

Pleomorphic Hyalinizing Angiectatic Tumor of Soft Parts – A Case Report –

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A case of rare pleomorphic hyalinizing angiectatic tumor (PHAT) of soft parts is reported. A 35-year-old woman presented with a subcutaneous solid mass in the left inguinal area, which had been present for 3 months, was presented to us. The tumor was histologically characterized by sheets of mitotically inactive oval and pleomorphic cells, mono- and multinucleated giant cells, intranuclear cytoplasmic inclusions, and prominent clusters of thin-walled ectatic vessels with perivascular hyalinization. A focal hemangiopericytoma-like vascular pattern, pseudovascular spaces, stromal collagen with degenerative change and abundant mast cells were observed. The tumor cells were reactive for vimentin and CD34. This tumor shared several features with malignant fibrous histiocytoma, ancient schwannoma, giant cell angiofibroma, giant cell fibroblastoma and solitary fibrous tumor. The patient was well with no evidence of disease for 10 months.

Key Words : Soft Tissue Neoplasms-Antiqens, CD34

The term pleomorphic hyalinizing angiectatic tumor (PHAT) of soft parts was recently coined by Smith *et al.* in 1996 to describe a low-grade sarcoma of uncertain lineage.¹ This neoplasm is characterized by sheets and fascicles of mitotically inactive, hemosiderin-stippled, spindle, and pleomorphic cells, situated around an angiectatic vasculature. There has been no other reported cases of this neoplasm in Korea. In the present report we describe the histopathologic and immunohistochemical findings of PHAT and discuss the main differential diagnoses.

CASE REPORT

We encountered a 35-year-old Korean woman presented with a slowly growing left inguinal mass, which was first noticed 3 months before. Physical examination and ultrasonography showed a well-circumscribed, elastic, soft mass in the subcutaneous tissue, measuring 4.5 cm in diameter. She had no specific medical and surgical histories. Chest X-ray showed no abnormalities. Baseline laboratory studies were within normal

limits. Marginal excision was undertaken. Macroscopically, the resected tumor, measuring 4.5 × 3.0 × 2.0 cm, was relatively well circumscribed and had a variegated grayish tan cut surface with foci of hemorrhage and cystic degeneration (Fig. 1). Microscopically, the tumor was unencapsulated but relatively well demarcated. An infiltrative border with trapping of normal adipose tissue at the tumor periphery was observed. At low magnification, the presence of clusters of thin-walled, ectatic blood vessels scattered throughout the lesion and hyalinized collagen deposition and prominent pleomorphism of the constituent cells were striking features (Fig. 2). Mono- or multinucleated giant cells were numerous and they tended to be located near the degenerative myxoid area and pseudovascular spaces (Fig. 3). Some of them had a floret-like or syncytial appearance. Hyalinized collagen deposition and clustered angiectatic vessels with perivascular hyalinization were prominent (Fig. 3), and there were foci reminiscent of hemangiopericytoma. The cellularity varied from area to area. The cellular areas showed predominantly diffuse or short fascicular arrangements of rounded, spindle-shaped, or pleomorphic cells. A focal palisading pattern was noted. The tumor cells were plump, oval and



Fig. 1. The tumor, measuring 4.5 × 3.0 × 2.0 cm, is relatively well circumscribed and variegated grayish tan cut surface with foci of hemorrhage and cystic degeneration.

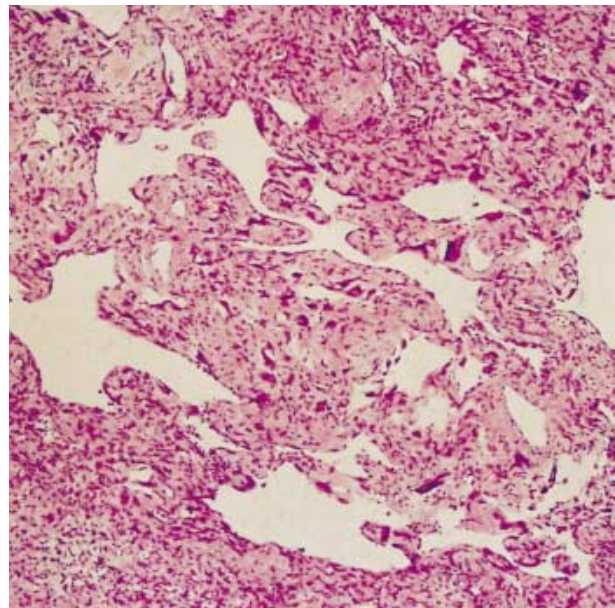


Fig. 2. At low magnification, presence of clusters of thin-walled, ectatic blood vessels scattered throughout the lesion, hyalinized collagen deposition and prominent pleomorphism of constituent cells are striking features.

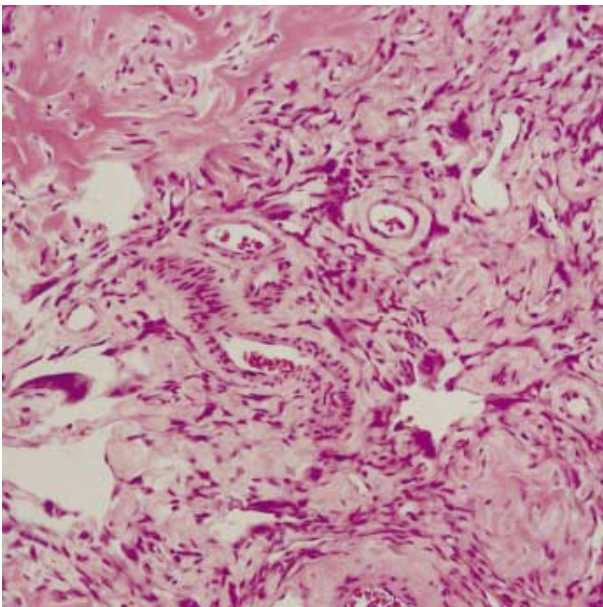


Fig. 3. Mono- or multinucleated giant cells are numerous and they tended to be located near degenerative myxoid area and pseudovascular spaces. Hyalinized collagen deposition, clustered angiectatic vessels with perivascular hyalinization are prominent.

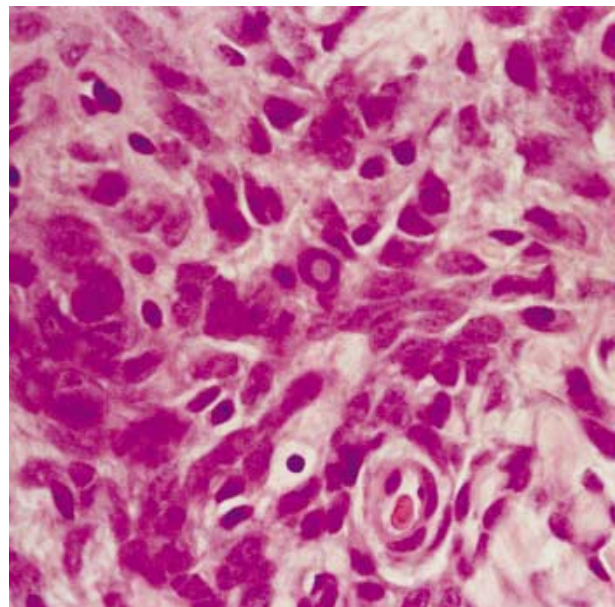


Fig. 4. The tumor cells are plump, oval and spindle-shaped with pleomorphic, hyperchromatic nuclei, inconspicuous nucleoli, and scant to moderate amount of indistinct basophilic cytoplasm. Intranuclear cytoplasmic inclusions are often seen.

spindled with pleomorphic, hyperchromatic nuclei, inconspicuous nucleoli, and scant to moderate amounts of indistinct basophilic cytoplasm. Binuclear cells and intranuclear cytoplas-

mic inclusions were often seen (Fig. 4). Cellular atypia was moderate and mitotic activities were less than one per 10 high-power fields. Moreover, no atypical features were present. Hypocellular areas were characterized by myxoid, degenerative,

or hyalinized stroma. Reticulin stains showed no characteristic patterns. There was no tumor necrosis. The tumor cells were negative for both periodic acid-Schiff stain and alcian blue stain. Small scattered aggregates of lymphocytes and mast cells were also present.

Immunohistochemically, the tumor cells were diffusely and strongly positive for vimentin (1:50, DAKO, Glostrup, Denmark) and CD34 (1:100, Neomarker, San Francisco, U.S.A.). The tumor cells were uniformly negative for S-100 protein (1:1,000, DAKO, Glostrup, Denmark), smooth muscle actin (1:100, DAKO, Glostrup, Denmark), desmin (1:50, DAKO, Glostrup, Denmark), CAM5.2 (1:50, PharMingen, San Diego, U.S.A.), epithelial membrane antigen (1:200, DAKO, Glostrup, Denmark) and factor VIII-related antigen (1:100, DAKO, Glostrup, Denmark). Ki-67 (1:100, PharMingen, San Diego, U.S.A.) index was approximately 1-2% of all tumor cell nuclei. Flow cytometric analysis revealed a diploid DNA content with a S-phase fraction of 4.8%. The patient was well with no evidence of disease for 10 months.

DISCUSSION

PHAT was recently delineated as a clinicopathologic entity by Smith *et al.*,¹ who reported a series of 14 cases. Following the original series, only six more cases have been reported.²⁻⁶ Of the total of 21 cases, including the case reported here, 14 (66.7%) occurred in women and 7 (33.3%) in men. All patients were adults, aged between 31 and 83 years (average, 55.8 years). Almost all patients were presented with slowly growing masses. Eighteen tumors (85.7%) had arisen in the subcutaneous tissue and three (14.3%) were intramuscular. In 11 patients (52.4%) the lesion was located in the lower leg. Other sites included the upper leg (4 cases), chest wall (2 cases), axilla, buttock, arm, and shoulder (one case each). Grossly, the lesions measured between 2.0 cm and 8.0 cm and were nonencapsulated; seven had well-circumscribed margins, while the others showed diffuse infiltration of the surrounding tissues. Histologically, PHAT is characterized by sheets and fascicles of mitotically inactive, oval, spindle, and pleomorphic cells and clusters of ectatic vessels with perivascular hyalinization. Other features include mast cell infiltration, hemosiderin deposits and focal calcifications. This case also showed short fascicular arrangements of spindle cells, the presence of mono- and multinucleated giant cells, a hemangiopericytoma-like pattern of vascularity, pseudovascular spaces, and stromal collagen with degenerative changes.

The histogenesis of the lesion remains unclear. Silverman *et al.*⁴ reported immunoreactivity for CD34 and Factor XIIIa and insisted that PHAT is a fibrohistiocytic tumor probably derived from proliferating microvascular CD34+ dendritic cells and Factor XIIIa+ dendrophages. Fukunaga *et al.*² suggests that these tumors may be histogenetically related with the solitary fibrous tumor (SFT) and giant cell angiofibroma because of their overlapping histologic features, the consistent expression of CD34 in SFT⁷⁻¹¹ and giant cell angiofibromas of the orbit¹² and the expression of CD34 in two-thirds of the cases of PHAT.¹⁻⁶ They considered that certain specific populations of primitive mesenchymal cells may give rise to PHAT, SFT, and giant cell angiofibroma that may be in the *same* family of low grade tumors. Gallo *et al.*³ also proposed a common origin of PHAT and SFT because of the same immunohistochemical features. But the expression of CD34 in PHAT is a less consistent finding than SFT. The present case shows diffuse and intense membrane staining for CD34. S-100 protein was uniformly negative in the original cases¹ and the present case. Since CD34 has been expressed in the endothelium, dermal dendritic cells, periadnexal cells, endocervical stromal cells, vascular tumors, nerve sheath tumors, smooth muscle tumors, SFT, dermatofibrosarcoma protuberans, epithelioid sarcomas, and gastrointestinal stromal tumors,¹³⁻¹⁷ its reactivity in twelve of 18 PHATs can not necessarily be helpful in the differential diagnosis of this lesion.¹⁻⁶ The presence of neuron specific enolase, glial fibrillary acidic protein, and α -smooth muscle actin may indicate abortive or primitive neural and muscle cell differentiation in some tumor cells¹⁰ or multipotential primitive mesenchymal cells, although neural or muscular differentiation was not confirmed in the present case. The presence of vimentin and CD34 in PHAT does not define the precise derivation of the cells, but it suggests their natures are that of primitive uncommitted mesenchymal cells, probably related to stromal fibroblasts.⁵

This tumor shared several features with SFT of various sites,^{1,3,6} giant cell angiofibroma,^{1,3,12} ancient neurilemmoma,^{1,3,4} and malignant fibrous histiocytoma (MFH).^{1,3,4} Giant cell angiofibroma occurs in the orbit of adults.¹² In histologically benign SFT and giant cell angiofibroma, nuclear atypia is less prominent than in PHAT and multinucleated giant cells are not a feature of SFT. In PHAT, prominent clusters of thin-walled ectatic vessels surrounded by perivascular hyaline material are described as characteristic, and substantial cellular atypia is present but mitotic figures are rare. These vascular changes, which are not uncommon in SFT and giant cell angiofibromas,

may not be specific for PHAT but secondary changes due to circulatory disturbances are often observed in slowly growing tumors. PHAT should be readily distinguished from neurilemmoma by the absence of a capsule, lack of associated nerve tissue and negativity for S-100 protein. MFH is characterized by pronounced nuclear pleomorphism. Cellular atypia in PHAT is less remarkable than those in MFH. Mono- and multinucleated giant cells in PHAT were observed predominantly in the degenerative areas. PHAT was composed of areas which were partly hemangiopericytomatous, but it differs from hemangiopericytoma because it has a more fascicular pattern, various proliferating patterns, and greater collagen production.

PHAT is a locally aggressive but not fully malignant neoplasm. This assumption is supported by the paucity of mitotic figures, the low grade of proliferation evidenced on Ki-67 index,^{1,4,5} and the absence of aneuploidy on flow cytometry.^{2,5} Flow cytometry was not studied in the original study. The present case has a diploid with low S-phase fraction, indicating benign or low grade malignancy. The low S-phase fraction is considered to be compatible with a low proliferating index by MIB1 immunostaining in the original PHAT.¹ Follow-ups of the eight patients in the series by Smith *et al.*¹ showed local recurrence in four. In the other published cases²⁻⁶ and in our case there was no evidence of disease after follow-up periods of 6 months to two years. To date, no patient has developed metastatic diseases. As this neoplasm is locally aggressive, wide local excision is an appropriate treatment and close follow up is required.

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