

## Malignant Schwannoma in von Recklinghausen's Disease: A Case Showing Glandular and Rhabdomyoblastic Differentiation

Jung Hee Cho and Je G. Chi

Department of Pathology, Seoul National University College of Medicine, Seoul 110-460, Korea

= Abstract = A rare case of malignant schwannoma showing both glandular and rhabdomyoblastic differentiation in the same tumor is reported. The patient was a 14-year-old girl with von Recklinghausen's disease, and the sciatic nerve was the site of occurrence. There were both pseudoglands and true glands, and the luminal content was PAS-positive and stained for mucin.

Key words: *Malignant schwannoma, Peripheral nerve tumor, Sciatic nerve, Neurofibromatosis Glandular schwannoma*

### INTRODUCTION

Unusual tissue elements may be encountered occasionally in malignant nerve sheath tumors. For instance, cartilaginous differentiation is seen in 11%, the foci of rhabdomyosarcoma in 15%, and areas showing bone formation may be seen in 4% of these tumors (Warner *et al.*, 1983). Rarely is more than one type of heterologous element discovered in the same tumor (Agostino *et al.*, 1963). Besides the above-mentioned histologic types, a glandular component can be seen, and in such cases the term glandular schwannoma has been applied. This is an exceedingly rare occurrence, and, to our knowledge, only 10 such instances have been reported to date. The histogenesis of these unusual variants of nerve sheath tumor is controversial.

We report herein a malignant nerve sheath tumor that shows heterologous elements comprised of true and pseudoglandular structure as well as rhabdomyosarcomatous element. This type of mixed components, to our knowledge, is the first case to be reported.

### CASE REPORT

A 14-year-old girl was admitted to Seoul

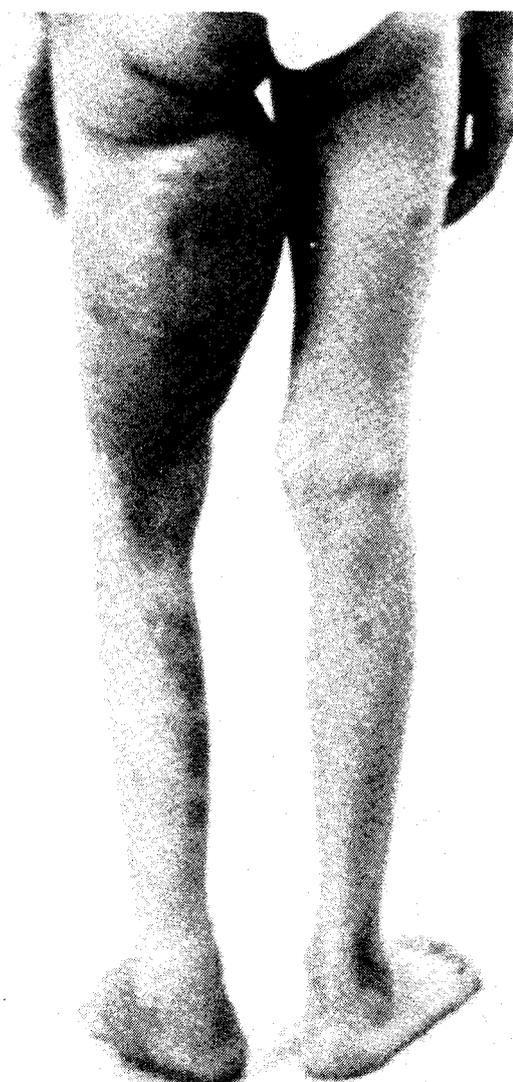


Fig. 1. A huge mass in the left thigh is covered by pigmented skin.

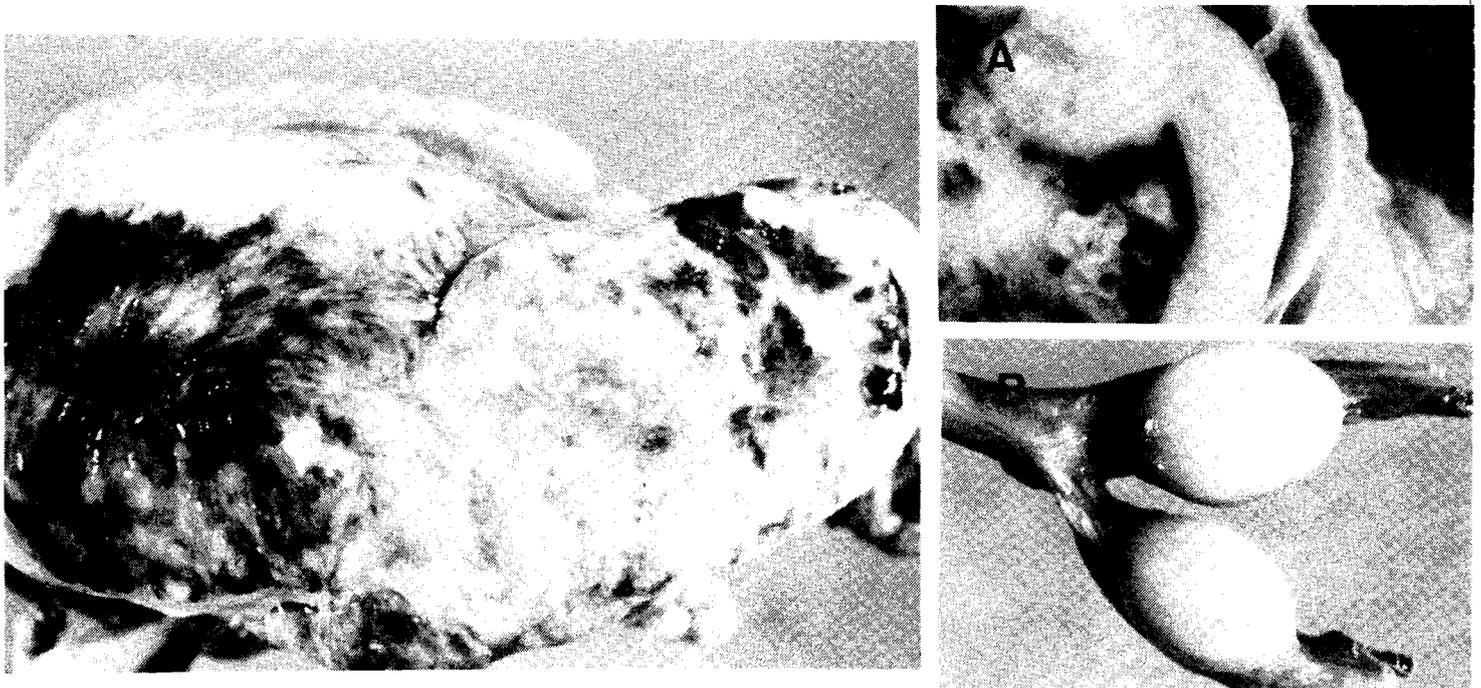


Fig. 2. Cut surface of the mass reveals a variegated appearance, partly myxoid and partly hemorrhagic–necrotic. In the periphery, small areas of microcystic portions (inset A) are found. A round mass (inset B) involving a diffusely thickened sciatic nerve shows a homogeneous gray cut surface.



Fig. 3. The bulk of the neoplasm is composed of spindle cells with tapered or blunt-ended nuclei in the intertwining fascicular arrangement.

National University Children's Hospital because of a rapidly growing huge mass in the left thigh

(Fig. 1). Four years prior to admission, she was first noted to have a walnut-sized mass in the

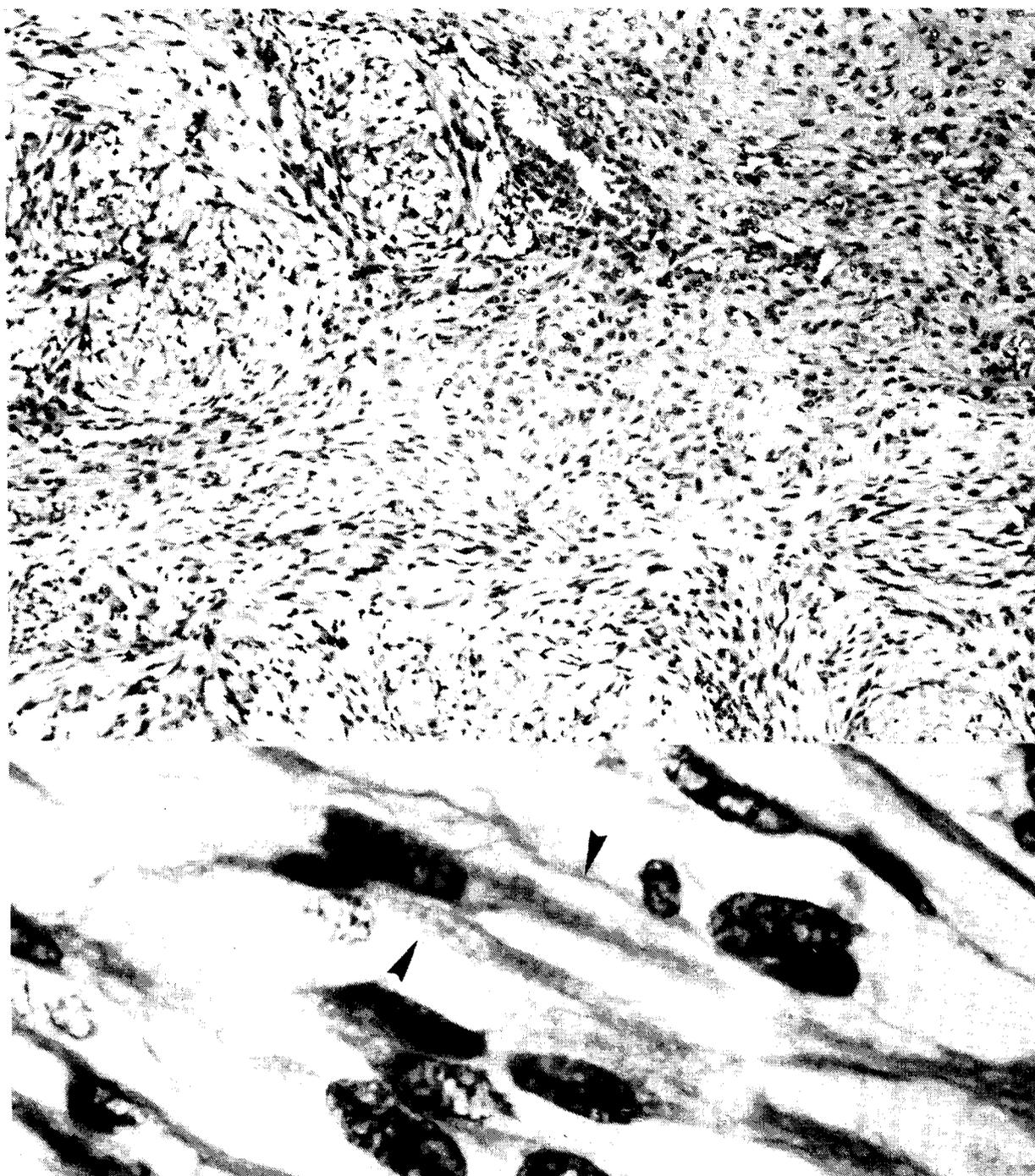


Fig. 4. Multiple islands of rhabdomyoblastic areas are scattered between the spindle cells. Frequent cross striation of the rhabdomyoblast is encountered (arrow heads).

left thigh. The mass grew rapidly to fetal-head size. Multiple cafe-au-lait spots were present on the whole body. The family history was non-contributory. The mass in the left thigh, which had undergone a biopsy one year earlier and was diagnosed as neurofibroma. It measured  $6 \times 5$  cm and was apparently fixed to the sciatic nerve trunk. Upon admission, a denervation pattern on electromyography was elicited in the regions of the common peroneal nerve and posterior tibial nerve, which supported the involvement of the sciatic nerve. Radical excision of the

mass together with the adjacent hamstring muscle was done.

#### PATHOLOGIC FINDINGS

The removed specimen consisted of an ellipse of skin,  $20 \times 15$  cm, and the subjacent large mass, adjacent muscle and a segment of sciatic nerve (Fig. 2). The overlying skin contained a large cafe-au-lait pigmentation. A whitish-yellow, well-circumscribed firm tumor, measuring  $30 \times 14 \times 13$  cm, was embedded entirely in the muscle. The tumor was faintly lobulated with a



Fig. 5. Areas having glandular structures (A) are separated by the necrotic area of spindle cells (B). Glandular lining cells have vacuolated cytoplasm and resemble goblet cells.

somewhat gelatinous and hemorrhagic appearance and also with a focus of microcystic area in the periphery. The involved sciatic nerve was diffusely thickened forming a round mass in the proximal one-third. It was firm and showed a homogeneous pale-yellow myxoid appearance.

Microscopically, the bulk of the neoplasm was composed of spindle cells with tapered or blunt-ended nuclei. They were arranged in intertwinning fascicles and sheets (Fig. 3). Occasionally, myxoid change and focal necroses were present. The tumor was well-demarcated but had

focally infiltrated the surrounding muscle. There were rhabdomyoblastic areas where the cells showed frequent cross striations (Fig. 4). Adjacent to these or apart from these there were glandular structures containing PAS-positive, diastase resistant mucinous material, which was carminophilic and stained positively with alcian blue. These glandular structures were lined by cells with vacuolated cytoplasm and resembled goblet cells. In another area, glandular clusters contained small dark cells resembling neuroendocrine cells which formed true rosettes or

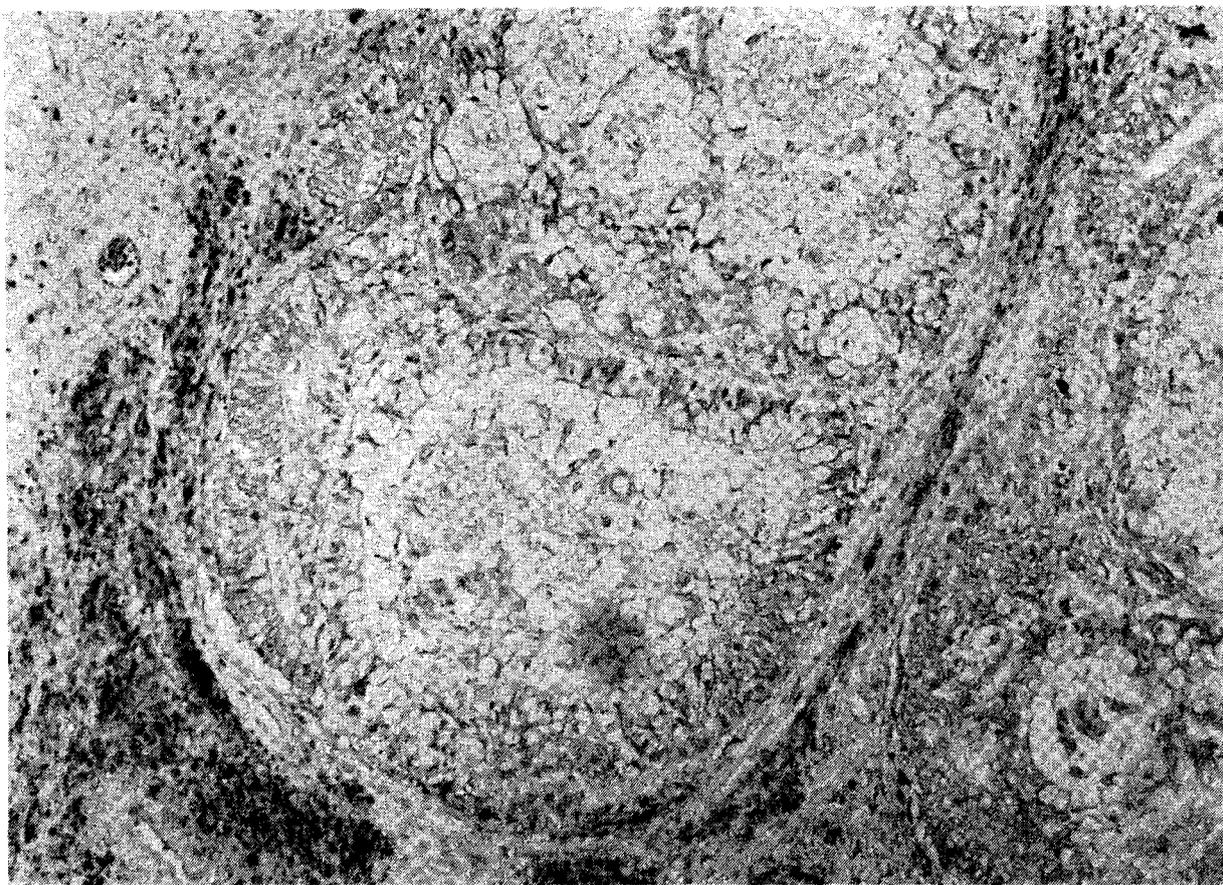


Fig. 6. Most spindle cells react with antiserum to S-100 protein with no reactivity in the areas of rhabdomyoblastic and glandular elements.

pseudorosettes. These cells were not stained by the argyrophil reaction or PAS. Between these glands, mucinous lakes, forming the pseudoglandular pattern without lining cells, were found. This area having glandular structures was separated by the necrotic area with spindle cells (Fig. 5). Mitosis, which was above 5/10 HPF, was found with ease, especially in cellular areas. By immunohistochemical study using the peroxidase-antiperoxidase method, most spindle cell elements reacted with anti-serum to S-100 protein (Fig. 6). However, rhabdomyoblastic components and glandular areas were not stained.

#### ELECTRON MICROSCOPIC FINDINGS

The glandular component showed polarity of the epithelial cells with acinar arrangement around a lumen which contained some amorphous material. The cells were invested by a basement membrane and were connected to each other by complex cell junctions. No transition between the epithelial and stromal cells was seen. The apical surface of the cells showed a packed arrangement of microvilli which were quite uniform and tall (Fig. 7). Microvillous core

rootlets, which were composed of fine filaments with long extensions into the apical cytoplasm, were present and well-developed. Also, a well-defined limiting membrane was present. The cytoplasm of the epithelial cells showed scattered mitochondria, dilated endoplasmic reticulum and conglomerated mucin globules. Few intracytoplasmic filamentous structures were admixed. However, no cilia, neurosecretory granule, or blepharoplasts were identified. The sarcomatous part showed features suggesting rhabdomyoblastic differentiation which was composed of well-developed myofilaments with dense Z band material in the cytoplasm of some cells.

#### DISCUSSION

Glandular schwannoma is a rare variant which, as its name implies, is characterized by focal benign glandular elements resembling intestinal or respiratory type epithelium, or ependyma. Over 80% of these tumors described previously have been malignant, and only rarely are glandular schwannoma benign. The majority of patients with glandular schwannoma have von Reckling-

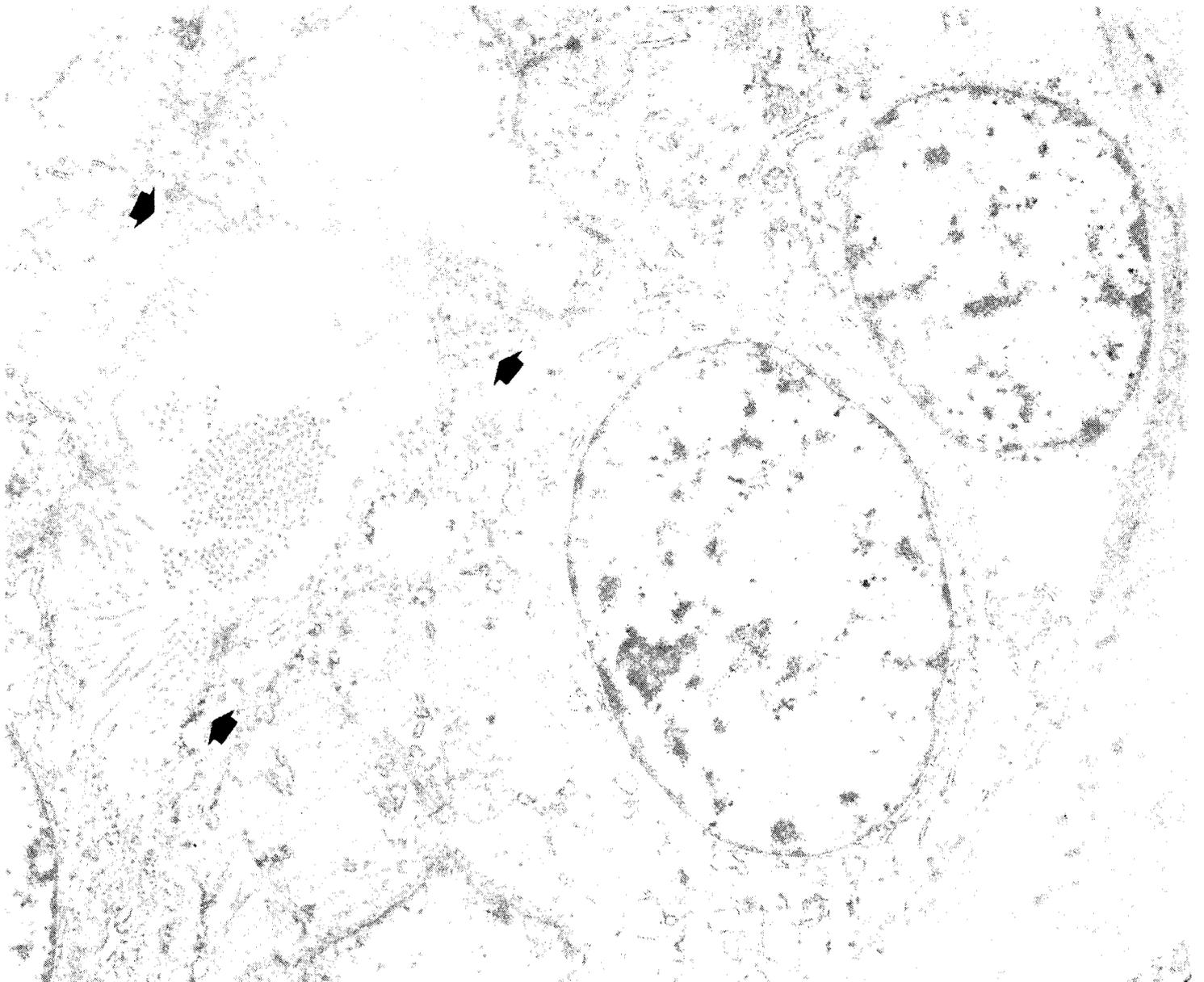


Fig. 7. The apical surface of the glandular lining cells shows a packed arrangement of uniform tall microvilli (arrows) and well-formed microvillous core rootlets (inset). No cilia, neurosecretory granules or blepharoplasts are identified.

hausen's disease, as is true in this case (Krumerman 1978).

Besides the location of the tumor and neurological findings distal to the sciatic nerve supported the sciatic nerve origin, this patient had multiple cafe-au-lait spots and characteristic plexiform neurofibroma could be found in the specimen removed. In our case, the malignant schwannoma started from preexisting neurofibroma rather than de novo origin.

The presence of both glandular and rhabdomyoblastic components in a same tumor as in our case is very unusual and fairly interesting. We could not find such a case in the literature, although only one case containing osteogenic

sarcoma as well as rhabdomyosarcoma and numerous atypical mucin-secreting glands has been reported as a brief communication (Woodruff, 1976). Rhabdomyosarcomatous differentiation is not very unusual in childhood cancers and is particularly common in Wilms' tumor.

The histogenesis of these heterologous elements of malignant schwannoma is debatable. The presence of such elements has been explained by the neuroectodermal origin of malignant peripheral nerve tumors and the potential of this neuroectoderm to undergo mesenchymal differentiation (Woodruff *et al.*, 1984). However, the presence of glandular element in this tumor has been much more difficult to explain. Garre

and Ferry *et al.* (Garre, 1892; Ferry and Dickersin, 1988) favored congenital displacement of the epithelium lining the neural tube which proliferated as a response to the malignant proliferation of schwannoma instead of teratomatous formation of glands. Other investigators believed this glandular space to be ependymal heterotopias (Foraker, 1948). In one study, electron microscopic findings were interpreted as showing ependymal differentiation which was thought to correlate well with the tendency for patients with neurofibromatosis to develop lesions of ependymal cells, including a high frequency of ependymal ectopia in the brain and spinal cord (DeSchryver K and Santa Cruz DS, 1984). In some cases, the concept of epithelial metaplasia of the neoplastic Schwann cells were thought to account for the glandular structures in light of the focal cytologic similarity between the gland lining cells and the surrounding Schwann cells. Recently, Ferry *et al.* (Ferry and Dickersin, 1988) described pseudoglandular schwannoma to support the metaplastic theory of the origin of the glands. Finally, Uri *et al.* (1984) proposed the possibility of pathologic induction–interaction between the neural crest and mesenchyme. It is well-known that during fetal development certain embryonic markedly influence the development of adjacent tissues. This influence, which acts for a limited time during early embryonic development, is known as induction. He reported a case of malignant glandular schwannoma showing glandular epithelium of the intestinal type to support the above proposal.

The neoplasm described here, unlike most pure glandular or triton tumors, was composed of neural, rhabdomyoblastic and glandular elements. In addition, these glandular structures were true glands, and the lining cells were

proven to be an intestinal type rather than of Schwann cell origin, both by immunohistochemical and ultrastructural examinations. Accordingly, on the bases of the presence of rhabdomyoblastic components and intestinal-type epithelium, such as in our case, the possibility of a pathological induction–interaction between the neural crest and the mesenchyme may be one of the most favored theories of pathogenesis in malignant schwannoma with heterologous elements including glandular components.

## REFERENCES

- Adostino AN, Soule EH, Miller RH. Sarcomas of the peripheral nerves and somatic soft tissues associated with multiple neurofibromatosis (von Recklinghausen's disease). *Cancer* 1963, 16: 1015–1027
- DeSchryver K, Santa Cruz DJ. So-called glandular schwannoma: ependymal differentiation in a case. *Ultrastruct. Pathol.* 1984, 6: 167–175
- Foraker AG. Gland-like elements in peripheral neurosarcoma. *Cancer* 1948, 1: 286–293
- Ferry JA, Dickersin R. Pseudoglandular schwannoma. *Am. J. Clin. Pathol.* 1988, 89: 546–552
- Garre C. Über Sekundär maligne Neurome. *Beitr Z Klin Chir* 1892, 9: 465–495
- Krumerman MS, Stingle W. Synchronous malignant glandular schwannomas in congenital neurofibromatosis. *Cancer* 1978, 41: 2444–2451
- Waner TFCS, Louie R, Hafez GR, Chandler E. Malignant nerve sheath tumor containing endocrine cells. *Am. J. Surg. Pathol.* 1983, 7: 583–590
- Woodruff JM. Peripheral nerve tumor showing glandular differentiation (Glandular schwannomas). *Cancer* 1976, 37: 2399–2413
- Woodruff JM, Chernik NL, Smith MC, Millett WB. Peripheral nerve tumors with rhabdomyosarcomatous differentiation (Malignant "Triton" tumor). *Cancer* 1973, 32: 426–439
- Uri AK, Witzleben CL, Raney RB. Electron microscopy of glandular schwannoma. *Cancer* 1984, 53: 493–497

악성신경종양에서 여러가지 이종요소의 존재는 드물지 않게 보고되어왔다. 예를 들면 연골 및 회문근 요소는 각각 11%와 15%의 경우 동반되는 것으로 알려져 있다. 최근들어 10예내외의 선형성 악성 신경종양이 보고되고 있다. 그러나 선형성 및 회문근 모세포 분화들 동시에 보여준 예의 보고는 아직까지 알려져 있지 않다.

저자들은 Von Recklinghausen 병을 가진 14세 여아의 대퇴부에 발생한 선형성 및 회문근 모세포성 분화를 보이는 악성신경종양 1예를 경험하고 전자현미경 및 면역조직학적 기색을 포함한 조직학적 소견과 여러가지 병인론을 재검토하여 보고하는 바이다.

조영희 · 지계근

서울대학교 의과대학 병리학교실

다발성 신경성분종양에 수반된 악성신경종양  
(선형성 및 회문근 모세포성 분화를 보이는 사례)

= 국문초록 =