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CASE REPORT

A Case of Pseudomyogenic Hemangioendothelioma of the Lower Extremity

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Pseudomyogenic hemangioendothelioma (PMH) is a rare vascular tumor and was recently recognized as a distinct entity. It has a predilection for young male adults and it frequently occurs in distal extremities. Although it is known to follow an indolent course, multi-focal presentation and local recurrence are common. PMH should be differentiated from epithelioid sarcoma, epithelioid hemangioendothelioma, dermatofibrosarcoma protuberans, and rhabdomyosarcoma. Its characteristic immunohistochemical staining pattern and recurrent translocation t(7:19)(q22:q13) are the basis for its diagnosis. Surgical excision is the mainstay treatment, although chemotherapy can be considered in non-operable patients. We present a rare case of a 40-year-old Korean male patient diagnosed with PMH through an excisional biopsy to facilitate the recognition PMH in the clinical practice. **(Ann Dermatol 32(5) 426～429, 2020)**

-Keywords-
Epithelioid cells, Hemangioendothelioima, Leg, Soft tissue neoplasms

INTRODUCTION

Pseudomyogenic hemangioendothelioma (PMH), also known as epithelioid sarcoma-like hemangioma, is a rare, indolent, low-grade vascular tumor. It was first described by Mirra et al.[1] in 1992 as a fibroma-like variant of epithelioid sarcoma. Billings et al.[2] proposed the term epithelioid sarcoma-like hemangioendothelioma in 2003 as they demonstrated the expression of endothelial markers in a series of soft-tissue neoplasms that have similar morphological and immunophenotypical features as those of endothelial sarcoma[3]. In 2011, Hornick and Fletcher[4] elucidated the clinicopathological identity of this disease and proposing to label it as PMH. The term "pseudomyogenic" refers to its histopathologic pattern which is similar to that of myoid and epithelioid tumors.

PMH usually presents as solitary or multiple, ill-defined, firm, cutaneous nodules and has a predilection for the lower extremities. The lesion can be asymptomatic or painful. It occurs in multiple anatomical sites including dermis, subcutaneous tissue, bone, and muscle.

Due to its rarity and clinicopathological similarity to other cutaneous, mesenchymal neoplasms, misdiagnosis can be made leading to inappropriate management. Although differential diagnosis includes comprehensive diseases, it is important to distinguish PMH from epithelioid sarcoma which follows a more aggressive course and with a poor prognosis. Herein, we present a rare case of a 40-year-old male patient diagnosed with PMH to guide proper diagnosis and management.

CASE REPORT

A 40-year-old male was referred to the dermatology department for multiple nodules on his left foot and left calf. It developed initially on the medial side of left first meta-

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tarsal 1 year prior and erythematous nodules on left calf progressively developed after the original lesion was detected. He had pain whenever he walked. The magnetic resonance imaging and positron emission tomography-computed tomography of his lower left leg revealed multiple nodules located in the skin and muscles and possibility of

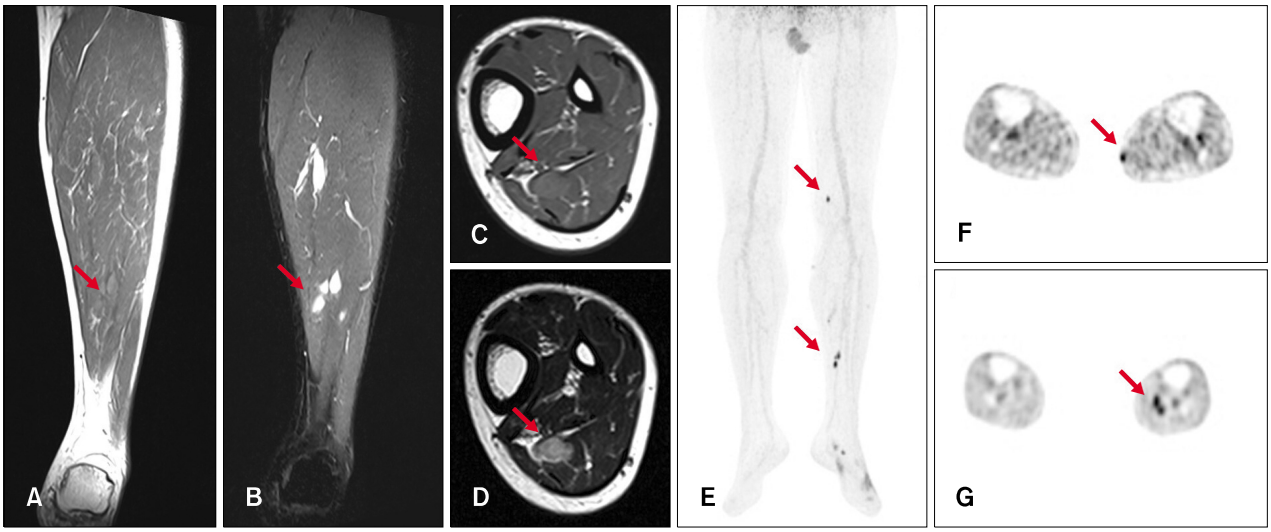

Fig. 1. Magnetic resonance imaging of pseudomyogenic hemangioendothelioma patient. (A～D) Magnetic resonance imaging of axial T1 image (A), axial T2 image (B), coronal T1 image (C), and coronal T2 fat-saturated image (D) shows several well defined nodules in the skin and gastrocnemius muscle with T1 intermediate, homogeneous enhance and T2 high signal intensity (arrows). (E～G) Positron emission tomography-computed tomography reveals multiple hypermetabolic lesions on skin and muscle (arrows).

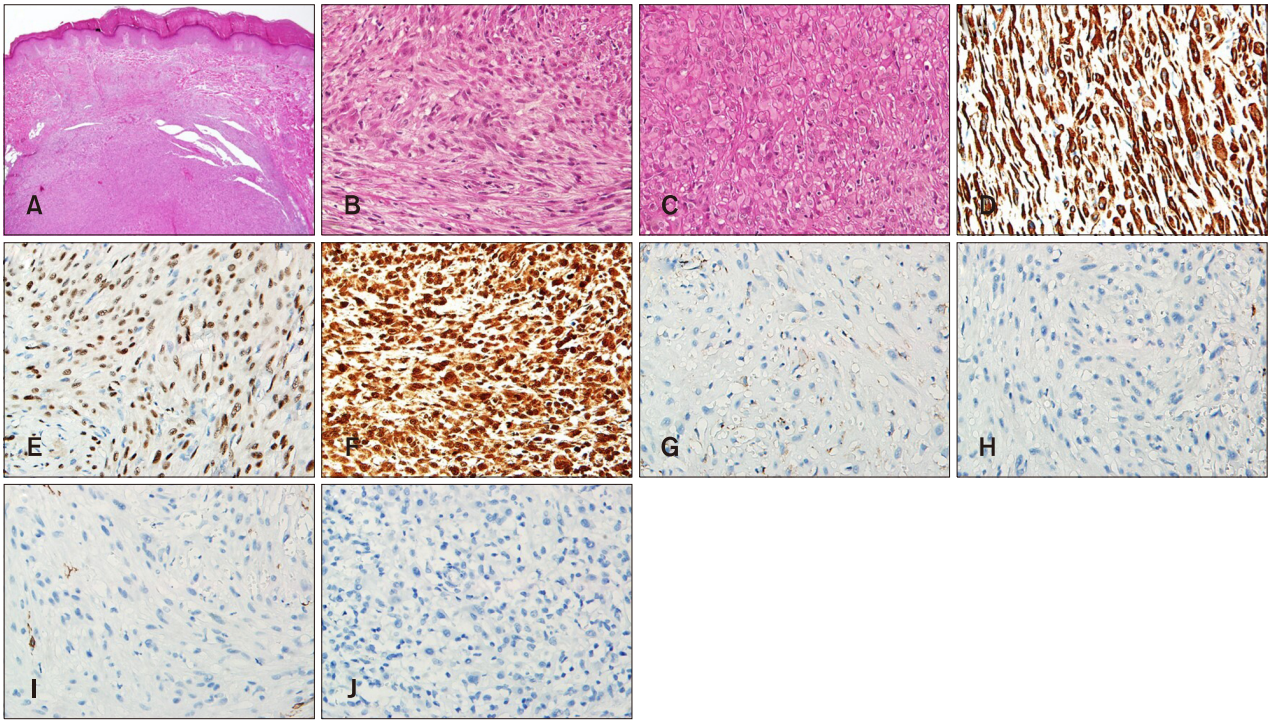

Fig. 2. Histopathological and immunohistochemical features of the pseudomyogenic hemangioendothelioma patient. (A) Histopathological staining reveals a lesion involving the middle and deep dermis on the scanning power (H&E, ×40). (B) Plump spindle cells arranged in a fascicles-like pattern can also be observed (H&E, ×200). (C) Rhabdomyoblastic-like to epithelioid type cells with abundant eosinophilic cytoplasm were noted (H&E×200). (D～J) The tumour cells are immunoreactive for (D) AE1/AE3, (E) nuclear ERG and expression of (F) INI-1 was intact while focal positivity for (G) CD31 and negative reaction for (H) CD34, (I) smooth muscle actin, and (J) desmin (×400).

myxoma was suggested (Fig. 1). The excision biopsy of his left foot and left calf performed at a private clinic two months previously had revealed Kaposi sarcoma. The patient denied any specific familial or personal history. Nodules were not palpable on the physical examination. The laboratory test was within the normal range. The histopathological review of the excised biopsy revealed pleomorphic spindle to epithelioid mesenchymal neoplasm with increased vascularity and inflammatory cell infiltration. Spindle-shaped cells had ovoid nuclei and prominent eosinophilic cytoplasm and showed fascicles-like arrangement (Fig. 2). Immunohistochemical staining showed that cytokeratin and nuclear ERG were positive and the expression of INI-1 was intact while CD31 was focally positive and CD34, smooth muscle actin, and desmin were negative (Fig. 2). Based on the clinical features of multiplicity and pain and the results of the immunohistochemical stain, the diagnosis of PMH was established. Following the diagnosis, the imaging workup including computed tomography, and whole-body proton emission tomography was performed and which excluded systemic metastasis. The patient was educated regarding the recurrent course of the disease and was referred to the oncology department for chemotherapy. However, the patient decided to follow up without additional treatment for a period of five months and without evidence of recurrence. The written informed consent about publishing all photographic materials was obtained from all patients.

DISCUSSION

PMH was included in the WHO classification in 2013 and is listed as an intermediate grade, rarely metastasizing vascular malignancy. It predominantly affects young adults ranging from 20 to 40 years of age and occurs more frequently in male patients and with a male:female ratio of 4.6:1[5,6]. The most frequent location is a lower extremity, accounting for 60% of the cases. However, the upper extremities, trunk, face, and scalp can also be involved[5]. Approximately 66% of these patients have multifocal or a single mass with satellite nodules at the time of their presentation, and thus implying local metastasis[7]. Interestingly, it can be developed in multiple planes of tissue, with muscle (34%) being the most common followed by dermis (31%), subcutaneous tissue (20%), and bone (14%)[8]. The tumor size usually ranges from 1 to 2.5 cm.

The exact etiology and pathogenesis remain obscure. Hornick and Fletcher[4] reported a recurrent translocation t(7:19)(q22:q13) resulting in fusion of SERPINE1 and FOSB in their studies of PMH. This specific genetic feature has not been observed in other neoplasms. Therefore, detection of nuclear FOSB with a specific antibody can be used for a more accurate differential diagnosis[9,10].

The diagnosis is made based on the histopathological and immunohistochemical staining. Microscopically, tumors are composed of plump spindle or polygonal cells with vesicular nuclei and small nucleoli[7]. However, the shape of cells can be variable and a rhabdomyoblast-like or epithelioid type with abundant eosinophilic cytoplasm can also be observed[6,7]. They are arranged in ill-defined sheets, infiltrating surrounding tissue. Nodules or a fascicles-like arrangement can also be seen. Cellular pleomorphism is occasionally prominent but atypia is minimal. The mitotic activity is low and necrosis is rare[2,5]. Conspicuous inflammatory infiltration is common and neutrophils are prominent in 50% of the cases[7].

Immunohistochemically, the tumors are characterized by the fact that they show a broad expression of cytokeratin (AE1/AE3)[2,5,7]. The nuclear FLI-1 and ERG are expressed in all cases and CD31 is expressed in 50% of the cases, implying endothelial differentiation[2,7]. However, inconsistency of CD31 reactivity and complete lack of CD34 expression as well as lack of apparent histologic evidence for endothelial differentiation are distinct feature of PMH compared to other hemangioendothelioma[4]. Moreover, nuclear INI1 is retained in contrast to epithelioid sarcoma. Staining for EMA is usually weak and smooth muscle actin is positive in one-third of the patients[4,5]. S100 protein, desmin, pancytokeratin MNF-116, podoplanin, Prox-1, and Lyve-1 are typically negative[5,9]. Differential diagnoses include epithelioid sarcoma, epithelioid hemangioendothelioma (EHE), dermatofibrosarcoma protuberans (DFSP), Kaposi sarcoma and rhabdomyosarcoma[5,11,12]. Due to its similarity, PMH is also referred to as epithelioid sarcoma-like hemangioma and it was initially considered as fibroma-like variant of epithelioid sarcoma. Epithelioid sarcoma lacks nuclear expression of INI-1 but expresses EMA, MMF116 as well as AE1/AE3 and CD34 in 50% of the cases[13]. It demonstrates more aggressive clinical and pathological features. EHE demonstrates a cordlike growth pattern with a myxochondroid background. Intracytoplasmic vacuoles are common in EHE. DFSP is distinctive in that it shows a storiform growth pattern and lacelike or honey-comb appearance which is characterized by interdigitating spindle cells within the subcutis. Moreover, DFSP is negative for cytokeratin AE1/AE3. Kaposi sarcoma typically shows sieve-like pattern with human herpes virus 8 positivity which is not observed in PMH. Lastly, spindle cell rhabdomyosarcoma shows more mitoses and expresses desmin and myogenin staining.

The treatment is mostly based on complete surgical excision with a narrow margin. Conservative management is

the mainstay of the treatment due to the indolent clinical feature. Metastasis is very rare, but local recurrence is relatively frequent, usually within two years[7]. Due to its recurrence and multifocality, systemic therapy can be considered, but only limited data are available. Gemcitabine/taxane chemotherapy and the mammalian target of the rapamycin inhibitor has been suggested for the treatment of PMH[14]. Moreover, there is a report that multiple lesions were treated with isolated limb perfusion of melphalan and the tumor necrosis factor alpha was followed by four cycles of ifosfamide and doxorubicin, which remained stable for nine months of follow-up[13]. Also, another study reported a response of multifocal PMH to oral cyclophosphamide and prednisolone[15]. Further studies and clinical trials are needed for establishing the treatment guideline.

In conclusion, we report a rare case of cutaneous PMH in a Korean patient and review its clinical and histopathological characteristics. Due to its rarity and clinically variable presentation, misdiagnosis can be made. Therefore, dermatologists should be aware of this entity for appropriate diagnosis and patient management.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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