

# High-Grade Myxofibrosarcoma Showing Pleomorphic Hyalinizing Angiectatic Tumor-like Appearance – A Case Report –

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Myxofibrosarcomas (MFSs), which consist of multiple nodules with a variable cellular population in a myxoid matrix, are primarily located in subcutaneous tissue. Pleomorphic hyalinizing angiectatic tumors (PHATs) are rare soft-tissue tumors characterized by a proliferation of highly pleomorphic spindle or polygonal cells and abundant ectatic blood vessels in cellular or myxoid stroma. We present here an unusual case of a high-grade MFS with a PHAT-like appearance. A 67-year-old man presented with an asymptomatic subcutaneous mass in the right forearm. The tumor had myxoid, hypo-, and hypercellular areas with highly pleomorphic spindle or polygonal tumor cells that showed frequent mitoses and nuclear pseudo-inclusions. Foci of punctuate necrosis and inflammatory infiltration were present throughout the tumor, and abundant ectatic, thick-walled vessels containing blood clots were noted. The tumor cells were immunohistochemically positive for vimentin but negative for CD34, S-100 protein, smooth muscle actin, desmin, and bcl-2.

**Key Words:** Soft tissue; Sarcoma

Myxofibrosarcomas (MFSs), one of the most common sarcomas appearing in adults, exhibit a wide range of cellularity, nuclear pleomorphism, and mitotic activity in a myxoid matrix.<sup>1</sup> Pleomorphic hyalinizing angiectatic tumors (PHATs) are soft-tissue neoplasms that most frequently occur in the subcutaneous tissue of the extremities. A PHAT was first described by Smith *et al.*<sup>2</sup> in 1996, who noted that it was characterized by a combination of markedly pleomorphic cells and numerous extensively hyalinized blood vessels. Although PHATs show severe nuclear pleomorphism and may be misdiagnosed as a sarcomatous lesion such as malignant fibrous histiocytoma, mitotic figures are scarce and necrosis is unusual. PHAT was recently included as a benign tumor type in the World Health Organization (WHO)'s classification of soft tissue tumors.<sup>1</sup>

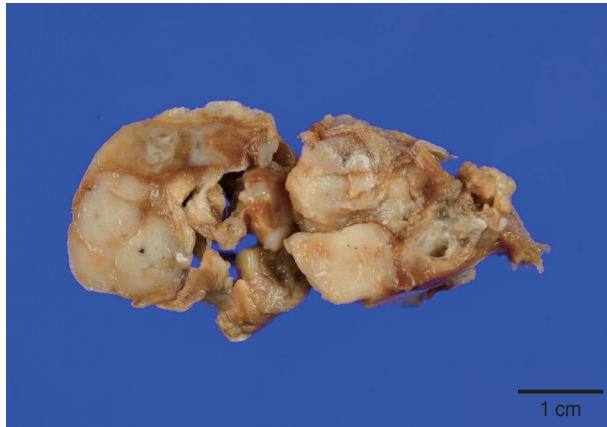
Some areas of sarcomatous lesions such as MFSs, pleomorphic lipomas, and pleomorphic sarcomas may resemble PHATs. The relationship between PHATs and sarcomatous lesions is not currently clear; such lesions arise rarely in PHATs or may merely have areas that resemble PHATs. A PHAT may not be a true clinicopathological entity, but merely a histological pattern.<sup>3</sup> We report here a case of a high-grade MFS with a typical PHAT-like appearance. Our goal was to raise awareness of the resemblance and to discuss the validity of PHATs as a separate entity.

## CASE REPORT

A 67-year-old man presented with an asymptomatic subcutaneous mass in the right forearm. The excised mass was 3.8 × 3.1 × 2.5 cm in size and had a well demarcated lobular appearance. The cut surface was solid and pale yellow to tan in color, with several pinpoint spaces containing blood clots in the deep dermis and subcutis (Fig. 1).

Microscopic observation showed that the tumor was not encapsulated and had infiltrated into the subcutaneous adipose tissue. Abundant ectatic, thick-walled vessels were observed in the center (Fig. 2A). A central hypervascular, angiectatic area was transformed into a cellular area (Fig. 2B). The vessels contained thrombi, and their walls showed severe hyalinized collagen deposition. We observed areas of hemorrhage and infiltrated tumor cells. These cells contained hemosiderin in their cytoplasm and showed highly pleomorphic nuclei with intranuclear pseudo-inclusions (Fig. 2C, D). This area made up more than 60% of the tumor, and was composed of myxoid, hypo-, and hypercellular areas with multinodular arrangements (Fig. 3A). Thin-walled curvilinear vessels were present within the myxoid hypocellular areas (Fig. 3B). Highly pleomorphic spindle or polygonal tumor cells were seen in hypercellular areas; these

cells exhibited atypical forms and frequent mitoses (> 10/10 high power fields) (Fig. 3C, D). Foci of punctuate necrosis and

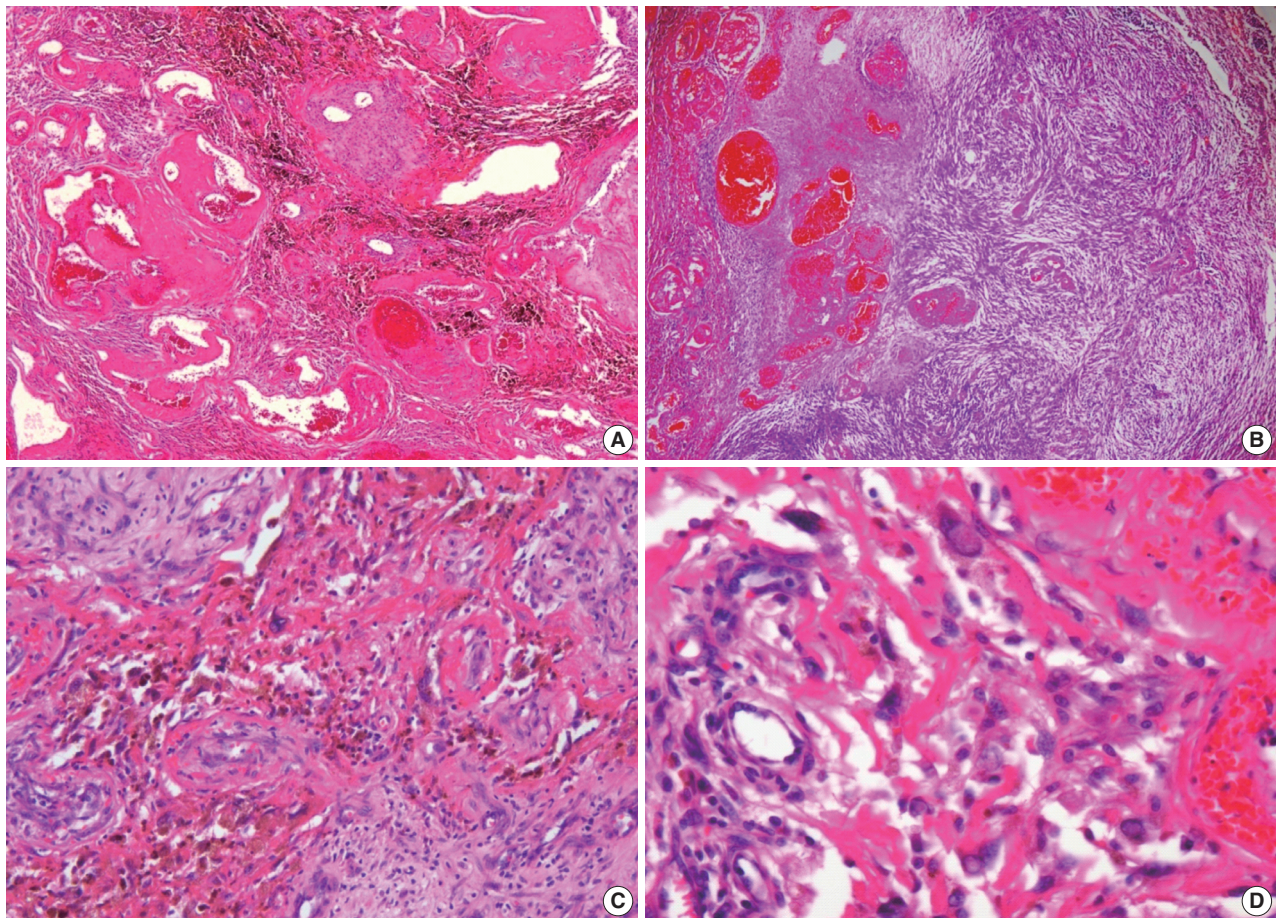


**Fig. 1.** The high-grade myxofibrosarcoma discussed in this case report. The tumor shows a multinodular growth pattern and a pale yellow to tan myxoid cut surface with foci of necrosis and cystic degeneration.

inflammatory infiltration were present throughout the tumor. Relatively bland-appearing tumor cells containing hemosiderin pigment had infiltrated the adipose tissue around the main lesion. We observed inflammatory infiltration in the walls of many small vessels. Immunohistochemical assays were done on tumor cells from central hypervascular areas and myxoid, hypo-, and hypercellular areas. These cells were positive for vimentin but negative for CD34, S-100 protein, smooth muscle actin, desmin, and bcl-2. This lesion was diagnosed as a high-grade MFS with focal PHAT features.

## DISCUSSION

An MFS is a soft-tissue sarcoma that was first described by Angervall *et al.*<sup>4</sup> in 1977. Although MFS was previously described as a myxoid variant of malignant fibrous histiocytoma, the WHO<sup>1</sup> has classified it as a fibrosarcoma. An MFS shows a



**Fig. 2.** A central hypervascular area with many ectatic thick-walled vessels (A) is transformed into a cellular area (B). The area contains tumor cells with hemosiderin in their cytoplasm (C) and highly pleomorphic nuclei with intranuclear pseudoinclusions (D).

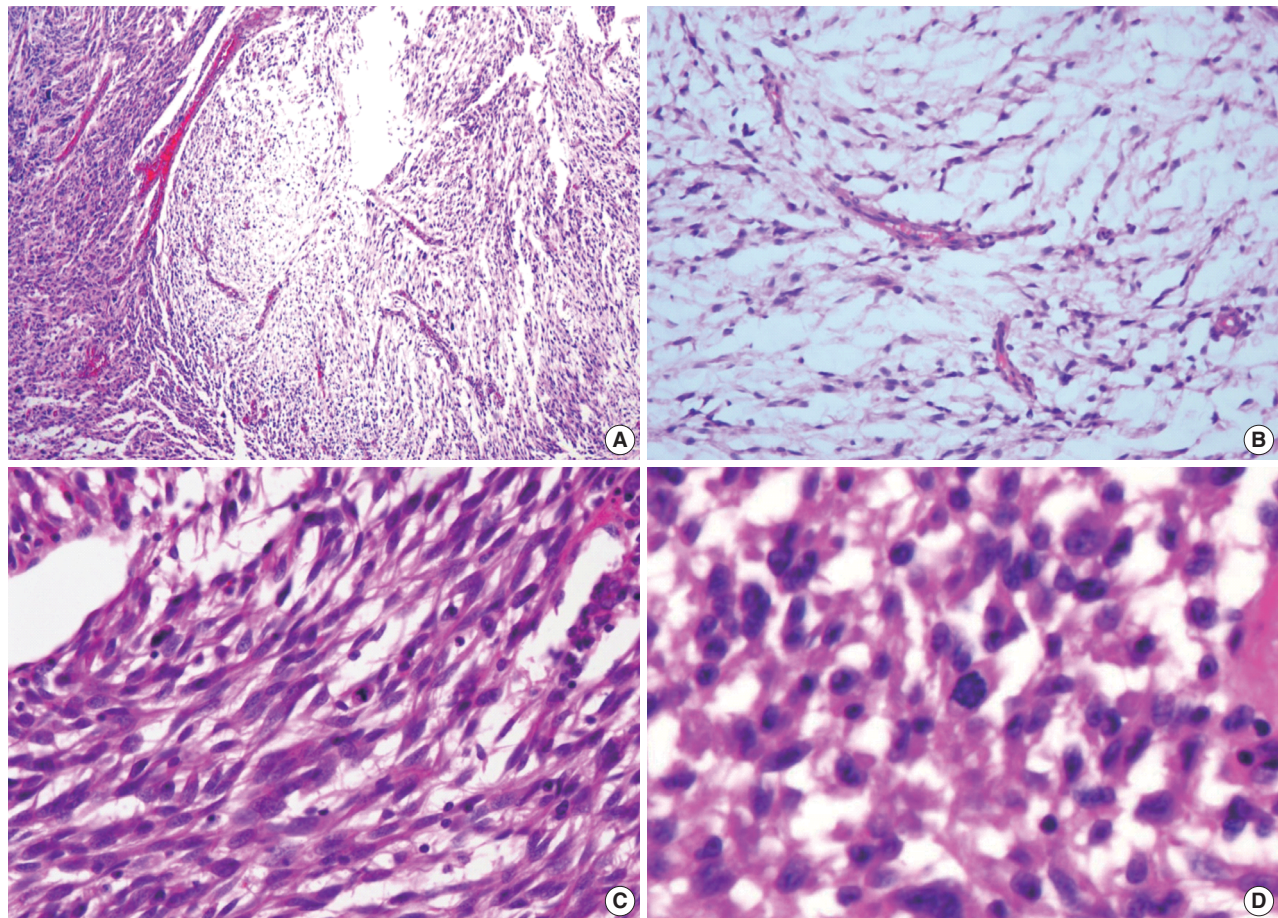
broad spectrum of cellularity, pleomorphism, and proliferative activity. Most patients present with a slowly enlarging and painless mass in the subcutaneous soft tissue of the extremities. Local recurrence occurs in up to 50-60% of cases and is unrelated to histological grade. Metastasis and tumor-associated mortality, however, are closely related to the histological grade of the tumor.

A PHAT is a rare, low-grade, soft-tissue tumor of uncertain histogenesis that principally involves the distal extremities.<sup>5</sup> It is characterized by the proliferation of highly pleomorphic spindle or polygonal cells and abundant ectatic blood vessels in cellular or myxoid stroma. The variously sized dilated blood vessels are lined with amorphous, eosinophilic material and scattered throughout the tumor. Although the tumor cells are highly pleomorphic and show locally infiltrative growth, mitotic activity and necrosis are unusual. Immunohistochemical studies have shown that most PHAT tumor cells (78%) express CD-34.<sup>2,6,7</sup> The tumor described in this case report, however, was

CD34-negative.

PHAT is not metastatic, but local recurrences have been documented and some recurrent tumors have shown histological features consistent with high-grade sarcomas.<sup>2,8</sup> Smith *et al.*<sup>2</sup> reported tumor recurrence in four cases and classified PHATs as low-grade sarcomas. Folpe and Weiss<sup>3</sup> described a local recurrence of "typical" PHATs showing myxoid pleomorphic sarcoma. Although they suggested that a PHAT was considered as a mesenchymal tumor of intermediate (borderline) malignancy, the WHO classifies it as benign.<sup>1</sup>

PHAT may also be seen as a component of other soft-tissue tumors. Mitsuhashi *et al.*<sup>8</sup> reported a case of a primary cutaneous MFS resembling a PHAT. The initial lesion was diagnosed as a PHAT, but the recurrence demonstrated high-grade MFS characteristics. Capovilla and Birembaut<sup>3</sup> observed typical PHAT-like areas in mesenchymal neoplasias such as MFSs, high-grade pleomorphic sarcomas, and pleomorphic lipomas. They argued that the diagnosis of PHAT should be rendered only af-



**Fig. 3.** The myxofibrosarcoma shows mixed hypo- and hypercellular areas with nodular growth (A). The hypocellular areas contain thin, curvilinear vessels in a myxoid matrix (B). The hypercellular areas show pleomorphic tumor cells with frequent mitoses (C) and atypical forms (D).

ter the exclusion of other tumor types. Preliminary cytogenetic results do not appear to indicate a specific, recurring chromosomal alteration that would indicate the validity of PHAT as a true clinicopathological entity.<sup>5</sup>

Smith *et al.*<sup>2</sup> postulated that the characteristic ectatic vessels of PHATs were due to the engulfment of the vessels by the advancing tumor front. This process would cause vascular damage and resultant plasma stroma leakage, organization, and subsequent perivascular hyalinization. In contrast, Flope and Weiss<sup>5</sup> suggested that the vascular changes of PHATs may be very early, and may occur even without significant spindle cell proliferation. They defined "early PHAT" as the distinctive hypocellular proliferation of generally bland, hemosiderin-laden spindle cells in a variable myxoid background. This stage of the tumor has been mistaken for benign lesions such as a spindle cell lipoma, benign fibrous histiocytoma, or nodular fasciitis.

The present case showed a high-grade MFS with focal areas that resembled a PHAT. The differential diagnosis included ancient schwannoma and other myxoid sarcomas (e.g., myxoid liposarcoma, extraskelatal myxoid chondrosarcoma, and low-grade fibromyxoid sarcoma) with angiectatic hyalinizing and/or fibrinoid vascular changes. Immunohistochemical assays of the tumor cells were negative for S-100 protein and CD34. An MFS typically arises in the subcutaneous tissue of the extremities of elderly patients, while fibromyxoid sarcoma commonly arises in the skeletal muscle of young patients.<sup>9</sup> A PHAT may evolve into a high-grade sarcoma, or it may be a histological pattern rather than a true disease entity. Mitsuhashi *et al.*<sup>8</sup> suggested that PHAT-like MFS cases may not be as rare as believed, although they did not find early PHAT lesions in their case.

In conclusion, a PHAT should be considered a provisional entity: a mesenchymal tumor of low to intermediate malignant potential, or a nonspecific morphological pattern associated with inflammatory vascular reactions in many soft-tissue tumors. We would argue that the current WHO classification of PHAT as a benign tumor should be revised. We also advise caution in the diagnosis of PHAT based on a small biopsy of a subcutaneous mass from the extremity of an elderly patient because some ar-

eas of a high-grade sarcoma may show PHAT-like features. Further cytogenetic and molecular studies with long-term clinical follow-ups are necessary to clarify the biological behavior of PHATs.

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