

# A Case of Neurilemmomatosis

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**Neurilemmomatosis is a clinical entity consisting of multiple cutaneous neurilemmomas, central nervous system tumors, and neurologic disorders. Since Shishiba et al first described the disorder in 1984, several cases have been reported. We report a Korean case of neurilemmomatosis showing multiple neurilemmomas of the skin and spinal cord, with associated motor and sensory nerve disturbance. Histologic, immunohistopathologic and electron microscopic studies confirmed the diagnosis. (Ann Dermatol 3:(1) 58–63, 1991)**

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*Key Words:* Neurilemmomatosis, Multiple neurilemmomas of the skin and spinal cord

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The neurilemmoma (neurilemoma or Schwannoma) is a solitary tumor arising from Schwann cell of the nerve sheath<sup>1, 2</sup>. It occurs along the course of peripheral nerves, but can be seen arising from cranial nerves. Although the tumor usually appears as solitary nodule, the tumors sometimes are multiple and have been reported as an isolated clinical finding<sup>4,6</sup> or as a clinical manifestation of neurofibromatosis<sup>7-9</sup>.

Shishiba et al<sup>4</sup> reported four cases of neurilemmomatosis showing multiple cutaneous neurilemmomas with central nervous system tumors, and proposed this as a clinical entity to be distinguished from neurofibromatosis of von Recklinghausen's disease. In 1989, Purcell et al<sup>5</sup> reported two non-Japanese cases of Schwannomatosis with manifestations of multiple cutaneous Schwannomas and central nervous system tumors.

In Korea, three cases of multiple neurilemmomas have been reported, one of which was associated with neurofibromatosis<sup>9-11</sup>. To our knowledge, there have been no reported cases of

multiple neurilemmomas with central nervous system tumors.

We report herein a case of neurilemmomatosis, manifested by multiple cutaneous and spinal neurilemmomas, and neurologic deficits.

## REPORT OF A CASE

A 48-year-old male patient visited our clinic in February 1990 for the evaluation of multiple cutaneous masses. He was admitted to the Neurosurgery clinic for neurologic deficits of 5 years duration, and was referred to our clinic to evaluate the skin lesions. The patient had been well until his twenties, when he noticed an asymptomatic bean-sized nodule on the dorsum of his right hand, which gradually increased in size. Similar asymptomatic nodular lesions developed gradually on the trunk and extremities with increasing size over time (Fig. 1). Five years prior to presentation, he felt weakness and an abnormal dull sensation in the lower extremities. During last 3 years, he experienced episodic attacks of tingling sensation and intermittent pain of his lower extremities. He also complained of hearing loss and tinnitus of the both ears. During last 2 years, his neurologic status worsened with the development of paraparesis, urination and defecation difficulties. His past history was remarkable for the presence of external ophthalmoplegia and

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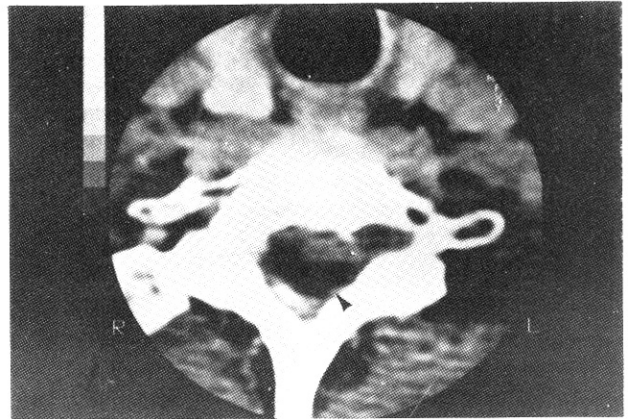


**Fig. 1.** Multiple nontender flesh-colored subcutaneous nodules on the neck, and the right arm.

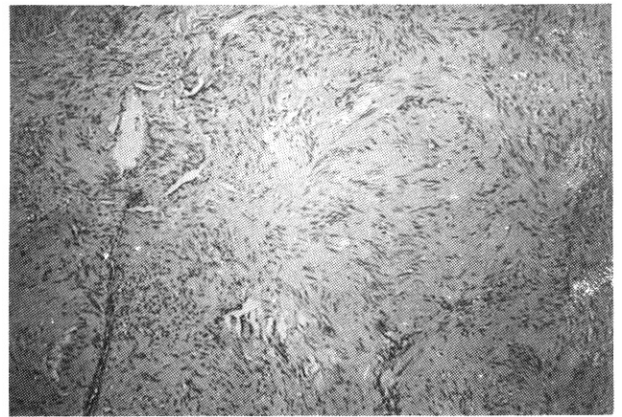
decreased visual acuity of the right eye after a head injury at the age of nineteen. His family history revealed no evidence of neurologic disorders, or phacomatosis.

Physical examination revealed multiple variable sized nodules measuring from  $0.5 \times 0.5$  cm to  $6.5 \times 4.0$  cm, located over his entire body surface excluding the face and the scalp. The lesions were asymptomatic, flesh-colored, oval or multilobulated, subcutaneous nodules which were adherent to the overlying skin but freely movable from the underlying subcutaneous tissue. There were no neurofibromas, café au lait spots, or freckles. Neurologic examination showed paraparesis of the lower extremities, hypesthesia and hypalgesia below the T-4 neurotome, and decreased anal sphincter tone.

The findings of laboratory evaluation including complete blood cell count, urinalysis, liver function tests, renal function tests, electrocardiogram, VDRL, and cerebrospinal fluid analysis were negative or within normal limits. Chest roentgenograms revealed an oval shaped soft tissue mass measuring  $4.0 \times 2.5$  cm in size on the right side lung field suggestive of extrapleural mass. An audiologic studies showed a bilateral hearing loss.



**Fig. 2.** A computer tomographic myelogram reveals a hypodense soft tissue mass lesion (arrow head) on C-7/T-1.

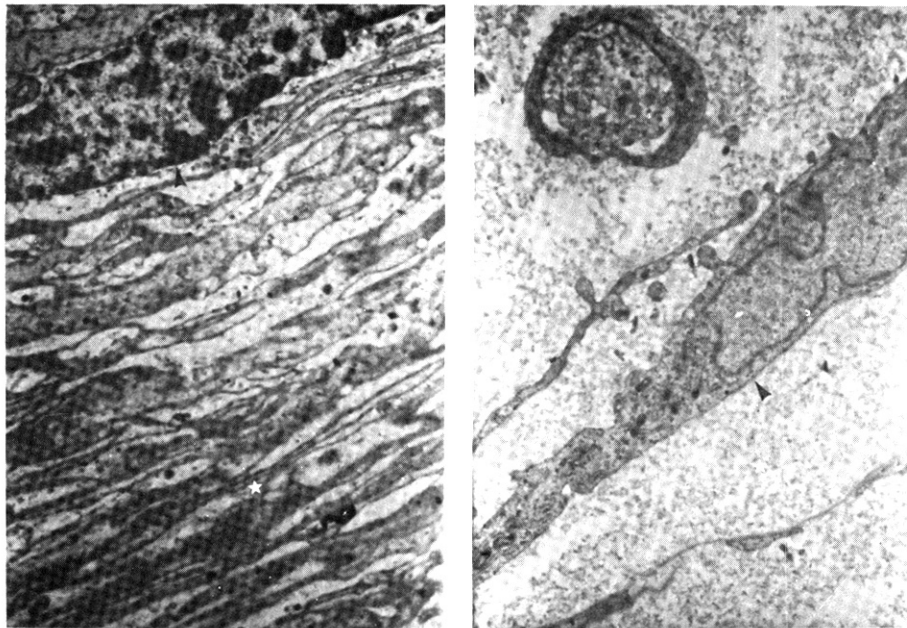


**Fig. 3.** Histologic features of the nodule on the right axilla. Tightly packed spindle cells are arranged in a streaming pattern. Verocay bodies formed by a palisade of nuclei and a space of homogeneous matrix are also noticed (Hematoxylin-eosin stain,  $\times 100$ ).

A total axial myelogram showed an extramedullary intradural mass lesion at C-7/T-1 and a paraspinal mass at T-3 (Fig. 2). Histologic examination of a right axillary nodule revealed numerous cellular nests or cords containing spindle cells with a fibrous capsule in the dermis and subcutis. Antoni A areas with tightly packed, spindle cells and well formed Verocay bodies (Fig. 3) alternated with the less cellular, looser stroma of the Antoni B areas. Immunohistopathology was positive for S-100 protein and negative for carcinoembryonic antigen. Electron microscopy revealed spindle shaped cells and numerous cellular processes covered with basal lamina in Antoni A tissue; loosely arranged cells separated

by a homogeneous matrix was observed in Antoni B tissue (Fig. 4). The tumor at C-7/T-1 was surgically removed, and histological examination revealed similar features as the cutaneous tumor. After surgical removal of the spinal cord mass, the patient showed improvement of motor and sensory disturbances.

case or in association with neurofibromatosis<sup>7-9</sup>. Izumi *et al*<sup>7</sup> reported a case of multiple neurolemomas associated with von Recklinghausen's disease, and Stout<sup>8</sup>, in his review of 50 patients with neurolemomas, reported three cases of von Recklinghausen's disease. The coexistence of neurilemmoma and neurofibroma is well known.



**Fig. 4.** Electron microscopic study showing spindle-shaped cells (arrow head) with plexus of cytoplasmic processes outlined by basal lamina (star) in Antoni A (left), and loosely arranged cells in a homogeneous matrix (star) in Antoni B (right) (Uranyl acetate and lead citrate stain,  $\times 11,200$ ).

## DISCUSSION

Neurilemmomas are benign nerve sheath tumors derived from Schwann cells. They usually occur as solitary firm nodules of variable size, and are seen along the main nerve trunks of the extremities, especially the flexor surface of the arms, wrists, and knees<sup>1,8</sup>. The lesions may arise along the course of cranial nerves, with the vestibular branch of the acoustic nerve most frequently involved<sup>5, 12</sup>. Our case showed multiple subcutaneous nodules on the neck, trunk, upper and lower extremities, and soft tissue tumors of the spinal cord. Multiple neurilemmomas have been reported as a rare isolated finding<sup>4,6</sup> as in this

and many authors attribute this association to their common cell of origin<sup>13-15</sup>. Electron microscopic<sup>13</sup>, tissue culture<sup>14</sup>, and histochemical studies<sup>15</sup> revealed that the cell origin of the neurilemmoma and neurofibroma is the Schwann cell. For example, Fisher and Vuzevski<sup>13</sup> in their electron microscopic study, asserted that the major difference in histologic appearance between the schwannoma and neurofibroma may be related to the degree of collagenization, but that both tumors are derived from Schwann cells. Winkelmann *et al*<sup>15</sup> stated that the neurilemmoma could be regarded as the same clinical entity as neurofibroma by the histochemical reaction of cholinesterase. Because of the common cellular

**Table 1.** Differences in clinical, histological, and ultrastructural features between neurilemmomatosis and neurofibromatosis

	Neurilemmomatosis	Neurofibromatosis
<b>Clinical</b>		
Caf'e au lait spots	—	+
Neurofibromas	—	+
Lisch nodules	—	+
Genetic background	—	+
Sites of predilection	extremities	trunk
Subjective symptoms	asymptomatic or painful, tender	asymptomatic
<b>Histological</b>		
Encapsulation	+	—
Antoni A and B	+	—
Verocay bodies	+	+/-
Malignant change	—	+/-
<b>Ultrastructural</b>		
Cytoplasmic process	ample	scant
Collagen amount	less	more
Myelinated axons	—	+

origin and coexistence with von Recklinghausen's disease, some regard neurilemmoma and neurofibroma as basically the same tumor. However, differences in clinical behavior, and gross and microscopic features make these neoplasms distinct entities<sup>16</sup> (Table 1). Clinically and histopathologically, neurilemmomas show some important differences from neurofibromas. Neurilemmomas are more common in the extremities, while the trunk is the common site of neurofibromas. In general, both tumors are asymptomatic, but neurilemmomas are often associated with pain or tenderness<sup>3, 7</sup>. Histologically, neurilemmomas are encapsulated tumors consisting of Antoni A and B tissue with characteristic Verocay bodies features, which are not found in neurofibromas<sup>3</sup>. The ultrastructural findings of the neurilemmomas are generally similar to those of the neurofibromas; however, the cytoplasmic processes appear more numerous, longer, and orient into parallel bands, particularly in Antoni A tissue of neurilemmomas<sup>13</sup>. In addition, the greater amount of collagen and the presence of myelinated axons enveloped within plasmalemmal invaginations are ultrastructural features of neurofibroma not found in neurilemmoma<sup>17</sup>.

In 1984, Shishiba et al<sup>4</sup> first described neuril-

emmatosis as a clinical entity consisting of multiple cutaneous neurilemmomas, and central nervous system tumors such as meningiomas, gliomas, and astrocytomas with associated neurologic disorders. They reported four cases and sixteen probable cases of neurilemmomatosis collected from the Japanese literature. Purcell and Dixon<sup>5</sup> reported two non-Japanese cases with features of neurilemmomatosis named as Schwannomatosis, and asserted that it should be regarded as a clinical entity distinct from neurofibromatosis. Similar to Shishiba's case, our case showed multiple cutaneous and spinal cord neurilemmomas, and motor and sensory nerve disturbances. According to the results of Shishiba's review, the incidence of neurilemmomas in the spinal cord was 33.3%<sup>4</sup>. Prevoo et al<sup>6</sup> also reported one case of neurilemmomatosis, in which they described abnormalities of the eye and congenital rib deformities that thus far had not been observed in the syndrome. Neurilemmomatosis differs from neurofibromatosis of von Recklinghausen's disease in that it does not manifest neurofibromas, caf'e au lait spots, or a genetic predilection. Our case showed absence of cutaneous signs of neurofibromas, caf'e au lait spots, and genetic background.

The light microscopic features of neurilemmomatosis are similar to those of a neurilemmoma in that the tumor nests are composed of Antoni A and Antoni B areas of growth, and surrounded by pseudocapsule<sup>3, 13, 16</sup>. The areas corresponding to Antoni A tissue show tightly packed spindle-shaped cells with alternating palisaded nuclei and anucleated bands called Verocay bodies. In contrast, Antoni B tissue shows loosely arranged cells among myxoid foci and microcysts. Our case showed typical histopathologic features of neurilemmomatosis including Antoni A and B tissue and Verocay bodies.

Sian and Ryan<sup>17</sup> stated three ultrastructural characteristics of neurilemmoma; a distinct basal lamina covering most of cells and their processes; extremely attenuated cell processes forming invaginations and wrapping structures, reminiscent of unmyelinated nerve fibers, and randomly arranged intracytoplasmic microfilaments. Additional cytoplasmic features were scant rough endoplasmic reticulum and Golgi apparatus. The other features of the tumor, common to Antoni A, Antoni B, and transition zones, were bundles of collagen in the intervening matrix and Luse bodies. In Antoni A tissue, the cells were spindle-shaped and their nuclei were sparse, and the anucleate zones of Verocay bodies were composed mainly of attenuated cell processes and their by a nonosmiophilic homogenous matrix with strands of fibrin, detached segments of basal lamina, and few Luse bodies. Electron microscopic findings of our case showed many spindle-shaped cells with irregular and peripherally condensed chromatin and extremely attenuated cellular processes covered with basal lamina. Wrapping tumor cell processes were also identified. There were scattered rough and smooth endoplasmic reticulum. Golgi apparatus, and mitochondria in the cytoplasm. These findings were compatible with those Antoni A. There were also a few spindle cells without basal lamina suggestive fibroblasts, but we could not found mast cell-like structures in our preparations. In Antoni B, there were loosely arranged spindle cells separated by homogeneous matrix. Luse bodies were not identified. The cytoplasm of the cells contained several dense osmiophilic granules, but collapsed myelin sheath-

structures were not observed. Unfortunately, we did not studied on the region of transition zone.

Neurilemmomatosis may be regarded as a type of phacomatosis, in that the disorder manifests cutaneous and central nervous system tumors, and should be distinguished from multiple neurilemmomas.

In conclusion our patient showed cardinal symptoms of neurilemmomatosis: multiple cutaneous neurilemmomas, neurilemmomas of the spinal cord, and neurologic deficits. The surgical removal of tumor on C-7/T-1 resulted in significant improvement of sensory and motor function. Hopefully more cases will be collected to study the genetic transmission of this unusual disorder.

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