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Original Article

Epithelioid hemangioma in the male breast: a rare case report and review of the literature

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Abstract: Objectives: Epithelioid Hemangioma (EH), also known as Angioblastic Lymphoid Hyperplasia with Eosinophilia (ALHE), is a rare benign vascular proliferative disease. Methods: A 61-year-old male presented with a mass in the upper outer quadrant of the right breast, and ultrasound suggested a BI-RADS category 4c lesion in the right breast. Pathological examination revealed vascular proliferation with endothelial proliferation on a background of collagenized fibrosis, with some endothelial cells showing epithelioid changes and protruding into the vascular lumen, accompanied by lymphocytes and a few eosinophilic granulocytes in the stroma. Results: The diagnosis of epithelioid hemangioma was made based on immunohistochemistry. Conclusion: We briefly analyzed the pathogenesis, imaging manifestations, histopathology, and treatment methods of epithelioid hemangioma.

Keywords: Male breast tumor, epithelioid hemangioma, diagnosis and treatment, case report

Introduction

Epithelioid Hemangioma (EH), also known as Angioblastic Lymphoid Hyperplasia with Eosinophilia (ALHE), is a rare benign vascular proliferative disease [1, 2]. It can occur in the skin, soft tissues, and even visceral organs [3], but is rarely found in the breast, and its occurrence in male breasts is even more uncommon, with no related reports to date. In this case report, we describe an extremely rare instance of epithelioid hemangioma in the breast of a 61-year-old male patient, and detail its breast ultrasound and histopathological characteristics.

Case report

A 61-year-old male presented to our hospital with the discovery of a mass in the right breast. The patient had a three-year history of hypertension and was being treated with slow-release nifedipine, valsartan, and hydrochlorothiazide. Additionally, the patient had a 40-year history of smoking and had not quit. The patient had no history of breast-related diseases, no history of radiation therapy, and no family history of breast or ovarian cancer. On clinical examination, a 2.0×1.5 cm mass was palpated in the upper outer quadrant of the right breast, which was hard in texture, ill-defined, with a rough surface, irregular in shape, and had poor mobility. There was also pigmentation of the skin above the mass. After admission, a breast ultrasound showed a 2.0×1.5×1.2 cm nodule at the 12 o'clock position in the right breast, with a ratio of the anteroposterior diameter to the greatest diameter greater than 1, irregular margins, and hypoechoic, heterogeneous internal echoes (**Figure 1A**). Color Doppler Flow Imaging (CDFI) showed abundant blood flow signals, and it was classified as BI-RADS category 4c (**Figure 1B**). A chest CT revealed a nodular shadow in the right breast (**Figure 2**). Based on the ultrasound findings, we suspected a high likelihood of malignancy and proceeded with a core needle biopsy of the breast mass. Rapid paraffin sectioning indicated proliferating fibrous and smooth muscle tissue, local endo-

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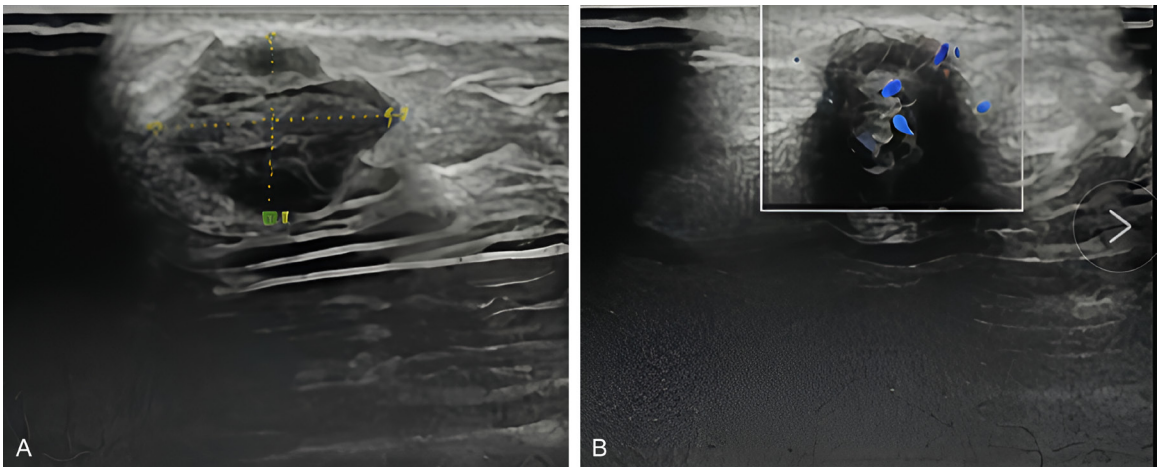

Figure 1. A nodule measuring 2.0×1.5×1.2 cm in the 12 o'clock position of the right breast, with an aspect ratio >1, irregular edges, and hypoechoic and heterogeneous internally. A: CDFI: Abundant blood flow signal. B: BI-RADS category 4c.

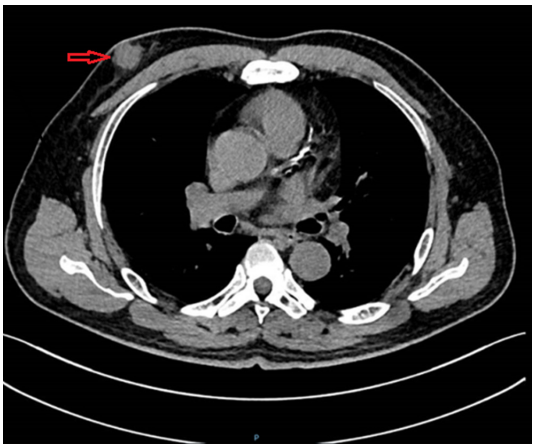

Figure 2. A nodular shadow in the right breast.

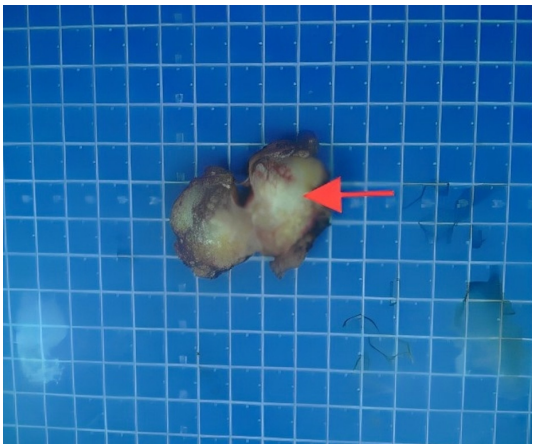

Figure 3. Upon cutting the grayish-yellow irregular tissue, a hard area was found measuring 1.5×1.3×1.2 cm, with a grayish-white cross-section and indistinct margins.

thelial proliferation, with a small number of eosinophilic granulocytes infiltrating and focal lymphoid hyperplasia. We performed a mass excision, and intraoperative frozen pathology suggested spindle cell proliferation with vascular proliferation and inflammatory cell infiltration, and partial endothelial epithelioid proliferation. Gross pathological examination revealed an irregular grayish-yellow tissue with a hard area measuring 1.5×1.3×1.2 cm, with a grayish-white cut surface and ill-defined borders (**Figure 3**). Microscopic examination showed vascular proliferation with endothelial proliferation on a background of collagenized fibrosis, with some endothelial cells exhibiting epithelioid changes and protruding into the vascular lumen, accompanied by lymphocytes and a few eosinophilic granulocytes in the stroma. Immunohistochemical results showed CK (-), CD31 (+), CD34 (+), CD3 (+), CD20 (+), SMA (-), Desmin (-), Ki67 (30%). Based on the immunohistochemical findings, the diagnosis was consistent with epithelioid hemangioma (**Figure 4A-G**). The patient recovered well postoperatively, was advised to have regular follow-ups, and was subsequently discharged.

Discussion

Hemangioma is a benign tumor that arises from vascular tissue and can be found in various parts of the body. Based on different histo-

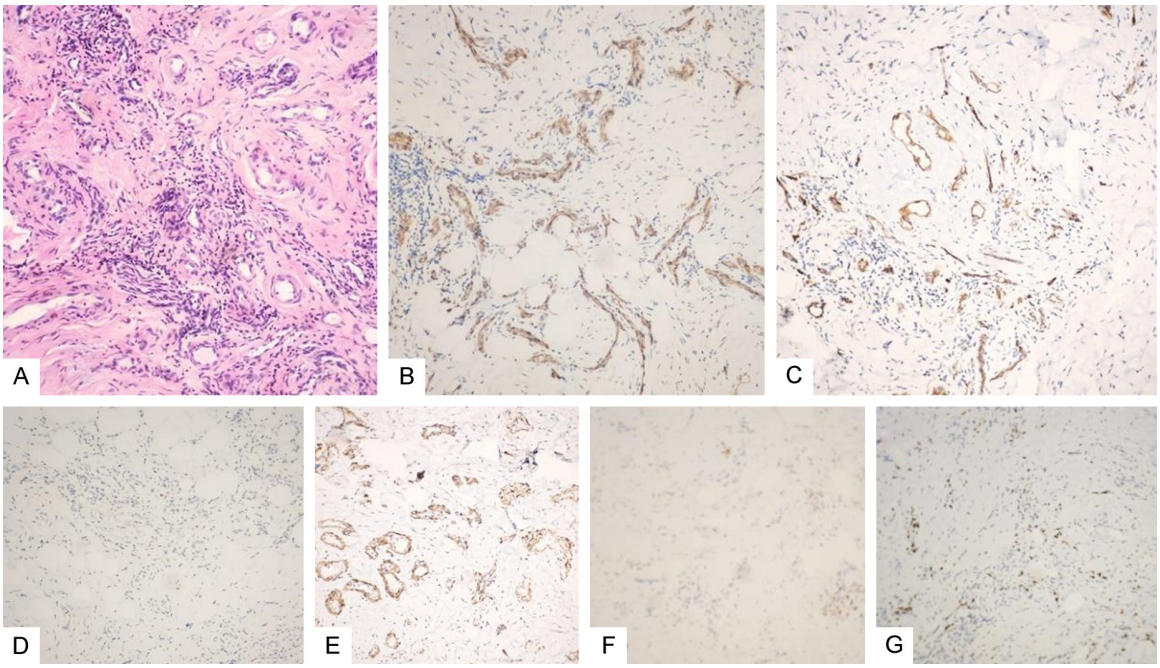

Figure 4. A: HE staining shows vascular proliferation with endothelial hyperplasia against a background of collagenized fibrous tissue, with some endothelial cells exhibiting epithelioid changes and protruding into the vascular lumen, and lymphocytes and a few eosinophilic granulocytes infiltrating the stroma (HE×200). B: CD31 staining is positive. C: CD34 staining is positive. D: CK staining is extensively negative. E: SMA staining is negative. F: Desmin staining is negative. G: Ki67 staining is 30%.

logical appearances, age, and location, hemangiomas can be classified into capillary hemangiomas, cavernous hemangiomas, intramuscular hemangiomas, spindle cell hemangiomas, epithelioid hemangiomas, and cardiac hemangiomas, among others [4]. Epithelioid Hemangioma (EH), also known as Angioblastic Lymphoid Hyperplasia with Eosinophilia (ALHE), is a rare benign vascular proliferative disease [1, 2]. It is most commonly seen in patients aged 20-50, with an average age of onset of 30-33 years [3], and is more common in Asian populations [5]. EH is most frequently found in the head and neck regions as well as around the ears. Less common sites of involvement include the orbit, oral mucosa, shoulder, hand, breast, liver, spleen, heart, bone, and penis [3, 6]. The occurrence of EH in male breasts is extremely rare, with no related reports to date. Twenty percent of EH patients exhibit systemic eosinophilia ranging from 6-34%, but serum eosinophilia is not consistent, and therefore cannot be used as a basis for diagnosing EH [7].

Regarding the pathogenesis of EH, there is still considerable debate. Some believe that EH is a tumor that develops from endothelial cells, with evidence suggesting its infiltrative growth and recurrence [8]; others consider it to be an inflammatory vascular response secondary to complex immune mechanisms [9]. In addition, some hypothesize that EH may be related to environmental factors such as insect bites, trauma, and infection [10]. Studies have suggested that the occurrence of EH may be associated with local hypoxia [10], and it has been proposed that local hypoxia may be related to arteriovenous malformations, vascular trauma, and injury. Kempf et al. evaluated seven patients with EH and found that five out of the seven patients showed clonal T-cell populations and proliferating T-cell activity, indicating that EH may be related to T-cell proliferation [11].

Breast hemangiomas typically appear on ultrasound and mammography as consistent with benign lesions, with the lesion being oval-shaped and having well-defined margins [12]. However, in our case report, the ultrasound showed an irregularly margined, hypoechoic, heterogeneous nodule with abundant blood flow signals, classified as a BI-RADS category

4c lesion, leading us to strongly suspect a malignant tumor. Surprisingly, the pathological results revealed EH, a rare benign tumor. We believe that the preoperative diagnosis of breast hemangiomas is quite challenging, as the imaging findings lack specificity and it is necessary to differentiate between benign and malignant lesions, such as fibroadenomas, hematomas, arteriovenous malformations, fibrosarcomas, and angiosarcomas.

Histopathology is the gold standard for diagnosing EH. The characteristic feature of EH is the proliferation of capillary-sized small blood vessels lined by plump epithelioid endothelial cells. The vessels often have an immature appearance; they may lack a well-defined lumen, but they have a single layer of endothelium and a complete pericyte or smooth muscle layer, with endothelial cells having amphophilic or eosinophilic cytoplasm [13]. The immunohistochemistry of hemangiomas is typically positive for CD31 and CD34, while S-phase kinase is negative, and the Ki-67 index is usually low [14]. However, CD34 and CD31 are also positive in angiosarcomas, and the distinction between the two should be based on the presence of S-phase kinase (positive in angiosarcomas), a higher Ki-67 index, and the existence of atypia [15]. Ki-67 immunostaining is helpful in atypical vascular lesions, with a Ki-67 index greater than 20%, a sensitivity of 90%, and a specificity of 95%, strongly suggesting angiosarcoma [16]. Surprisingly, in our pathological report, the Ki-67 was 30%, and combined with the immunohistochemical results and histopathological morphology, it was confirmed as EH. Ki-67 is a marker of cellular proliferation activity. An index of 30% indicates that a significant proportion of tumor cells are in the cell cycle. For typical EH, this is an extremely strong outlier, which strongly suggests that the tumor may not be a quiescent benign lesion, but rather an actively proliferating tumor. High proliferative activity means that the tumor grows faster, and it may be more difficult to completely remove it through local excision. The possibility of local recurrence is significantly higher than that of typical EH with a Ki-67 index <5% [17]. Typical EH rarely metastasizes. However, atypical cases with a high Ki-67 index have unpredictable behavior. There are indeed a very small number of EH cases reported in the literature that have metastasized to regional lymph nodes or even distant sites, and these cases are often associated with atypical histological features, such as cellular atypia, high mitotic rate, with high Ki-67 being an objective indicator of this “atypicality”. Therefore, this case must be regarded as a tumor with potential metastatic risk [18]. Given the uncertainty, the patient needs to undergo long-term and regular follow-up, such as clinical examination and imaging tests every 6-12 months, to monitor for signs of local recurrence and distant metastasis. According to the current follow-up results, the patient has not experienced recurrence or metastasis. There has always been controversy surrounding the malignant transformation of hemangiomas into angiosarcomas, with some authors even doubting its existence [12]. For example, atypical hemangiomas, if pathology shows endothelial cell atypia, increased mitotic figures, or infiltrative growth, should raise suspicion for malignant potential and need to be differentiated from angiosarcoma. Angiosarcoma is a highly malignant vascular tumor that grows rapidly and is prone to metastasis, which is quite different from typical hemangiomas. Local complete excision and follow-up are the best methods for treating EH. It has been reported that one-third of patients will experience local recurrence [19]. According to our previous report [20], there is still a possibility of recurrence after the excision of breast hemangiomas, and even transformation into angiosarcoma. Therefore, for high-risk EH, complete excision is necessary, and when necessary, margin biopsies should be taken or total mastectomy should be performed.

Conclusion

Epithelioid hemangioma of the male breast is extremely rare, and its preoperative diagnosis is challenging due to nonspecific imaging findings, which often require histopathological diagnosis. For high-risk breast EH, complete surgical excision with margin biopsies or mastectomy when necessary is currently the most ideal treatment method, and close follow-up after surgery is essential.

Disclosure of conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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