or mass effect.<sup>14</sup> The aim of surgery in these patients would be to decompress the nerves and not so much for total resection.<sup>14</sup> Further treatment with radiotherapy or chemotherapy is best decided on an individual basis, after inputs from the oncologist and radiotherapist. The overall prognosis for these patients was felt to depend on the primary tumour and its control.<sup>14</sup>

MME is an aggressive tumour with an average survival rate of 6 to 13 months and is resistant to current treatment options.<sup>3</sup> The treatment of MME is generally palliative. Treatment modalities currently used are surgery (pleurectomy/decortication), chemotherapy and radiotherapy.<sup>4</sup> Systemic therapy is the only treatment option for most of the patients.<sup>1</sup> Most evaluated chemotherapy drugs achieved response rates below 20% and the median survival is less than 1 year.<sup>1</sup> It has been reported that most patients with intramedullary metastases who underwent resection did not show any neurological improvement.<sup>5</sup>

In our case, the presence of incidental left sciatic nerve masses in a patient with previous mesothelial hyperplasia diagnosed 8 years ago and with a family history of asbestos exposure and mesothelioma raised the rare possibility of MME metastatic to the left sciatic nerve. The immunophenotype for pleural fluid was suspicious but not conclusive for malignant mesothelioma. It was the biopsy results of the left sciatic nerve masses that led to a conclusive diagnosis of metastatic MME for which patient was given appropriate chemotherapy. Her disease has shown radiological stability since chemotherapy.

## Conclusion

In conclusion, this is the first reported case of MME with metastasis to a peripheral nerve. Although MME spread to the nervous system is rare, this is a consideration in patients with a prolonged course of disease, especially if the patient is symptomatic.

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