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# Soft Tissue Perineurioma
## – A Case Report –

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Soft tissue perineurioma is a very rare tumor composed of entirely of neoplastic perineurial cells. A 54-year-old woman presented with a palpable mass in the right lower leg. The mass was excised. Grossly, the tumor measured 2.0×2.0×1.5 cm. The cut surface was well circumscribed, pale pinkish gray, and rubbery soft. Histological examination showed that the tumor was composed of spindle cells within collagenous and myxoid stroma. The tumor cells had elongated, tapering nuclei with long and thin cytoplasmic processes, and were arranged in fascicular, whorled, and storiform pattern. The tumor cells were positive for epithelial membrane antigen and collagen type IV and negative for S-100 protein. Ultrastructurally, tumor cells showed long and thin cytoplasmic processes, pinocytic vesicles, and incomplete external lamina. The diagnosis of soft tissue perineurioma was confirmed by immunohistochemical stain and ultrastructural study.

**Key Words :** Perineurioma; Immunohistochemistry; Ultrastructure

Perineuriomas are uncommon benign peripheral nerve sheath tumors that include soft tissue, intranueural, sclerosing and reticular variants.[1-3] Soft tissue perineuriomas were first described in 1978 by Lazarus and Trombetta based on ultrastructural features of perineurial cells in the calf of a 45-year-old male.[4] It accounts for approximately 1% of soft tissue neoplasms.[5] It arises often in middle-aged adults. Females are more frequently affected. Soft tissue perineuriomas are generally found in subcutaneous sites and only infrequently affect deep soft tissues of the extremities or trunk.[6] Soft tissue perineuriomas have been described in the literature.[1,7-11] Recognition of soft tissue perineuriomas is important because it can easily be mistaken for other soft tissue neoplasms. Here, a case of soft tissue perineurioma arising in the right lower leg of a 54-year-old woman is reported.

## CASE REPORT

A 54-year-old woman presented with a palpable mass in the right lower leg. The mass had been present for six months. Her medical history was noncontributory. Physical examination revealed a movable, rubbery soft mass in the anterior side of the right lower leg. Pain and tenderness were absent. Magnetic resonance images showed a soft tissue mass in the lateral subcutaneous layer of the right lower leg (Fig. 1). The mass revealed low signal intensity on the T1-weighted image, high signal intensity on the T2-weighted image, and homogeneous contrast enhancement. Excision of the mass was performed.

Grossly, the mass measured 2.0×2.0×1.5 cm in size (Fig. 2). It was a well-circumscribed, pale pinkish gray, and rubbery soft. On microscopic examination, the mass was composed of spindle-shaped tumor cells. The spindle cells were arranged in fascicular, whorled, and storiform pattern (Fig. 3A, B). The stroma was collagenous and myxoid. The nuclei were elongated, slender, and wavy, with tapered ends (Fig. 3C). The long, thin cytoplasmic processes were present. Mitotic count was 1 per 50 high power fields. Some cells showed ovoid or fusiform nuclei (Fig. 3D). The chromatin was finely dispersed. Small nucleoli were noted. Mast cells were occasionally found. In some areas, nuclear hyperchromasia was seen. No necrosis was present. On the immunohistochemical stain, tumor cells showed positivity for EMA and collagen type IV (Fig. 4). Cytokeratin (AE1/AE3), S-100 protein, smooth muscle actin, and desmin were all negative in the tumor cells. Electron microscopy of the formalin-fixed tumor

was performed. Tumor cells showed long and thin cytoplasmic processes, running in parallel (Fig. 5). Incomplete external lamina and pinocytotic vesicles were occasionally found. The extracellular collagen fibers were present. The tumor was diagnosed soft tissue perineurioma. Twenty-six months after surgery, the patient remains in good health, with no evidence of recurrence or metastasis.

## DISCUSSION

Soft tissue perineurioma is a distinctive type of peripheral nerve sheath tumor composed of perineurial cells. It occurs preferentially in adults and may arise in a wide variety of anatomic sites, including retroperitoneum, breast,[1] gastrointestinal tract,[12] and kidney.[13] It is typically not associated with nerve and are usually benign. Soft tissue perineuriomas are solitary, generally small (1.5-7 cm) and well circumscribed but not encapsulated. Histologically, the tumor cells have elongated spindle shaped nuclei with long, slender, bipolar cytoplasmic processes.[6] Approximately 20% of soft tissue perineuriomas show atypical histologic features, including hyperchromatic nuclei, pleomorphic cells, and infiltrative margin.[1] In the present case, microscopic findings are suggestive of soft tissue perineurioma.

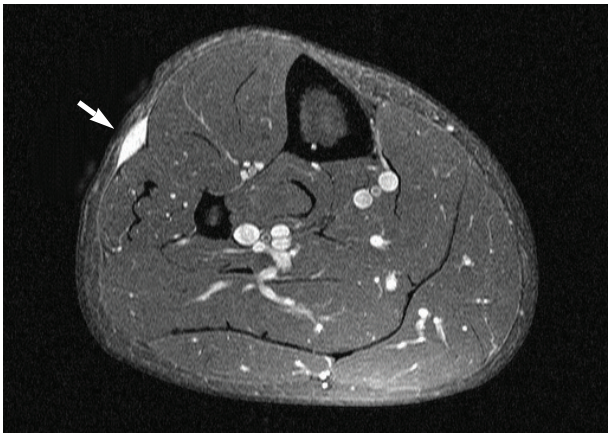

Fig. 1. Magnetic resonance image. Axial T1-weighted image with fat saturation shows contrast enhanced, high signal intensity (arrow) in the subcutaneous tissue of the right lower leg.

Immunohistochemically, soft tissue perineuriomas usually show EMA staining and lack S-100 protein reactivity. In the present case, the positivity of EMA supports the perineurial cell nature. Recently, claudin-1 and GLUT-1 have been diagnostically useful markers of normal and neoplastic perineurial cells.[5] Ultrastructurally, soft tissue perineuriomas show elongated cell processes with external lamina and pinocytotic vesicles.[1,4] In the present case, immunohistochemical and ultrastructural findings are characteristic of soft tissue perineurioma.

Cytogenetically, monosomy of chromosome 22 and loss of chromosome 13 have been reported in soft tissue perineuriomas.[5,8] Loss of chromosome 10 and a small chromosome 22q deletion involving NF2 have also been documented.[5]

The histologic differential diagnosis of soft tissue perineurioma includes benign and malignant spindle cell tumors with a

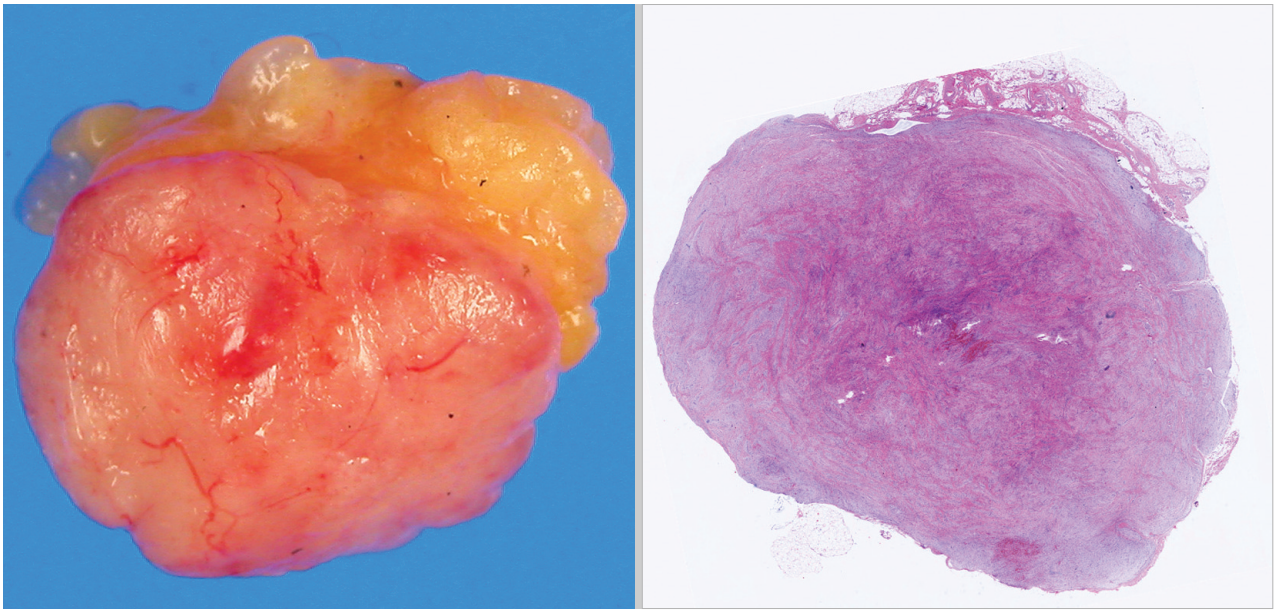

Fig. 2. Gross finding and whole mount section. The tumor is well-circumscribed, pale pinkish gray, and rubbery soft. The whole mount section shows a well circumscribed mass with collagenous and myxoid stroma.

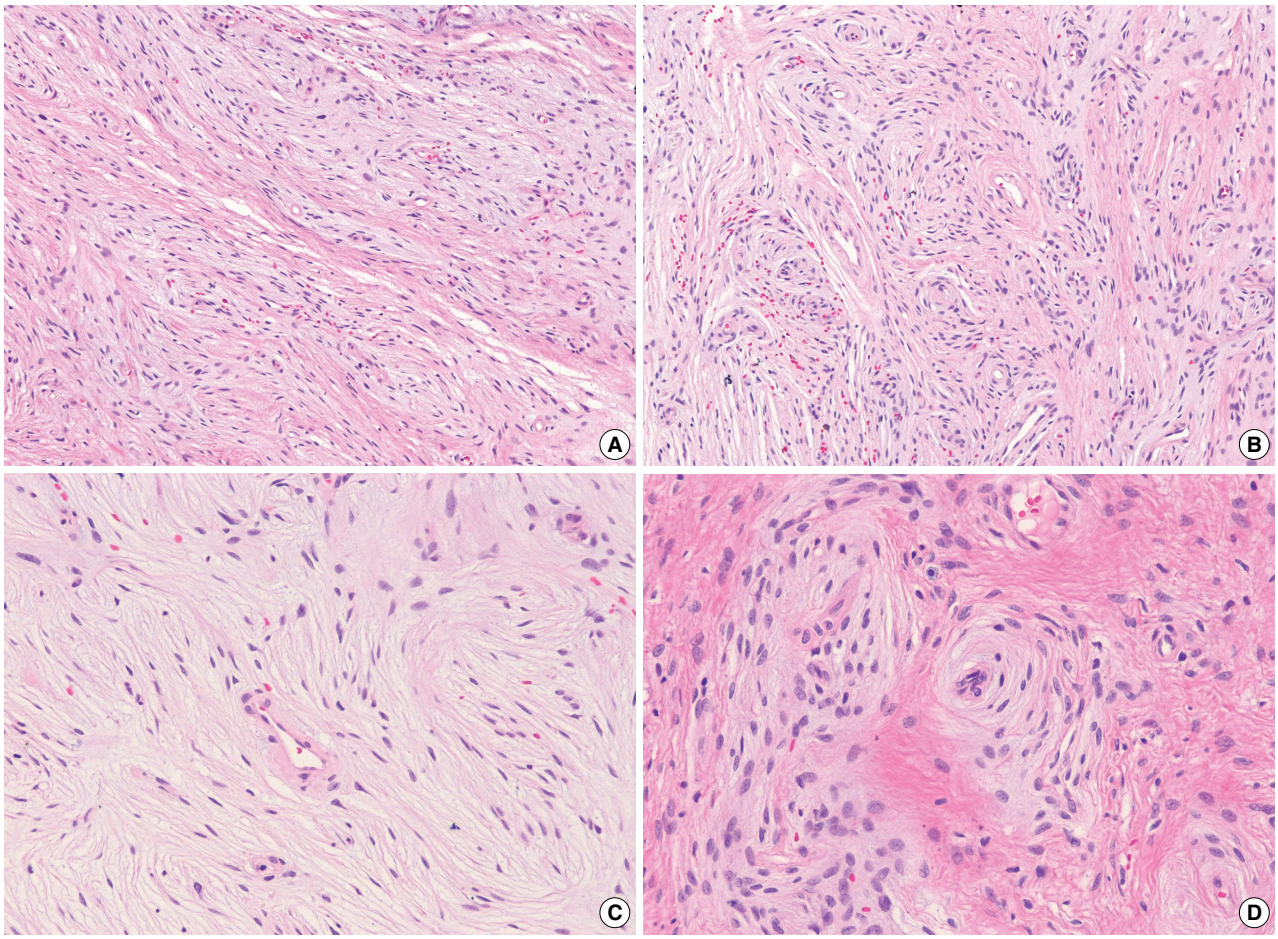


Fig. 3. Microscopic findings. (A) The spindle cells are arranged in fascicular pattern within collagenous and myxoid stroma. (B) The spindle cells are arranged in whorled pattern. (C) The spindle cells have elongated nuclei with tapering ends, and long, thin cytoplasmic processes. (D) The tumor cells have ovoid or fusiform nuclei with finely dispersed chromatin.

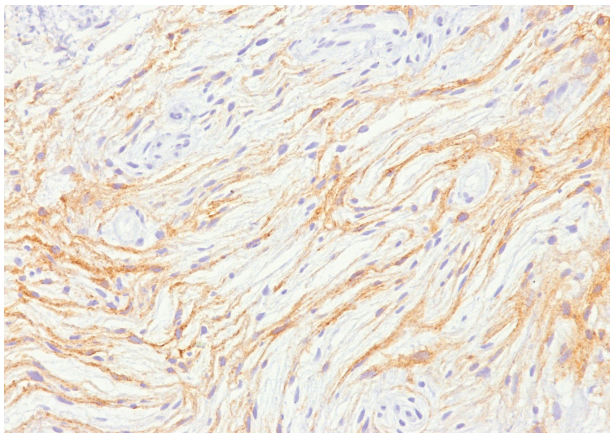

Fig. 4. Immunohistochemical stain. The tumor cells show positivity for epithelial membrane antigen.

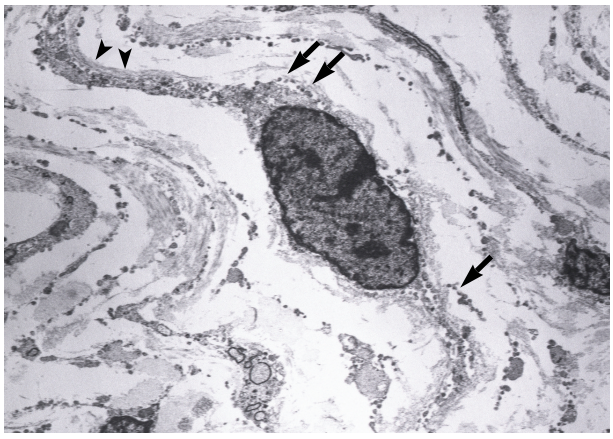

Fig. 5. Ultrastructural finding. The tumor cells show long and thin cytoplasmic processes. Occasional pinocytic vesicles (arrows) and external lamina (arrowheads) are present (original magnification, ×5,000).

collagenous or myxoid stroma, including neurofibroma, extracranial meningioma, deep benign fibrous histiocytoma, smooth muscle tumors, dermatofibrosarcoma protuberans, solitary fibrous tumor, low grade fibromyxoid sarcoma, and malignant peripheral nerve sheath tumor.[1,14,15] Soft tissue perineuriomas should be distinguished from neurofibromas. The remarkably elongated, slender spindle cells of soft tissue perineuriomas differ from the buckled spindle cells commonly found in neurofibromas. Neurofibromas are positive for S-100 protein and negative for EMA, whereas perineuriomas are negative for S-100 protein and positive for EMA. Extracranial meningiomas may be confused with soft tissue perineuriomas. The tumor cells of perineuriomas show more elongated, bipolar cytoplasmic processes than do meningothelial cells and tend to be arranged in fascicular or storiform pattern.[16] Deep benign fibrous histiocytomas with storiform pattern resemble soft tissue perineurioma.[17] Deep benign fibrous histiocytomas are negative for EMA. Smooth muscle tumors have blunt-ended nuclei with eosinophilic fibrillary cytoplasm and positive for smooth muscle actin and desmin. Soft tissue perineuriomas with storiform pattern resemble dermatofibrosarcoma protuberans. Soft tissue perineuriomas are often positive for CD34, which may lead to difficulties in differential diagnosis.[1] Dermatofibrosarcoma protuberans shows dermal origin and a characteristic pattern of infiltration through the subcutaneous adipose tissue (honeycombing), in contrast to the circumscription of soft tissue perineuriomas. Solitary fibrous tumors show prominent hemangiopericytoma-like vascular pattern and hyalinized stromal collagen. Solitary fibrous tumors are negative for EMA. Perhaps the closest histologic mimic of deep-seated soft tissue perineuriomas is low-grade fibromyxoid sarcoma (LGFMS).[1] LGFMS is characterized by cytologically uniform bland spindle cells in alternating zones of collagenous/hyalinized and myxoid stroma. Such alternating stroma is unusual in perineurioma and the arcades of small blood vessels typical of LGFMS are not seen in soft tissue perineuriomas. Malignant peripheral nerve sheath tumor (MPNST) may show perineurial differentiation.[18] Cytologically significant atypia, hypercellular perivascular accentuation of tumor cells, and the presence of heterologous elements favor a diagnosis of MPNST.

The clinical course of soft tissue perineuriomas is almost always benign. Local recurrence is extremely uncommon.[1] Malignant soft tissue perineuriomas are uncommon and characterized by hypercellularity, hyperchromasia, and variable, often brisk mitotic activity, and necrosis.[5] Malignant transformation of benign soft tissue perineuriomas has yet to be documented. In the present case, the patient has been alive 26 months after surgery, with no evidence of recurrence or metastasis.

In conclusion, soft tissue perineurioma is a recently characterized, benign peripheral nerve sheath tumor composed of perineurial cells with characteristic immunohistochemical and ultrastructural features. Soft tissue perineuriomas should be considered in the differential diagnosis of soft tissue tumors composed of spindle cells. Immmunohistochemical stain and electron microscopy are helpful in confirming a diagnosis of soft tissue perineurioma.

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