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Case Report

Fatal poorly differentiated angiosarcoma of the scalp

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Abstract: Cutaneous angiosarcoma is a very rare but aggressive tumor. Angiosarcoma of the scalp is very rare, and a review of the world literature revealed less than 60 cases. Here, the author reports a case of poorly differentiated angiosarcoma of the scalp. The pathological diagnosis was very difficult. A 70-year-old Japanase man was admitted to our hospital complaining of red mass of the scalp. An excisional biopsy was done. The biopsy showed proliferation of malignant spindle cells in the dermis. Apparent differentiation was not recognized. Invasion into the lateral dermis and subcutis was recognized. There were many mitotic figures and a few foci of necrosis. The size was 2 x 2 x 3 cm. Intracytoplasmic vacuoles were recognized in the malignant tumor cells in some places. A few vague vasoformative features were recognized in one very small area. Immunohistochemically, the malignant spindle cells were positive for factor VIII-related antigen (F-VIII-RA), Ulex lectin, CD31, CD34, vimentin, p53 protein. The Ki-67 labeling was 76%. In contrast, the tumor cells were negative for cytokeratins, epithelial membrane antigen, desmin, S100 protein, α-smooth muscle antigen, bcl-2, melanosome, and myoglobin. The intracytoplasmic vacuoles were strongly positive for F-VIII-RA, Ulex lectin, CD31, and CD34, The abortive vasoformative channels were moderately positive for these endothelial markers. A pathologic diagnosis of angiosarcoma of the scalp was made. Chemoradiation and immunotherapy were performed. However, the tumor recurred several times, and ultimately metastasized to the systemic bones and lungs. The patient died of systemic carcinomatosis 33 months after the first manifestation.

Keywords: Cutaneous angiosarcoma, scalp, for factor VIII-related antigen (F-VIII-RA), Ulex lectin, CD31, CD34, vimentin, p53 protein

Introduction

According to WHO blue book, cutaneous angiosarcoma is defined as a malignant neoplasm of endothelial cells [1]. Almost all cataneous angiosarcomas are aggressive tumors, and are in one of the following settings: the head and neck of predominantly male elderly patients (the most common setting) [2], the chest of the patients who have undergone mastectomy for breast cancer (Stewart-Treves syndrome) [3], lymphoedema (congenital and acquired) or post irradiation [4]. Although angiosarcoma can occur in any locations of the skin, the most common sites are head and neck regions [1, 2]. Here, the author reports a fatal case of poorly differentiated angiosarcoma of the scalp.

Case report

A 70-year-old man noticed a red mass of the scalp. It enlarged gradually, so that he consulted to our hospital. The tumor was present in the scalp, and was a red mass with hard consistency. It measured 3 x 3 x 4 cm. An excisional biopsy of the tumor was performed. Microscopically, the tumor was located in the dermis. The tumor consisted of proliferation of malignant spindle cells without apparent differentiation (**Figure 1A**). The tumor cells were seen to invade into the surrounding dermis and subcutaneous tissue. Many mitotic figures were scattered, and there were a few areas of necrosis. Intracytoplasmic vesicles were recognized (**Figure 1B**) in several areas. A few abortive vasoformative channels were recognized in one very tiny area (**Figure 1C**).

An immunohistochemical study was performed with the use of Dako Envision method (Dako, Glostrup, Denmark). The antibodies used were as follows: cytokeratin (AE 1/3, Dako), cytokeratin (CAM5.2, Beckton-Dickinson, CA, USA), epithelial membrane antigen (E29, Dako),

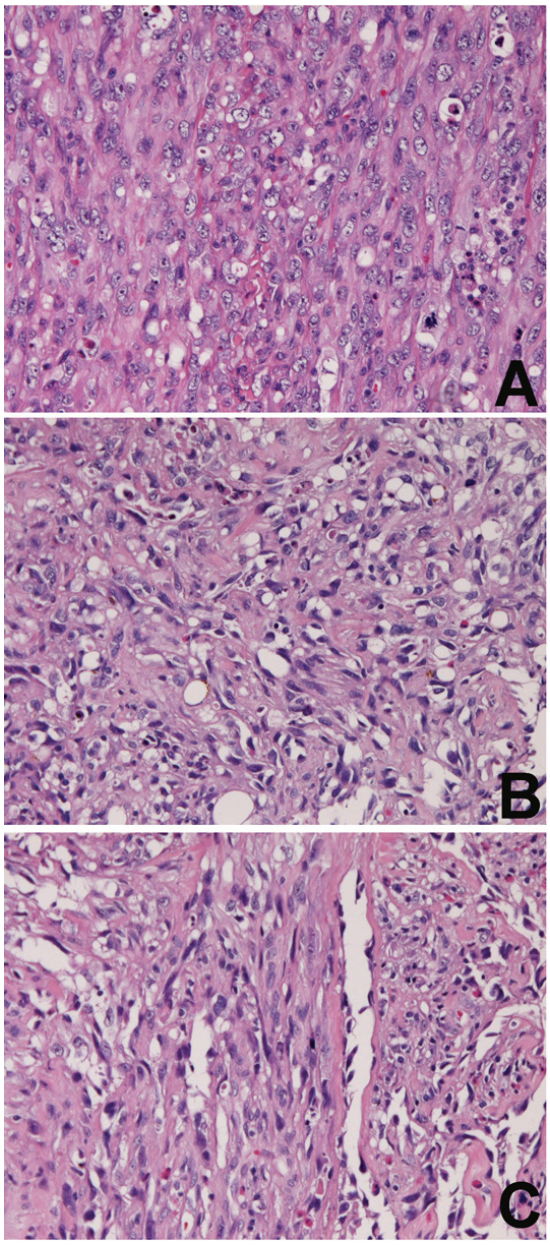

Figure 1. Histological features of the tumor. A: The tumor is composed of malignant spindle cells with hyperchromatic nuclei. No apparent differentiation is recognized. Many mitotic figures are seen. HE, x100. B: Some parts of the tumor contains tumor cells with intracytoplasmic vacuoles. HE, x100 C: A few abortive vascular structures are seen only in one tiny focus. HE, x100.

CD34 (NU-3A1, Dako), S100 protein (polyclonal, Dako), desmin (D33, Dako), α-smooth muscle antigen (1A4, Dako), vimentin (Vim 3B4, Dako), CD31 (JC70A, Dako), p53 protein (DO7, Dako), Ki-67 (MIB-I, Dako), melanosome (HMB 45, DAKO), factor VIII-related antigen (F-VIII-RA) (36B11, Novocastra, Newcastle upon type, UK), bcl-2 (124, Dako), and myoglobin (polyclonal, Dako).

Immunohistochemically, the malignant spindle cells were positive for factor VIII-related antigen (F-VIII-RA), Ulex lectin, CD31 (**Figure 2A**), CD34, vimentin, and p53 protein (**Figure 2B**). The Ki-67 labeling was 76% (**Figure 2C**). In contrast, the tumor cells were negative for cytokeratins, epithelial membrane antigen, desmin, S100 protein, α-smooth muscle antigen, melanosome, bcl-2, and myoglobin. The intracytoplasmic vacuoles were strongly positive for F-VIII-RA (**Figure 2D**), Ulex lectin, CD31, and CD34, The very small number of the abortive vasoformative channels were moderately positive for these endothelial antigens.

A pathologic diagnosis of poorly differentiated high grade angiosarcoma of the scalp was made. The pathologic diagnosis was very difficult because the tumor was very poorly differentiated, and apparent differentiation was not recognized. Chemoradiation and immunotherapy (interleukin 2) were performed. However, the tumor recurred several times, and ultimately metastasized to the systemic bones and lungs. The patient died of systemic carcinomatosis 33 months after the first manifestation.

Discussion

Angiosarcoma of the scalp is very rare. A review of the world literature revealed less than 60 cases [2, 5-7]. In the present report, all the references are not cited because of the space limitation. All cases except for Holden et al [2] are case reports. The review of the literature revealed that the angiosarcoma of the scalp occurs in elderly person [2, 5-7]. Male are much more affected than female [2, 5-7]. The biological behaviors vary, but most showed aggressive growth with metastasis [2, 5-7]. Four cases were associated with Kazabach-Merritt syndrome [6].

The pathologic diagnosis of angiosarcoma is easy when tumor cells forms vascular cannels. However, in the present study the diagnosis of angiosarcoma was very difficult because apparent vascular cannels were not recognized. Instead, the present study, there were foci of

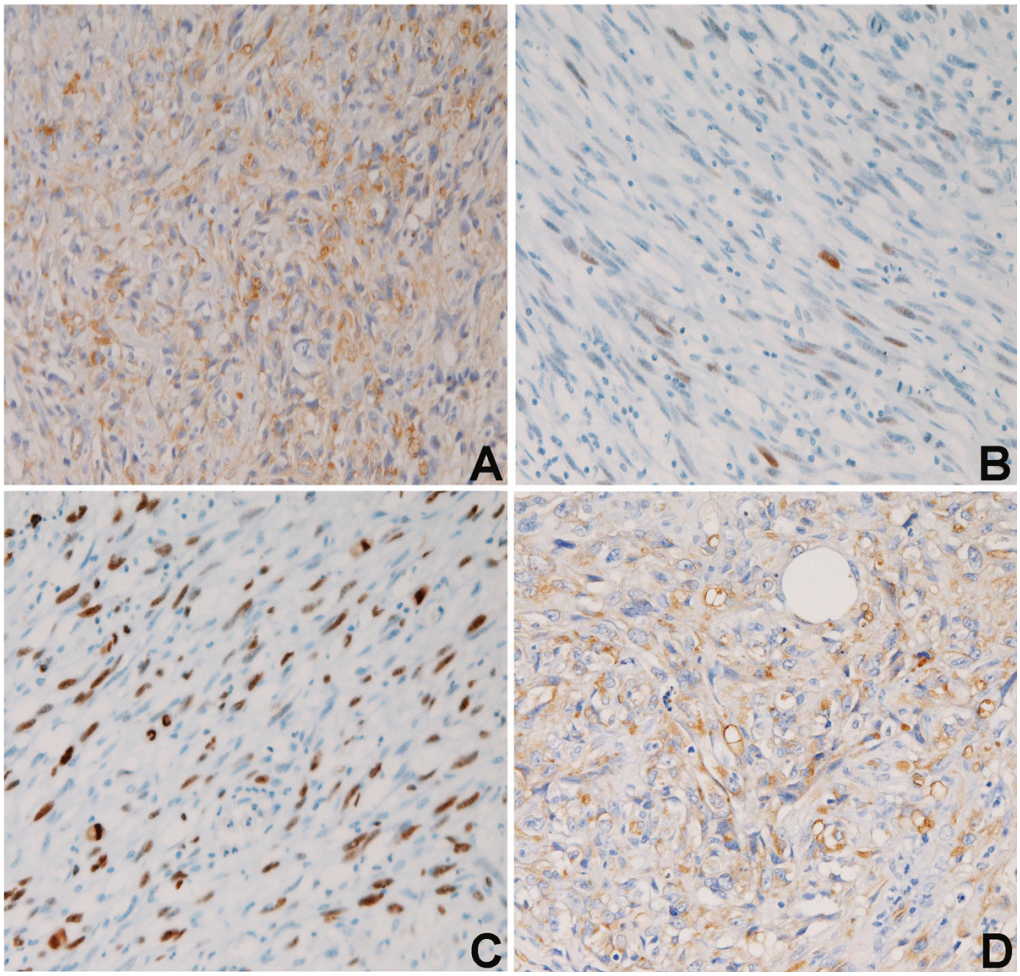

Figure 2. Immunohistochemical features of the tumor. A: The tumor cells are positive for CD31. x100. B: p53 is positive. x200. C: Ki67 labeling is high. x100. D: The tumor cells and intracytoplasmic vacuoles are positive for factor VIII-related antigen. X100

intracytoplasmic vacuoles. They are not pathognomotic for angiosarcoma, but they are suggestive for angiosarcoma [1]. The intracytoplasmic vacuoles may be the only clue of poorly differentiated angiosarcoma, as in the present study. The author could suspect angiosarcoma because of the presence of these structures, but other sarcomas were also possible.

Immunohistochemistry is a powerful tool in the diagnosis of the angiosarcoma, particularly in poorly differentiated angiosarcoma. Well known endothelial antigens are F-VIII-RA, CD31, CD34, and Ulex lectin [8]. Orchard et al [8] reported that Ulex lectin and CD31 are the most sensitive and specific markers of endothelial cells of cutaneous angiosarcoma.

In the present study, the malignant spindle cells were negative for cytokeratins and epithelial membrane antigen and positive for vimentin, indicating that the present tumor was not an epithelial tumor but a mesenchymal tumor. The malignant histologies and immunoreactivities of p53 protein and high Ki-67 labeling (76%) indicated that the present tumor is malignant, i.e. sarcoma. The absence of immunoreactivities of desmin, S100 protein, α-smooth muscle antigen, bcl-2, and myoglobin highly suggests that the present sarcoma is not neurogenic, rhabdomyogenic, smooth muscle myogenic, and lipogenic tumors. The absence of melanosome and S100 excludes malignant melanoma. The presence of F-VIII-RA, Ulex lectin, CD31 and CD34 in the present study highly suggested the endothe-

lial natures of the tumor. The intracytoplasmic vacuoles were strongly positive for F-VIII-RA, Ulex lectin, CD31, and CD34, indicating that these structures are early phase of angiogenesis [1]. Thus, the immunohistochemistry was very useful in making the diagnosis of poorly differentiated angiosarcoma of the present study.

The pathogenesis of angiosarcoma is unclear. In addition to these endothelial antigens, a recent report suggested that Fli-1, which is a nuclear transcriptional factor expressed Ewing sarcoma, is diagnostic marker of vascular neoplasms [9]. Shuborg et al [10] demonstrated that angiosarcomas show frequent rearrangements of 5pter-p11, 8p12-qter, 20pter-q12, losses of 7pter-p15, 22q13-qter, and –Y. There have been no other studies on the pathogenesis other than these reports, to the best of the author's knowledge.

The present angiosarcoma recurred several times, and metastasized to bones and lungs. The patient died of systemic carcinomatosis 33 months after the first presentation. In general, cuteneous angiosarcoma is an aggressive tumor [1]. Holden et al [2] reported that angiosarcomas of head and neck regions have poor prognosis. One half of the patients died within 15 months of presentation [2]. Only 12 % of the patients survived 5 years or more. They also reported that early therapy yielded better survival; thus exact pathologic diagnosis in early state is mandatory [2].

In the present case, the patient was treated by chemoradiation and immunotherapy (interleukin 2). The effects of chemoradiation have been established. The interleukin 2 immunotherapy is effective [11]. Heavy proton bean is suspected to be useful in the treatment of angiosarcoma [2].

In summary, the author reported a fatal case of poorly differentiated angiosarcoma of the scalp. The pathologic diagnosis was very difficult, but an immunohistochemical investigation was very useful.

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