Malignant Myopericytoma: Report of a New Case and Review of the Literature

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Abstract: Malignant myopericytoma is a rare entity with only 8 cases reported in the English literature. The authors report a case of a 65-year-old man with a slow-growing 8-cm nodule on the right arm. Marginal excision was performed, and a diagnosis of malignant myopericytoma was made based on histopathologic and immunohistochemical aspects. These tumors are characterized by a proliferation of round-to-spindle cells of myoid appearance in a concentric perivascular arrangement, along with malignant cytological findings. By immunochemistry, the cells were positive for smooth muscle actin and negative for desmin, cytokeratin AE1/AE3, S100 protein, Melan-A, p63, CD99, bcl-2, CD10, and STAT-6. No membranous expression of type IV collagen was observed. These tumors are associated with aggressive biological behavior and most develops metastases.

Key Words: malignant myopericytoma, perivascular neoplasm, myoid, skin, soft tissue

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INTRODUCTION

After Stout's original description of hemangiopericytoma,[1] it seems that a variety of "vascular" benign and malignant tumors may have a hemangiopericytic pattern. Relationship between hemangiopericytoma and pericytes was frequently not confirmed by ultrastructural and immunohistochemical evaluation. In 1996, Requena et al[2] proposed the term myopericytoma as an alternate name for solitary myofibroma, basing their argument on its myopericytic differentiation. In 1998, Granter et al[3] adopted the term myopericytoma and argued that myopericytoma, myofibromatosis, solitary myofibroma, and infantile hemangiopericytoma form a single morphological spectrum of tumors that show differentiation toward perivascular myoid cells/pericytes. In 2002, McMenamin and Fletcher[4] broadened this spectrum with a report of 5 malignant myopericytomas (MMPCTs) and showed that they are associated with aggressive biological behavior. We performed a review of the English literature and found 3 additional cases described in the last 9 years.[5–7] Finally, we report a new case of MMPCT that shares the histological and immunohistochemical findings as described by McMenamin and Fletcher.[4]

CASE REPORT

We report a 65-year-old man who presented with a painless tumor, which had been growing slowly for a few months on the right arm. Physical examination revealed an 8-cm nodular tumor on otherwise normal skin. His medical history was not significant. The main clinical differential diagnosis was dermatofibrosarcoma protuberans. A surgical total excision was tried, and the specimen was sent for histopathologic examination. Macroscopic examination revealed a 7.6 × 6.0 cm nodule covered by a focally ulcerated epidermis (Fig. 1). On section, the lesion occupied the entire dermis and the subcutis with gray-whitish appearance and pushing rather than infiltrating borders. Microscopic examination showed a dermal–hypodermal unencapsulated confluence of poorly defined nodules around discrete hemangiopericytoma-like vascular spaces (Fig. 2A). Perivascular concentric growth of tumor cells was present (Fig. 2B). These nodules were composed of round-to-oval or short spindle-shaped cells with amphophilic or eosinophilic pale cytoplasm. The cells showed ill-defined borders, vesicular nuclei, and myoid features. Some areas of cells with central nuclei had glomus

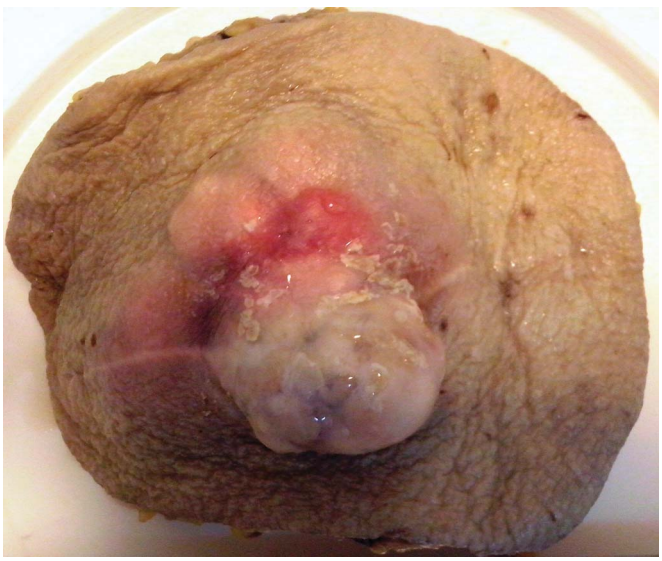

FIGURE 1. Malignant myopericytoma. Ex vivo photography of the cutaneous nodule.

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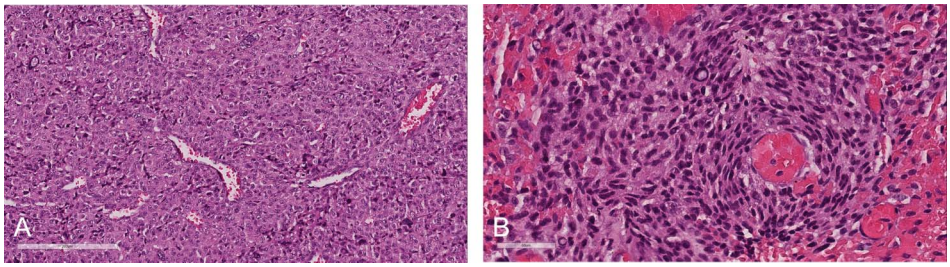

FIGURE 2. A, Malignant myopericytoma. Tumor cells around discrete hemangiopericytoma-like vascular spaces (H&E, ×200). B, Malignant myopericytoma. Perivascular concentric growth of tumor cell (H&E, ×400).

appearance (Fig. 3A). Nuclear pleomorphism was widespread with large size, anisocariosis, multilobulation, macronucleoli, and giant pseudoinclusions (Fig. 3B). A mitotic count of 22 mitoses per 10 high power fields (HPF) was identified. Necrosis "en masse," lymphovascular invasion, and neural permeation were also observed (Figs. 4A and B). Tumor cells stain diffusely for smooth muscle actin (SMA) (Fig. 5) and calponin, and they were negative for desmin, cytokeratin AE1/AE3, S100 protein, Melan-A, p63, CD99, bcl-2, CD10, and STAT-6. No membranous expression of type IV collagen was observed. Stain for CD34 was positive for the normal endothelial cells and negative for tumor cells. The spectrum of histomorphological and immunohistochemical findings was congruent with a diagnosis of MMPCT. Staging studies were negative for metastatic disease.

DISCUSSION

In 1998, Granter et al[3] adopted the term myopericytoma to describe a benign tumor with concentric perivascular proliferation of oval-to-spindle cells that show apparent differentiation toward perivascular myoid cells/pericytes. MMPCT shows the same histological and immunohistochemical characteristics but exhibit malignant features of the tumor cells as high cellularity, high mitotic index, pleomorphism, necrosis, and sometimes lymphovascular invasion and perineural infiltration. MMPCT are exceedingly rare and only 8 cases have been reported in the English literature. We report a new case of MMPCT based on the histopathologic and immunohistochemical features described by McMenamin and Fletcher,[4] in the dermis and subcutis of the right arm. In Table 1, we present an overview of the clinical data, gross findings, treatment, and follow-up of these 9 cases. The largest series of 5 cases was published by McMenamin and Fletcher[4] in 2002, and 3 others authors[5–7] reported isolated cases. In this review, the median age of occurrence was 54.5 years and the male:female ratio was 5:3. The tumors reported had a wide anatomical distribution, arising subcutaneous/dermal or intramuscular in the extremities (n = 4), neck (n = 1), or deep-seated location, mediastinum (n = 1) with disseminated metastatic disease at presentation, periampullary (n = 1), and left atrium (n = 1). Our case, like most, occurred in a male and was located in the subcutaneous/dermal tissue of an extremity. The presenting symptoms in 5 cases were a growing mass,[4,5] painful (cases 2 and 3),[4] or painless (cases 1 and 4).[4] Macroscopically, the average size of the tumor was 5.82 cm (1.5–13 cm). The size was not specified in 1 case.[5] Most cases appeared well-defined but not encapsulated. Two cases were ill-defined.[4,5] The color of the lesions varied (white, gray purple, tan, or red). Microscopically, 6 cases showed a perivascular concentric growth accentuation.[4,7] This striking tendency for concentric perivascular growth is not a feature in malignant glomus tumors.[8,9] Vascular holes with a staghorn pattern were present in 4 cases.[4,7] Focal myxoid stroma was described in 3 cases.[4,6] A focal morphological overlap with malignant glomus tumor was reported.[4] The

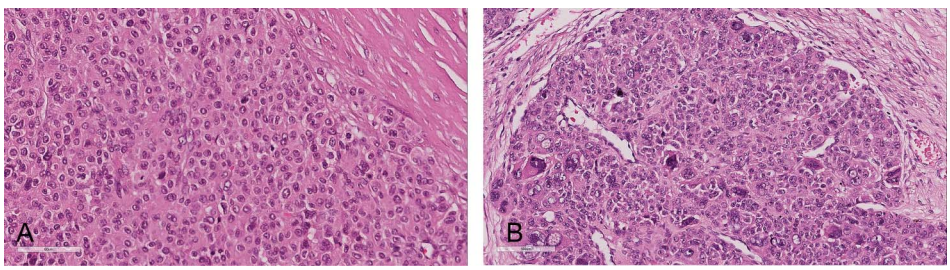

FIGURE 3. A, Malignant myopericytoma. Areas of cells with glomus appearance (H&E, ×400). B, Malignant myopericytoma. Round-to-oval cells with marked nuclear pleomorphism (H&E, ×400).

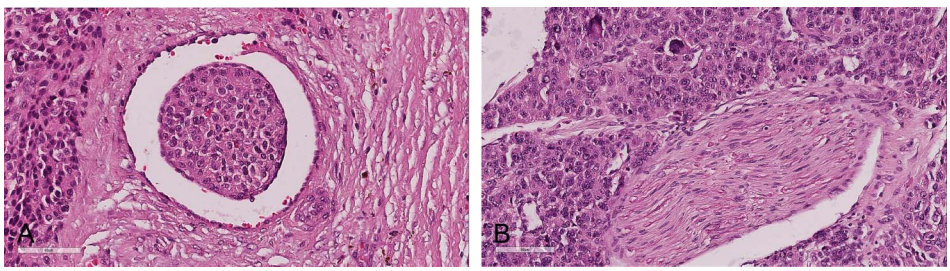

FIGURE 4. A, Malignant myopericytoma. Lymphovascular invasion (H&E, ×400). B, Malignant myopericytoma. Neural permeation (H&E, ×400).

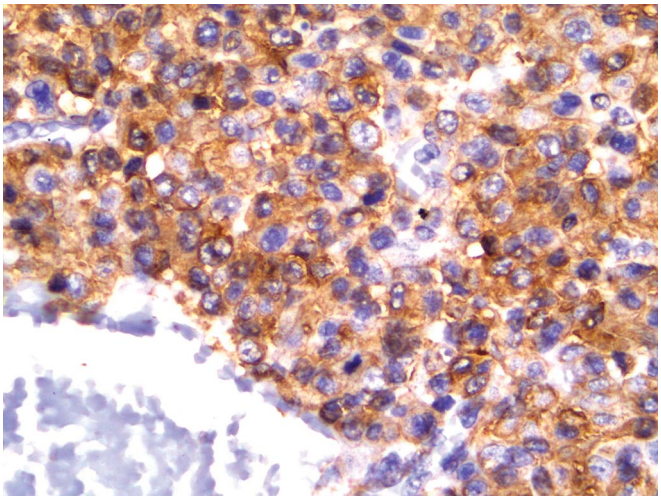

FIGURE 5. Malignant myopericytoma. Tumor cells stain diffusely for smooth muscle actin (H&E, ×400).

tumor cells were round, oval, or spindle shaped. Nuclear pleomorphism was seen with prominent nucleoli, hyperchromatism, and multilobulation in most tumors. Mitoses were numerous in all cases with an average of 27/10 HPF (12–48/10 HPF), and atypical mitotic figures were frequently described. Necrosis was a feature in 5 cases.[4,6,7] Vascular invasion was a feature in 2 cases.[4,6] Immunohistochemical studies revealed that 7 cases were positive for SMA,[4,5,7] in 1 case h-caldesmon was positive and SMA was not discussed.[6] McMenamin and Fletcher[4] interestingly described a case where tumor cells were positive for SMA, and focally for EMA and cytokeratin (AE1/AE3), the unique case in their study with this immunohistochemical particularity. Desmin expression was focally positive in case 3 of the McMenamin series with a "dot-like" pattern of staining.

In view of the morphological findings, 2 pertinent differential diagnoses are worth considering. Malignant glomus tumor (glomangiosarcoma) is a closely related entity within the pericytic family of tumors and can show morphologic overlap. In contrast to MMPCTs, they do not show the characteristic perivascular concentric multilayering of cells. On occasion, there may be a residuum of precursor glomus tumor around the malignant counterpart.[8–11] It is now well-established by some authors that malignant glomus tumors have an immunohistochemical membranous expression of collagen type IV.[9–11] No evidence of membranous expression of collagen type IV was found in our case.

Malignant solitary fibrous tumor is exceedingly rare; all cutaneous tumors reported so far have behaved in a benign fashion. Typical histologic features for malignant solitary fibrous tumors are small fibroblast-like cells

TABLE 1. Clinical Features of All Reported Cases of Malignant Myopericytoma

Cases	References	Sex/ Age	Site	Presenting Symptoms and Relevant History	Gross Description	Treatment	Follow-up
1	McMenamin and Fletcher[4]	F/81	Soft tissue of the left side of neck	Rapidly growing painless mass of 2 mo history. Previous site of a resected melanoma in situ	2.0-cm subcutaneous mass	Marginal excision	Liver metastasis 9 mo after diagnosis. Alive with disease at 24 mo
2	McMenamin and Fletcher[4]	M/46	Intermuscular mass of the left posterior thigh	Painful mass of unstated duration	13.0-cm intermuscular mass, myxoid with central firm area	Marginal excision, postoperative external beam radiation	Metastasis to the heart, brain, liver, and bone after 6 mo. Dead of disease at 7 mo
3	McMenamin and Fletcher[4]	M/19	Dermis/Subcutis of the right foot heel	Enlarging painful mass. History of multiple poorly circumscribed glomus tumors of the sole of right foot × 6 yrs. External Beam radiation 5 yrs earlier.	4.0-cm infiltrative tumor in the dermis/subcutis invading muscle and calcaneus bone	Below-knee amputation	Metastatic disease and death within 1 yr (exact time of death not available)
4	McMenamin and Fletcher[4]	F/80	Superficial mass of the left upper arm	Painless superficial mass of unstated duration	1.5-cm mass	Marginal excision followed by wide excision	No metastasis. Discharged after 8 mo of follow-up. Patient as not represented since. Believed to be disease free at 20 mo

(*continued on next page*)

TABLE 1. (*Continued*) Clinical Features of All Reported Cases of Malignant Myopericytoma

Cases	References	Sex/ Age	Site	Presenting Symptoms and Relevant History	Gross Description	Treatment	Follow-up
5	McMenamin and Fletcher[4]	F/67	Mass in the superior mediastinum	Short history of superior vena cava syndrome. Large mediastinal mass found on imaging. Multiple cutaneous and subcutaneous metastases developed rapidly	10.0-cm mass abutting the lung and lower pole of enlarged thyroid (goiter)	Excision of 1 cutaneous metastatic deposit	Metastasis disease to the skin and subcutis. Dead of respiratory failure within 1 mo
6	Mentzel et al[5]	M/61	Lower leg	Subcutaneous mass of unstated duration	Ill-defined mass (size not specified)	Marginal excision, recurrence after 12 mo treated by wide excision with negative margins	Free disease at 3 yrs
7	Ramdial et al[6]	M/30	Periampullary	Obstructive periampullary mass with jaundice that indented the duodenum and bulged into the common bile duct lumen in a HIV patient	5.0-cm circumscribed pseudocapsulated mass	Biopsy and pancreaticoduodenectomy 2 mo later	Liver metastasis 8 mo after diagnosis
8	Mainville et al[7]	M/52	Floor of the left atrial wall	Sudden decrease in left vision. Work-up revealed right occipital mass (metastasis) and left atrial mass. Vertebral and liver metastases discovered 3 mo later	5.3-cm rubbery atrial mass with focal hemorrhage and necrosis	Marginal excision of cardiac mass. Positive margins. Excision of metastatic brain tumor followed by γ-knife radiotherapy. Laminectomy and vertebral fixation	Alive with metastatic disease at 8 mo
9	Our case	M/65	Dermis/subcutis of the right arm	Enlarging painless mass of unstated duration	8.0-cm infiltrative tumor in the dermis/subcutis. Unencapsulated, with pushing borders. Tan-white cut section with areas of hemorrhage and necrosis	Marginal excision of the mass. Positive margins	Free of disease after 5 mo

arranged in the well-characterized "patternless pattern" of architecture, hemangiopericytoma-like vessels and areas with dense collagen along with malignant cytological features, lymphovascular invasion, and neurotropism. In contrast to MMPCTs, they do not show the characteristic perivascular concentric multilayering of cells. By immunochemistry, these tumors express Vimentin, CD 34, CD99, bcl-2, and STAT-6. In contrast to MMPCTs, they do not show expression for SMA.

The therapeutic options were individually decided. Marginal excision is the major option when metastases are excluded after proper staging and was practiced in 5 cases.[4,5,7] Three patients died after developed metastasis[4] and 5 were alive,[4–7] 3 of the 5 with metastatic disease.[4,6,7]

In summary, we have reported a new case of the rare entity MMPCT and review the 8 cases published in the English literature. A careful examination of a proliferation of round-to-spindle cells with myoid appearance in a concentric perivascular arrangement along with malignant cytological findings, and positive immunophenotype for the SMA, will facilitate a prompt diagnosis and the initiation of appropriate therapy. MMPCTs showed aggressive biological behavior with metastases occurring within the first year of evolution. Only 2 cases were free of

metastatic disease, remarkably one of these cases showed a focal positivity for cytokeratin (AE1/AE3).[4] The follow-up period for our patient is as yet short-term; the patient is free of disease after 5 months. It is clear in this study, however, that metastatic disease can appear later and a long-term follow-up period is strongly recommended.

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