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Plexiform Malignant Peripheral Nerve Sheath Tumor(MPNST) in Infancy and Childhood

—A case report—

Eun-Sook Nam, M.D., Young-Chae Chu, M.D.,* In-Sun Kim, M.D.**

Department of Anatomical Pathology, Eulji Hospital, Inha University Hospital and Korea University Anam Hospital**, Seoul, Korea*

We present a congenital plexiform cellular tumor with high mitotic activities arising in the right thigh of a 3-days-old infant. This subcutaneous tumor measured 6.5×4.5cm in diameter with multinodular, whitish, elastic cut surface. Microscopically, the tumor was composed of fascicles of closely packed uniform spindle cells with frequent nuclear palisadings. The most remarkable finding was frequent mitoses(4-5/10 HPF). The tumor cells were strongly positive for S-100 protein, myelin basic protein and vimentin, and weakly positive for Leu 7. On electron microscopic examination, the spindle cells were found to be surrounded by continuous basal lamina and had interlocking long cytoplasmic processes. Although the prognosis of this tumor is difficult to predict, aggresive behavior such as recurrences may be suggested, but it is less likely to be metastatic. Further accumulation of similar unusual cases may be helpful in evaluation of its biologic behavior.

Key Words : *Malignant peripheral nerve sheath tumor, Plexiform, Childhood.*

INTRODUCTION

Malignant peripheral nerve sheath tumors(MPNST) in children are rare. MPNSTs in children may show histologically rather primitive foci and have proliferative activities according to age, which gives frequent difficulty in diagnosis(Meis et al., 1992 ; Meis and Enzinger, 1993). Also the diagnosis of MPNSTs has been complicated by unclear criteria for determining the malignancy of a tumor originating in the nerve. Since Harkin et al.(1978) first reported plexiform schwannoma, several authors have reported plexiform schwannoma unassociated with von Recklinghausen's disease, which usually show benign histologic features (Woodruff et al., 1983 ; Barbosa and Hansen, 1984 ; Lee et al., 1989 ; Guarino, 1993).

We present an unusual case of congenital plexiform MPNST composed of mainly cellular Antoni A areas with high mitotic activities.

Address for correspondence : *Eun-Sook Nam, M.D., Department of Anatomical Pathology, Eulji Hospital, 302-1, Euljiro-3, Joon-gu, Seoul, 100-193, Korea. Tel : (02)266--3134(Ext 203).*

CASE REPORT

A three days old male infant was referred to the pediatric department of Eulji hospital from a local obstetric clinic due to a palpable subcutaneous mass in the right thigh. The infant was born by normal vaginal delivery at 3.34 Kg in weight with good Apgar scores. He was a first baby whose parents and family did not have any stigmata of von Recklinghausen's disease. On physical examination, no other masses or cafe au lait spots were found. The resected mass measured 6.5×4.5×1.5cm. The cut

surface was whitish, elastic, and multinodular. Microscopically, the tumor was organized into small and large nodules which were continuous with each other. Each nodule was encased by its own thin fibrous capsule which were seen in apparent continuity with perineurium of the adjacent nerve fiber (Fig. 1). The nodules were composed of fascicles of closely packed uniform spindle cells with fibrillar, eosinophilic cytoplasm mimicking to Antoni A areas of schwannoma. Nuclear palisadings were frequently found with Verocay bodies. The nuclei of spindle cells had fine chromatin and indistinct nucleoli. There were not Antoni B areas, thick-walled hyalinized vessels, and secondary degenerative changes. The most remarkable findings were frequent mitoses(4-5/10 HPF) with occasional atypical mitoses(Fig. 2). Marked cellular atypia, peripheral neuroectodermal tumor(PNET)-like foci, and necrosis were lacking. Two months later, two subcutaneous nodules, 1.2cm and 0.5cm in diameter each, were found adjacent to the previous biopsy site. The nodules revealed the same histology as the original tumor except for more infiltrative growth. It was considered to be residual tumor rather than recurrence because of incomplete resection of the original tumor and the short duration.

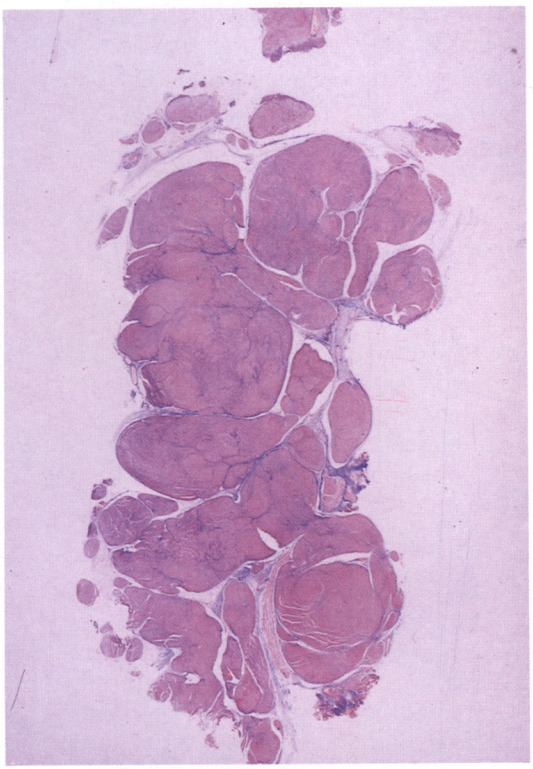

Fig. 1. The tumor is organized into small and large nodules continuous with each other. Each nodule was encased by its own thin fibrous capsule in continuity with perineurium of adjacent nerve fiber(Masson's trichrome, × 1)

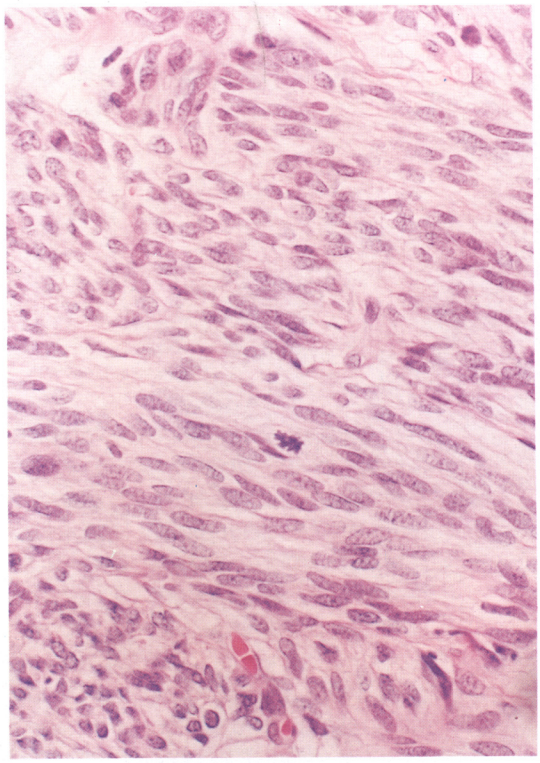

Fig. 2. The spindle cells have fibrillary, eosinophilic cytoplasm showing nuclear palisadings with frequent mitoses(H & E, ×400).

IMMUNOHISTOCHEMICAL RESULTS and EM FINDINGS

The tumor cells showed strongly positive reaction for S-100 protein(Fig. 3), myelin basic protein and vimentin, and also weakly positive reaction for Leu 7. Immunohistochemical staining for desmin, neuron specific enolase, glial fibrillary acidic protein and CAM 5.2 revealed negative reaction. Electron microscopic examination showed the tightly packed spindle cells surrounded by continuous basal lami-

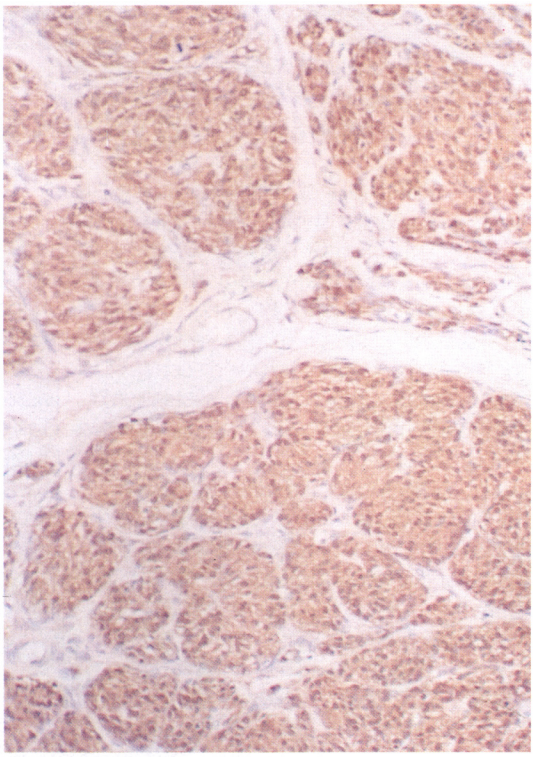

Fig. 3. Immunohistochemical reaction showed a strongly positive reaction for S-100 protein.

na, with interlocking long cytoplasmic processes (Fig. 4), which are consistent with schwann cells.

DISCUSSION

With respect to malignancy in cases of nerve sheath tumors, some of the usual indicators of malignant behavior in a neoplasm such as cellularity or infiltrative border are not highly discriminatory. Increased cellularity and pleomorphism may be consistent with a completely benign course such as ancient schwannoma. Infiltrative borders may be a feature of neurofibroma. Trojanowski et al.(1980) diagnosed the malignancy of the nerve sheath origin based on the presence of one of the following ; 1) the presence of more than a rare or isolated mitosis(usually seen in the context of pleomorphism and increased cellularity), and 2) extensive invasion by the tumor in a previously unoperated field. They said that mitoses were exceedingly rare in neurofibromas and schwannomas and therefore identifica-

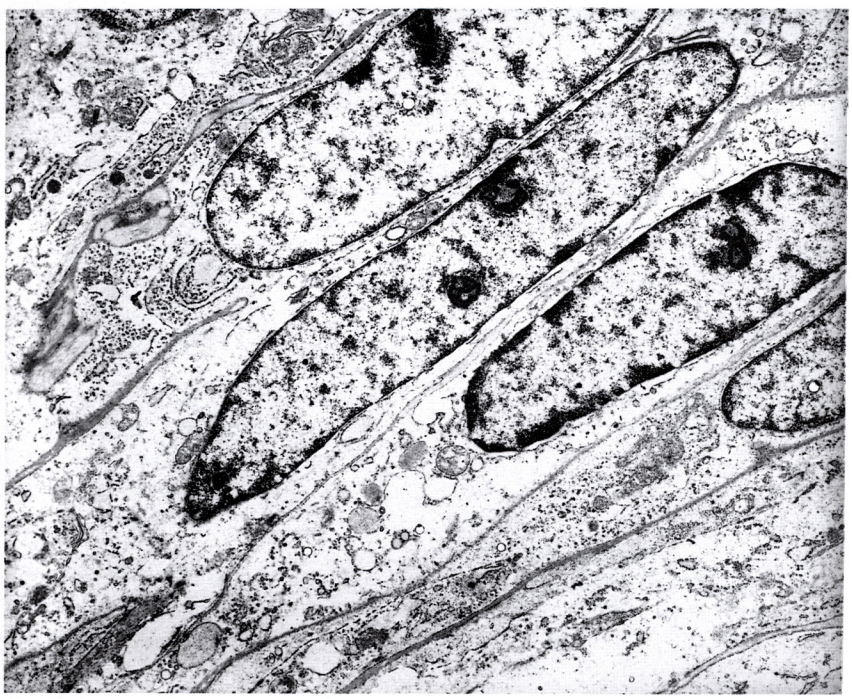

Fig. 4. On electron microscopic examination, the spindle cells are surrounded by continuous basal lamina and have interlocking long cytoplasmic processes(×4000).

tion of even a single mitosis necessitated careful scrutiny of a neoplasm for additional mitotic figures. However, there are exceptional cases in which the absence of mitoses does not preclude malignant behavior(Trojanowski et al., 1980). Also cellullar schwannoma with benign course may exhibit considerable mitoses(Woodruff et al., 1981 ; White et al., 1990). According to the study of White et al.(1990) who analyzed 57 cases of cellular schwannoma, only three of them revealed a local recurrence but no cases metastasized and no patient died of the tumor. All but two cases did not exceed 4 per 10 HPF. Two exceptions had 11 and 10 mitoses per 10 HPF. The mitotic activity did not have no prognostic import in those tumors. Horak et al.(1983) evaluated the clinicopathologic features of 87 fully documented primary and recurrent nerve sheath tumors. They suggested that neurofibroma and schwannoma displayed similar courses, but cellular tumors were more disposed to recur and undergo malignant transformation than typical tumors. They considered cellularity in peripheral nerve sheath tumor to be a morphologic factor influencing prognosis. Harkin et al.(1978) first reported benign plexiform schwannoma in 6 patients in aged from 9 to 39 years old in 1978. In the review of succeeding reported cases of plexiform schwannoma, most schwannoma showed sparse mitosis except one case, which was a large vulvar mass about 15cm in diameter in a 26-year-old woman, growing as a multinodular tumor(Woodruff et al., 1983). Mitoses were sparse (<1/20HPF) in most nodules with the exception of one nodule showing 8 mitoses in 10 contiguous high powers. The tumor recurred twice without metastasis. The problem gets more complicated in children because of the rarity of reported series and high proliferating activities. Among the reported 78 cases of MPNST in children by Meis et al.(1992), two cases were congenital. Whether they had plexiform pattern or not was not mentioned. The majority of lesions were chiefly composed of spindle cells arranged in fascicles with variable mitotic rates from one to 83 per 10 HPF(median 12/10 HPF). Tumor necrosis was not striking. Twenty-seven(36%) had no necrosis. They suggested that age older than 7 years, male sex, presence of von Recklinghausen's disease, central location, tumor size larger than 6cm, and tumors with more than 25% necrosis would be potentially significant prognostic indicators, but degree of cellularity, mitotic rate, heterologous elements, and the presence of PNET-like foci did not have an adverse impact on survival. Present case had only two factors including male sex and tumor size among the above adverse prognostic factors. So, we considered that the prognosis of our case may not be so bad.

The most pertinent differential diagnosis of our case was infantile fibrosarcoma, cellular schwannoma and conventional MPNST. Adjacent nerve bundles, plexiform pattern, palisadings of serpentine nucleus and absence of herringbone pattern made us favor the nerve origin. The results of immunohistochemical and electron microscopic studies confirmed the diagnosis of nerve sheath tumor. Cellular shcwannomas, although they have considerable mitoses, can be identified by feaures seen in more usual schwannomas such as Antoni B areas, secondary degenerative changes, and hyalinized, thick-walled blood vessels(White et al., 1990). Two-thirds of conventional MPNST show a geographic type necrosis and the cells are mostly anaplastic with widespread mitotic figures (usually more than 10/10 HPF). Because the cells of conventional MPNST are mostly dedifferentiated or poorly differentiated, reactivities for S-100 protein are variable, in contrast to strong positive reaction in cellular schwannoma and well differentiated MPNST(Daimaru et al., 1985). Our case can be distinct from cellular schwannoma and conventional MPNST by the absence of those features. Meis and Enzinger(1993) recently described nine cases of plexiform MPNST of infancy and childhood, similar to our case, characterized by plexiform pattern of growth and a high level of differentiation with median 4/10 HPF mitotic rates. 5 among 6 cases with available follw-up had local recurrence within 8-31 months, following excision of initial lesion and one with an orbital tumor died of locally invasive disease within a year. They suggested that distinction of this variant of MPNST from cellular and plexiform schwannoma or neurofibroma and harmatomatous lesions of childhood was important. More accumulation of such cases and follow up will define the appropriate biologic behavior.

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