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Case Report

Intimal sarcoma of the abdominal aorta and common iliac arteries presenting as epithelioid angiosarcoma of the skin: a case report

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Abstract: Intimal sarcoma (IS) is the most common type of sarcoma of the aorta. IS tumor emboli can involve various organs, including the skin. However, a limited number of IS cases with an initial presentation of skin metastasis has been reported. Cutaneous metastasis as a form of epithelioid angiosarcoma (EAS) has not been well described. Herein, we present a 61-year-old Japanese man with an initial presentation of EAS of the skin, followed by multiple metastases to the skin as a form of EAS prior to detection of IS of the infrarenal aorta and common iliac arteries. In our case, the IS was CD31 and cytokeratin positive but did not express CD34 and factor VIII-related antigen. The EASs in our case exhibited diffuse CD31 expression, and focal factor VIII-related antigen and cytokeratin expression were observed throughout the tumor, including the neoplastic vascular structure; CD34 expression was not identifiable. IS metastasis to the skin has been documented as a form of angiosarcoma. However, IS metastasis has not been well described as a form of EAS. Our case could prove a morphological change from IS to EAS. Given the rarity of primary cutaneous EAS, it is recommended that primary sites other than the skin should be thoroughly investigated when EAS of the skin is encountered.

Keywords: Intimal sarcoma, aorta, common iliac artery, metastasis, skin, epithelioid angiosarcoma

Introduction

Two types of aortic sarcoma, intimal and mural, have been reported [1]. The intimal type extends along the lumen and often forms intraluminal polyps that cause aortic obstruction or peripheral emboli; the mural type develops in the media or adventitia and usually grows

extramurally to para-aortic tissues [2-4]. The luminal-type intimal sarcoma (IS) is the most common sarcoma of the aorta [5]. IS often involves the abdominal aorta among other large systemic arteries, and it is occasionally observed to span both the abdominal aorta and the iliac artery [5, 6]. Tumor emboli of IS involve various organs, including the skin, brain, lungs, bowels, kidneys, liver, and bones [7]. However, only a few cases of IS presenting initially as skin metastasis have been reported [7, 8]. IS metastasis to the skin has been documented as a form of angiosarcoma [5, 8]. However, IS metastasis as a form of epithelioid angiosarcoma (EAS) has not been well described.

Herein, we present a 61-year-old Japanese man who presented initially with EAS of the skin, followed by detection of IS of the infrarenal aorta and common iliac arteries.

Clinical summary

A 61-year-old Japanese man was seen at an outpatient clinic because of a painful nodule on the penile skin. The patient reported that he had noticed the nodule approximately 1 month before presentation and had not experienced with any recent trauma. At the outpatient clinic, he reported no fever, fatigue, or other specific complaints. Upon clinical examination, a 1-cm nodule was found on the penis. Apart from the penile nodule, his physical examination results were unremarkable, and no swollen lymph

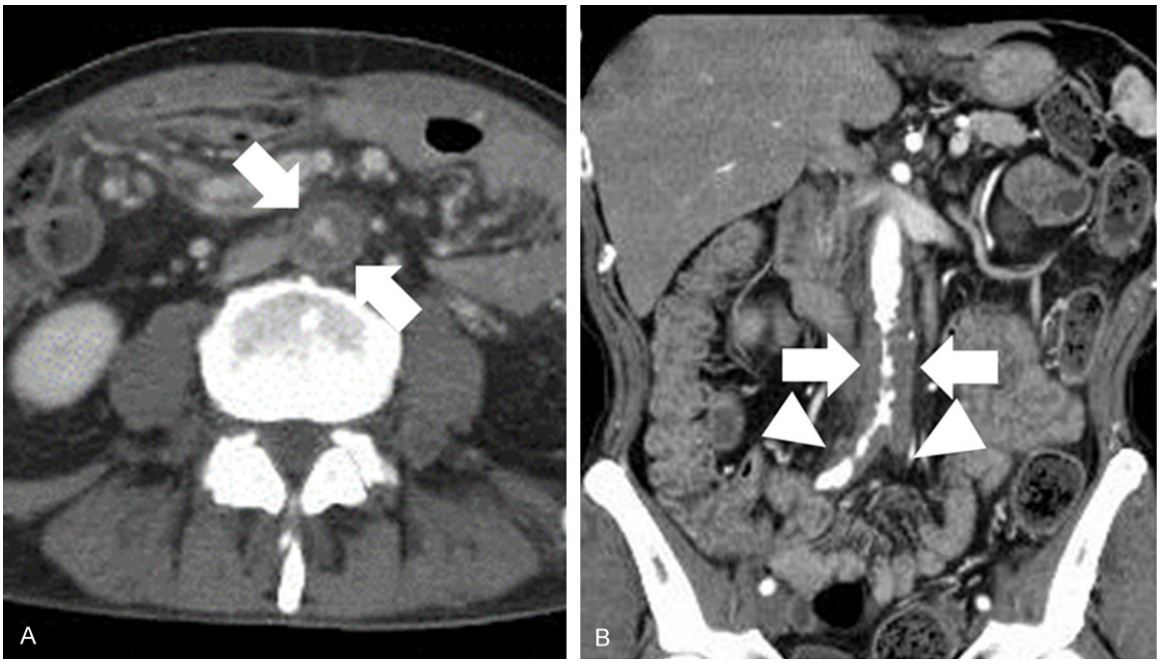

Figure 1. Contrast-enhanced computed tomography. A. Markedly narrowed intraluminal space with a thickened abdominal aortic wall (arrows). B. Wall thickening from below the level of the renal arteries to the bilateral common iliac arteries. Arrows indicate the infrarenal aorta; arrowheads indicate the bilateral common iliac arteries.

nodes were observed. Subsequently, excision of the penile skin nodule was performed. The pathological diagnosis was angiosarcoma. An enhanced computed tomography (CT) scan revealed a few nodules in the lungs; these considered metastases of the cutaneous angiosarcoma to the lung. The patient was referred to our hospital 1 month after presentation at the clinic for intensive examination and treatment. He then complained of another painful nodule on his left abdomen. Another skin excision was performed, and the biopsy results were consistent with angiosarcoma. Positron emission tomography (PET) demonstrated increased tracer uptake in the L5 vertebral body, the left side and S3 level of the sacrum, and the left calcaneus. At that time, primary cutaneous angiosarcoma and metastasis to multiple sites were not considered. Extradermal primary sites were investigated but could not be confirmed. The patient received 5 cycles of docetaxel-based (60 mg/m^2) chemotherapy. Seven months after the initial diagnosis, he developed metastatic disease on his back, groin, and penis. These lesions were excised and he began to receive pazopanib (200 mg/day) therapy. Two months after the excision, he began to exhibit intermittent claudication, and contrast-enhanced CT showed an exacerbating thickened abdominal aortic wall from below the level of the renal arteries to the bilateral common iliac arteries (**Figure 1A**, **1B**). The patient was admitted for vascular surgery. A transplant from the infrarenal aorta to the bilateral common iliac arteries was performed. Pathological findings revealed an IS. Proximal and distal surgical margins were all positive. Besides pain from the left fibula metastasis, the patient recovered well from this major surgical intervention.

Pathological findings

All the skin excision specimens revealed a tumor in the dermis, with a hemorrhagic appearance (**Figure 2A**). The constituent tumor cells, which were nearly identical among the specimens, formed a focal vascular structure (**Figure 2B**). The tumor cells exhibited an epithelioid morphology with enlarged nuclei and prominent nucleoli; some cells had intracytoplasmic lumina (**Figure 2C**). Immunohistochemistry (IHC) revealed that the tumor cells were strongly positive for CD31 (JC70A, 1:100; Dako, Glostrup, Denmark) (Figure 2D), focally positive for factor VIII-related antigen (F8/86, 1:100; Dako) (**Figure 2E**), and strongly positive for pan-cytokeratin, including the area of vascu-

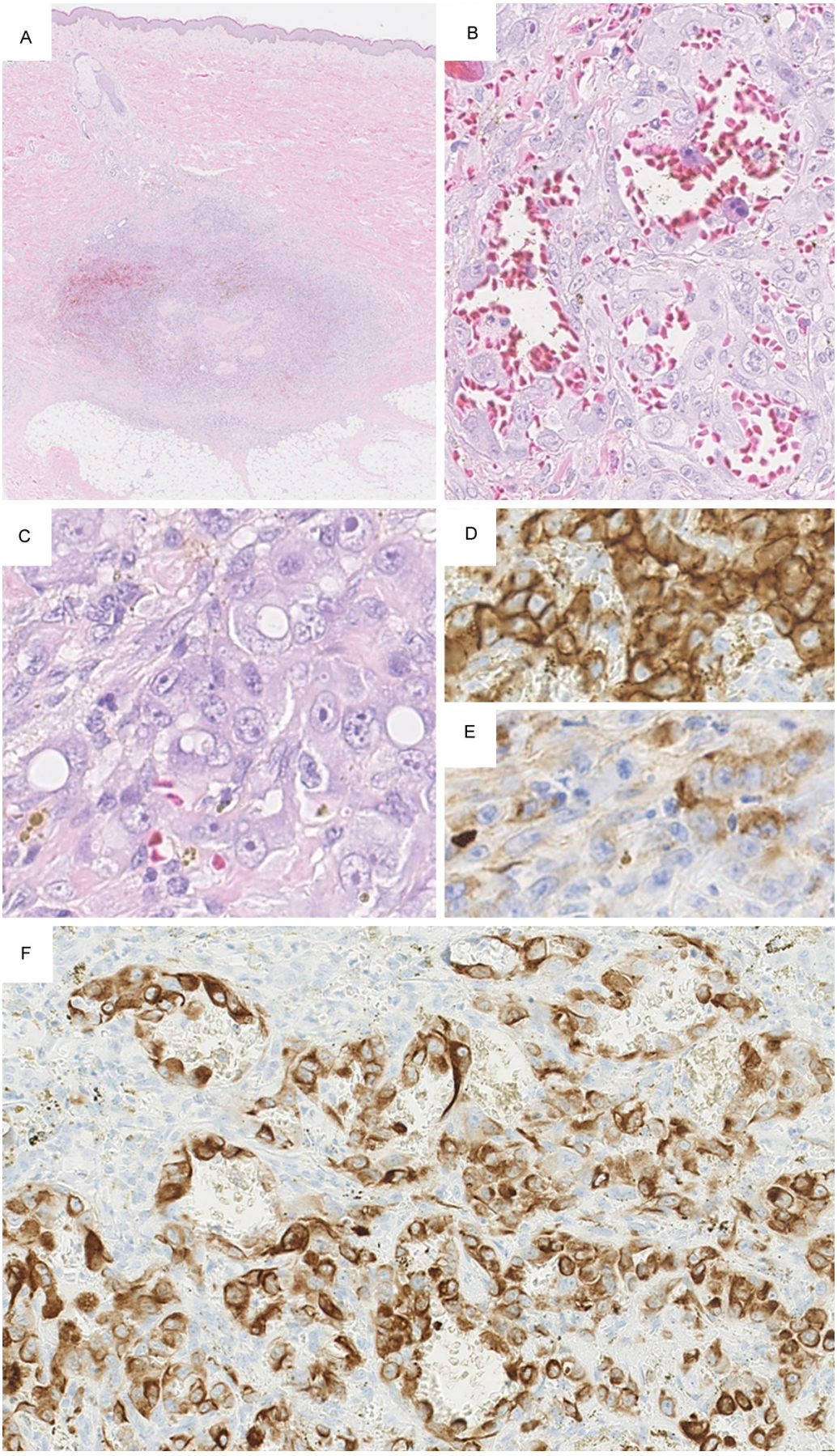
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Figure 2. Microscopic findings of skin excision specimens. A. Representative specimen showed a tumor in the dermis with a hemorrhagic appearance (1.25× magnification). B. Constituent tumor cells were nearly identical among the specimens and formed focal vascular structures (400×). C. Tumor cells exhibited an epithelioid morphology with enlarged nuclei and prominent nucleoli; some cells had intracytoplasmic lumina (600×). D. Tumor cells exhibited strong immunostaining for CD31 (400×). E. Tumor cells exhibited focal immunostaining for factor VIII-related antigen (400×). F. Tumor cells exhibited strong immunostaining for pan-cytokeratin, including the area of vascular formation (400×).

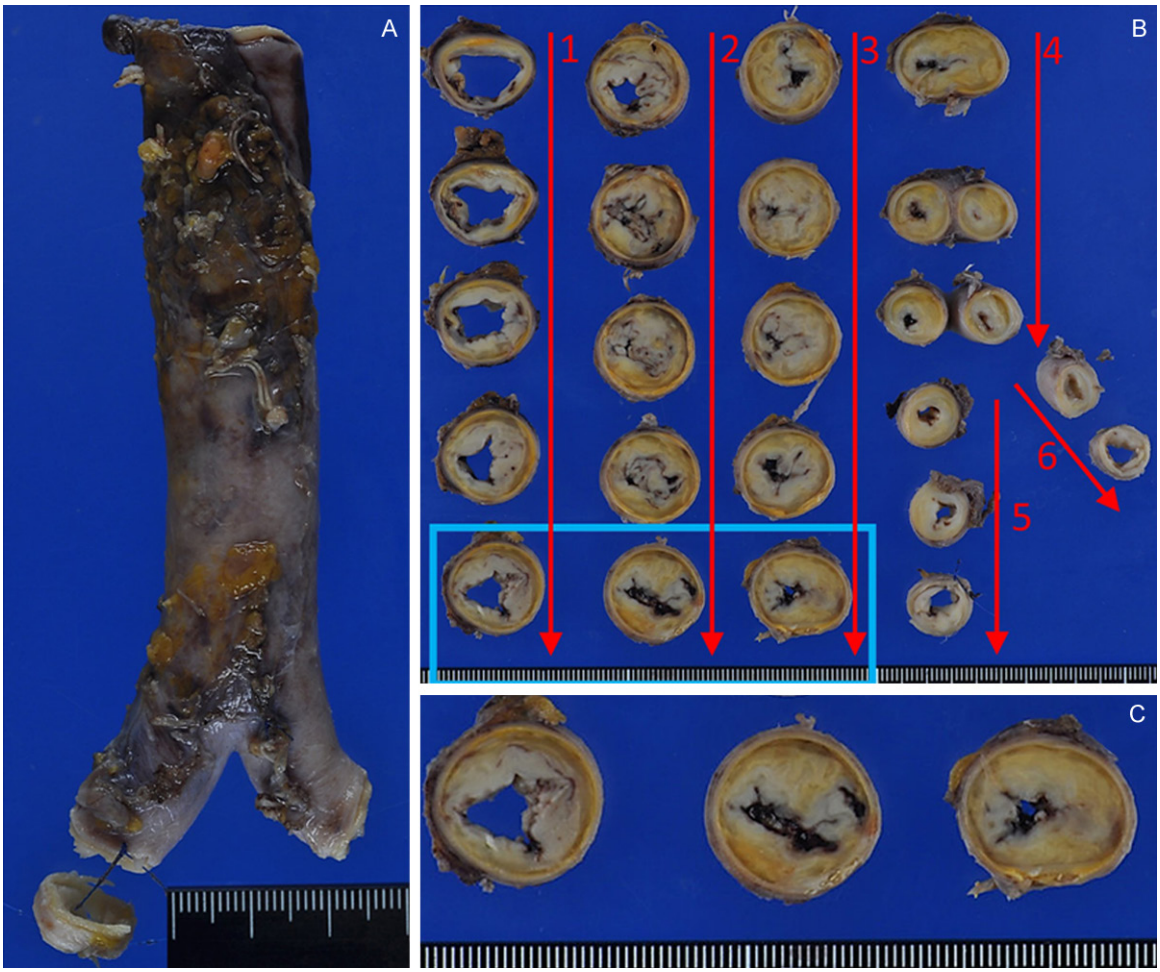

Figure 3. Macroscopic findings of the surgically resected infrarenal aorta and common iliac arteries. (A) Nine centimeters of the infrarenal aorta, 3 cm of the right common iliac artery, 0.5 cm of additional tissue, and 2.5 cm of the left common iliac artery were resected. (B) Cut surfaces are arranged in the direction indicated by arrows from the proximal (1) to the distal (4) portion of the abdominal aorta; the common iliac arteries are indicated by (5) (right) and (6) (left). The cut surface revealed the formation of a whitish thrombus along the entire length of the resected aorta and common iliac arteries. This thrombus nearly occluded the lumen at the center of the resected aorta. (C) Closer view of the boxed area in (B). Yellowish atherosclerosis was observed beneath the whitish thrombus; no mass was apparent.

lar formation (AE1/AE3, 1:100; Dako) (**Figure 2F**); however, the samples were negative for CD34 (QBEnd 10, 1:100; Dako). A diagnosis of angiosarcoma was rendered for each excised specimen.

The surgically resected abdominal aorta and common iliac arteries included 9 cm of the infrarenal aorta, 3 cm of the right common iliac artery, 0.5 cm of additionally resected tissue, and 2.5 cm of the left common iliac artery (**Figure 3A**). The cut surface revealed the formation of a whitish thrombus along the entire length of the resected aorta and common iliac arteries; this thrombus nearly occluded the lumen in the center of the resected aorta

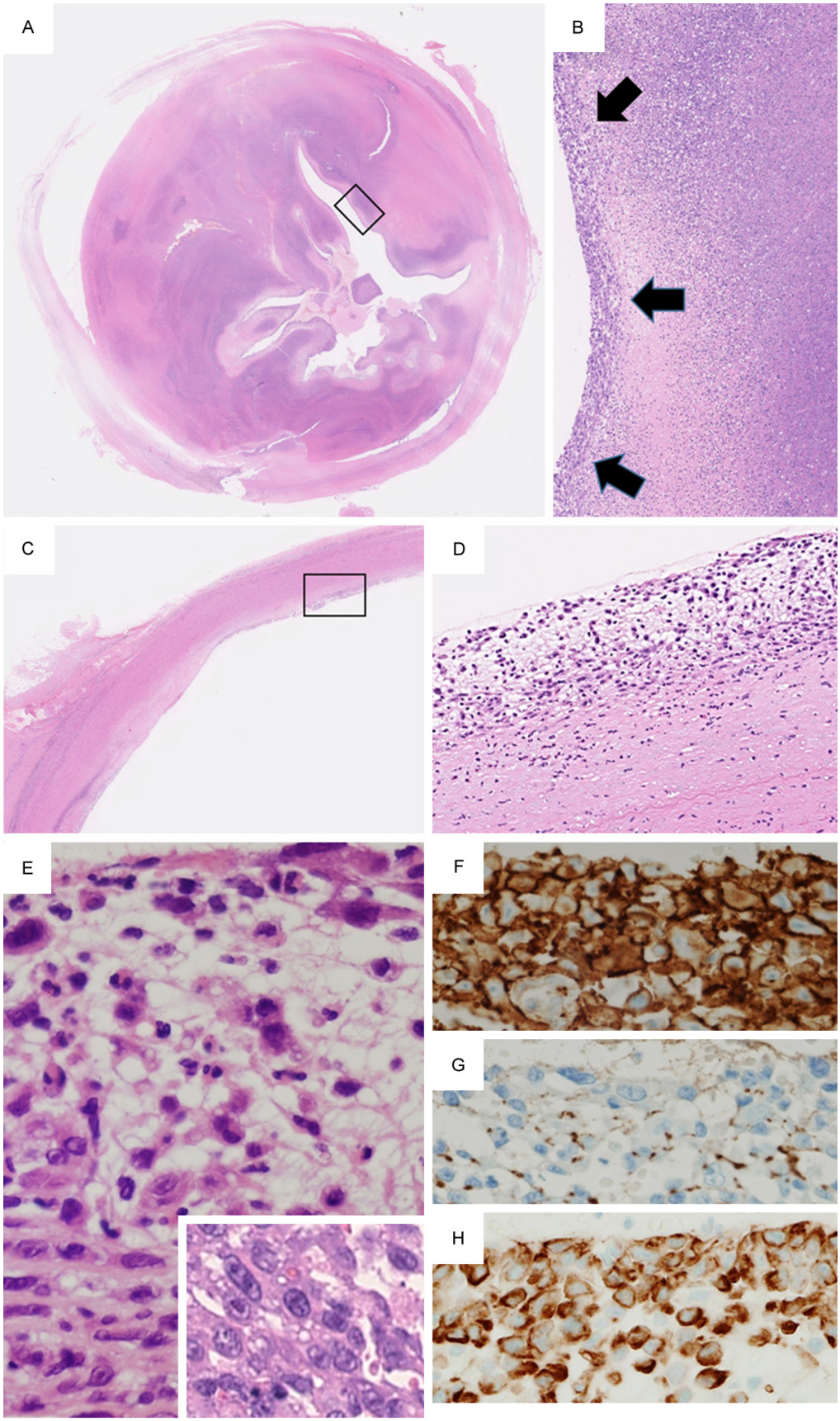
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Figure 4. Microscopic findings of the surgically resected infrarenal aorta and common iliac arteries. (A) A large circumferential thrombus, especially at the central part of the infrarenal aorta (1.25× magnification). (B) Higher magnification of the boxed area in (A). The thrombus surface features a tumor cell layer (arrows) (40×). (C) The thrombus was smaller at the proximal and distal margins and exhibited a patchy distribution, leaving areas with no thrombus present (20×). (D) In areas lacking the thrombus, tumor cells were in direct contact with the intima (200×). (E) Tumor cells with short-spindled to epithelioid morphology formed a layer with polygonal cells at the luminal side and short-spindled cells at the opposite side (400×). Inset: These cells exhibited enlarged nuclei with prominent nucleoli (600×). (F) Tumor cells exhibited strong immunostaining for CD31 (400×). (G) The cells did not exhibit immunostaining for factor VIII-related antigen. However, plasma antigen was immunostained (400×). (H) The cells exhibited positive immunostaining for pan-cytokeratin (400×).

(**Figure 3B**). Yellowish atherosclerosis was observed beneath the whitish thrombus, and no mass was apparent (**Figure 3C**). Histopathological examination of the surgically resected specimen revealed a large circumferential thrombus, particularly at the central part of the infrarenal aorta (**Figure 4A**). A tumor cell layer was present on the thrombus surface (**Figure 4B**). At the proximal and distal margins, the thrombus was smaller and patchily distributed, resulting in areas without thrombus (**Figure 4C**); these areas showed direct contact between the tumor cells and the intima (**Figure 4D**). Tumor cells with a short-spindled to epithelioid morphology formed a layer with polygonal cells at the luminal side and short-spindled cells at the opposite side (**Figure 4E**). These cells had enlarged nuclei with prominent nucleoli (**Figure 4E**, inset). IHC revealed that these cells were strongly positive for CD31 (**Figure 4F**), negative for factor VIII-related antigen (**Figure 4G**) and CD34, and positive for pan-cytokeratin (**Figure 4H**). A diagnosis of IS was rendered.

Upon reviewing the biopsy specimens, we considered that this angiosarcoma might be better classified as EAS, given the epithelioid morphology and pan-cytokeratin positivity.

Discussion

Reports of IHC-detected CD31 and cytokeratin expression in IS vary among studies. CD31 expression, including focal positivity, was previously reported in 13 of 13 cases (100%) [5], 0 of 42 cases (0%) [9], and 13 of 26 cases (50%) [6]; cytokeratin expression was observed in 2 of 13 cases (15%) [5], 6 of 42 cases (14%) [9], and 10 of 26 (38%) [6]. Some authors define CD31-positive IS as angiosarcoma and CD31- and cytokeratin double-positive IS as EAS even if the morphological features of vascular differentiation are not apparent [6]. However, we did not want to describe a case of IS as angiosarcoma if CD31 expression did not accompany morphological vascular differentiation. This viewpoint is supported by a study in which IS was shown to express at least focal CD31 [5]. In our case, although the IS strongly expressed CD31 and cytokeratin, we did not diagnose it as EAS because of its lack of morphological vascular differentiation.

In contrast, the skin metastases of IS in our case expressed these markers along with vascular formation and epithelioid morphology in more than 90% of the constituent tumor cells. The term EAS should be strictly applied to tumors in which more than 80-90% of constituent cells exhibit epithelioid morphology [10]. It was therefore valid to designate the metastatic skin lesions in our case as EAS.

Both primary and metastatic cutaneous angiosarcomas are rare among malignant tumors of the skin. Primary cutaneous angiosarcomas arise in three main settings [11-13]: the head and neck of elderly patients; post-radiotherapy; and in association with lymphedema. Focal epithelioid changes are frequently observed in angiosarcomas arising in these three main settings; however, EAS is more often encountered outside of these settings. EAS is most commonly observed in deep, soft tissue and is rarely encountered as a primary skin tumor [10]. Therefore, when encountering EAS of the skin, it would be wise to consider the possibility that it might be a cutaneous metastasis rather than primary cutaneous tumor. Although cases of cutaneous metastasis of EAS originating in a non-skin site are exceptional [10], cutaneous metastases from cardiac and mediastinal EAS have been documented [14, 15]. In cases such as ours involving multiple skin and internal organ lesions, it would be impossible to determine whether the skin lesion was a primary cutaneous or metastatic lesion [10].

In conclusion, at the metastatic site, IS could change to EAS with vascular formation. Given the rarity of primary cutaneous EAS, primary sites other than the skin should be thoroughly evaluated when encountering EAS of the skin.

Disclosure of conflict of interest

None.

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