We describe a case of intraneural metastasis of a synovial sarcoma, the first published case of a metastasis of a soft-tissue sarcoma to a peripheral nerve.

Synovial sarcoma is a high grade malignancy, usually occurring in adolescents and young adults between 15 and 40 years of age. It occurs primarily in the para-articular regions of the extremities, usually in close association to tendon sheaths, bursae, and joint capsules. Metastatic lesions develop in half the cases, most commonly in the lung, followed by the lymph nodes and bone marrow. However, there have been no previous reports of intraneural metastasis of synovial sarcoma to a peripheral nerve.

Case report

In January 2001, a 28-year-old man presented with a mass 10 mm in diameter in the right scapular region. Biopsy revealed a spindle-cell neoplasm growing in a fascicular fashion with the vascular pattern of a haemangiopericytoma suggestive of a monophasic synovial sarcoma. Molecular genetic studies performed on frozen-tissue samples using reverse transcriptase polymerase chain reaction (RT-PCR) showed the fusion transcript for SYT-SSX1, confirming the diagnosis of synovial sarcoma. A CT scan of the chest revealed multiple pulmonary metastases. The diagnosis was monophasic synovial sarcoma, with an American Joint Committee for Cancer Staging System classification of T2b, N0, M1, stage IV. After two cycles of pre-operative chemotherapy, a wide excision of the primary tumour was undertaken. The patient received three cycles of post-operative chemotherapy and underwent excision of left pulmonary metastases five months later. He received a further two cycles of chemotherapy and at follow-up 16 months later complained of the acute onset of severe pain in the dorsolateral aspect of the forearm. He developed a complete high radial nerve palsy within five days of the onset of the pain. There was marked tenderness 7 cm proximal to the lateral humeral epicondyle. No abnormality of the radial nerve in the upper arm was identified on MRI and there were no abnormalities on MRI of the brain and cervical spine.

He underwent exploration of the left radial nerve. A 1.5 cm segment of the nerve at the exit of the spiral groove in the lateral third of the humerus was swollen and grey. Histopathology of frozen sections indicated synovial sarcoma and a wide excision of the nerve was performed. Nerve grafting was not undertaken because of the poor prognosis. Also, the patient had refused nerve grafting as functional recovery would take a long time. At pre-operative counselling, he gave informed consent for...
a functional orthosis for the predicted permanent radial nerve palsy. Macroscopic examination of the excised radial nerve showed that tumour tissue occupied about 4/5 of the cross-section of the nerve, and occupied a 1.8-cm length of the longitudinal section (Fig. 1) and histopathology confirmed an identical appearance to the synovial sarcoma which had originally been removed from the right scapular region (Fig. 2).

Although the intractable neuralgia resolved the patient subsequently died from metastatic pulmonary disease about 18 months later.

Discussion
A common neurological complication in advanced stages of various malignancies is direct invasion of cranial nerves, the epidural space, or spinal nerve roots. However, intraneural metastasis to peripheral nerves is very rare. Eleven cases have been reported (Table I). There have been no reports of intraneural metastasis of synovial sarcoma to a peripheral nerve.

The metastatic process consists of various stages of detachment, migration, arrest in the target organ, formation of micrometastases, and vascular neogenesis leading to overt tumour formation. Why is a metastasis of a tumour to a peripheral nerve so rare? The axonal environment in the endoneurium of the peripheral nervous system is isolated from the general extracellular space of the body by a diffusion barrier called the blood-nerve barrier, which is similar to the blood-brain barrier. The blood-nerve barrier consists of tight and adherence junctions, both between perineural and endothelial cells in the endoneurium.

Table I. Case reports of intraneural metastasis of malignancy to the peripheral nerve of extremities

<table>
<thead>
<tr>
<th>Authors</th>
<th>Gender / age</th>
<th>Location</th>
<th>Diagnosis</th>
<th>Symptom</th>
<th>Utility of images for diagnosis</th>
<th>Treatment</th>
<th>Recovery of palsy</th>
<th>Pain relief</th>
<th>Oncological status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lusk, Kline and Garcia³</td>
<td>F/26</td>
<td>Brachial plexus</td>
<td>Melanoma</td>
<td>Pain</td>
<td>ND</td>
<td>S</td>
<td>ND</td>
<td>N</td>
<td>NED</td>
</tr>
<tr>
<td>van Bolden et al⁴</td>
<td>M/60</td>
<td>Radial nerve</td>
<td>Lymphoma</td>
<td>Palsy</td>
<td>ND</td>
<td>S, RT</td>
<td>N</td>
<td>-</td>
<td>NED</td>
</tr>
<tr>
<td>Artico et al⁵</td>
<td>F/66</td>
<td>Brachial plexus</td>
<td>Breast cancer</td>
<td>Pain, palsy</td>
<td>N</td>
<td>S, C</td>
<td>C</td>
<td>N</td>
<td>NED</td>
</tr>
<tr>
<td>Kline and Hudson⁶</td>
<td>ND</td>
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<td>Melanoma</td>
<td>ND</td>
<td>ND</td>
<td>S, RT</td>
<td>ND</td>
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<td>ND</td>
</tr>
<tr>
<td></td>
<td>ND</td>
<td>Brachial plexus</td>
<td>Melanoma</td>
<td>ND</td>
<td>ND</td>
<td>S, RT</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Meller et al⁷</td>
<td>M/65</td>
<td>Brachial plexus</td>
<td>Laryngeal cancer</td>
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<td>S, C</td>
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</tr>
<tr>
<td></td>
<td>F/42</td>
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<td>Breast cancer</td>
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<td>S, RT</td>
<td>N</td>
<td>Y</td>
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</tr>
<tr>
<td></td>
<td>F/62</td>
<td>Brachial plexus</td>
<td>Breast cancer</td>
<td>Pain, palsy</td>
<td>N</td>
<td>S, C</td>
<td>N</td>
<td>Y</td>
<td>NED</td>
</tr>
<tr>
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<td>F/32</td>
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<td>Y</td>
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<tr>
<td></td>
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<td>Pain, palsy</td>
<td>N</td>
<td>C, RT</td>
<td>N</td>
<td>Y</td>
<td>DOD</td>
</tr>
<tr>
<td>Cantone, Rath and Richter⁸</td>
<td>M/50</td>
<td>Sciatic nerve</td>
<td>Melanoma</td>
<td>Pain, palsy</td>
<td>MRI</td>
<td>S, RT</td>
<td>N</td>
<td>Y</td>
<td>NED</td>
</tr>
</tbody>
</table>

* F, female; M, male
† ND, not determined; N, No; Y, yes
‡ C, chemotherapy; RT, radiotherapy; S, surgery
§ DOD, dead of disease; NED, no evidence of disease

Microscopic finding of a transverse section of the radial nerve. Figure 2a – Low magnification view showing infiltration of synovial cells into endoneurium. Note the intact perineurium (haematoxylin and eosin, x40). Figure 2b – High magnification view showing monophasic synovial sarcoma, identical to the original biopsy (haematoxylin and eosin, x40).
gested that synovial sarcoma cells penetrated the blood-nerve barrier, although the molecular mechanism of this transmigration across the vascular endothelium is obscure.

It is still unclear why the prevalence of metastases to peripheral nerves differs among tumours, most involve carcinoma, and there have been no previous reports of cases involving sarcoma. Modern neuro-imaging techniques have revealed that brain metastases occur in 20% to 35% of patients with primary carcinoma and in 5.6% of patients with sarcoma. However, histological analysis has revealed a high incidence of metastasis to the brain in cases of sarcoma: in all of three angiosarcomas, three of four alveolar soft-tissue sarcomas and four of eight haemangio-pericytomas, all of which had histologically epithelioid features. This indirect clinicopathological evidence could indicate that neural metastasis through the blood-brain barrier or blood-nerve barrier is closely related to the expression of molecules associated with the maintenance of the epithelioid phenotype of the tumour cells.

Surgical exploration is sometimes the only way to arrive at a correct diagnosis of intraneural metastasis because the lesion may be too small to be detected by imaging methods.

In a report of five cases, radiotherapy to the isolated metastasis in a brachial plexus provided good symptomatic relief to all patients and brought about local arrest of the disease in four of the five patients. If an intraneural metastasis is diagnosed by MRI in a patient with a radial nerve palsy, radiotherapy might be an option for treatment. However, in the present case, because a precise diagnosis could not be made, excision was undertaken after obtaining informed consent. It may be that the lesion was too small to be detected by MRI scan. Segmental resection of the involved nerve, followed by nerve grafting if technically possible, may be an alternative option for obtaining relief from pain.

We have described the first published case of metastasis of a synovial sarcoma to a peripheral nerve. The patient had a progressive neural palsy with intractable neuralgia. The possibility of intraneural metastasis should be considered in a patient with a history of sarcoma who has a progressive nerve palsy and intractable pain without evidence of spinal metastasis. We recommend that in patients who have a peripheral neuropathy and a previously identified malignancy, surgical exploration should be considered.

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References