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Case Report

Anastomosing Hemangioma of the Breast: An Unusual Case at an Unusual Site

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Conflict of Interest
The authors declare that they have no competing interests.

ABSTRACT

Anastomosing hemangioma (AH) is an unusual benign vascular lesion that commonly occurs in the kidney and genitourinary tract. We report a case of AH in a 49-year-old woman presenting as a mass in the breast, a site which, to the best of our knowledge, has not been previously documented in the English literature. Microscopic examination of the mass revealed a well-demarcated proliferation of anastomosing vascular spaces lined by bland endothelial cells, with focal hobnailing and scattered intravascular fibrin thrombi. No mitotic activity was observed and the Ki-67 proliferative index was low. These features were interpreted as AH, a lesion that may be difficult to distinguish from low-grade angiosarcoma or other benign vascular lesions of the breast which may demonstrate anastomosing channels. Due to the presence of atypical histologic features which can raise suspicion for angiosarcoma on biopsy, complete excision of these lesions is recommended for optimal treatment.

Keywords: Anastomosing hemangioma; Angiosarcoma; Breast; Hemangioma

INTRODUCTION

Anastomosing hemangioma (AH) is a recently described, rare benign vascular neoplasm characterized by prominent interanastomosing architecture that, as a result, often resembles low-grade angiosarcoma histologically [1]. While originally described as most commonly occurring in the kidney and genitourinary tract, cases of AH have also been reported in most parenchymal organs and a variety of soft tissue locations. Here, we report a case of AH of the female breast, a site that, to the best of our knowledge, has not been previously described in the English literature. In addition, we discuss relevant histopathological features of AH and differential diagnostic considerations of vascular lesions displaying anastomosing channels in the breast. Approval and requirement of formal written consent were waived by the Institutional Review Board of Houston Methodist Hospital.

Author Contributions

Conceptualization: Ro JY; Data curation: Mehta RR, Ro JY; Writing - original draft: Lin MS; Writing - review & editing: Ngo T, Schwartz MR, Ayala AG, Ro JY.

CASE REPORT

A 49-year-old woman with a history of endometrial endometrioid adenocarcinoma underwent screening mammography, which detected a 1-cm lobulated mass in the posterior medial left breast. The subsequent diagnostic mammogram demonstrated a persistent ovoid lobulated hyperdense 7-mm mass in the posterior medial aspect of the left breast (**Figure 1A**). High-resolution ultrasound demonstrated an irregular hypoechoic mass in the 9-o'clock position of the left breast, which correlated with the mammographic findings (**Figure 1B**). The overall radiographic impression was Breast Imaging Reporting and Data System (BI-RADS) 4. An ultrasound-guided biopsy was performed and the findings were interpreted as atypical vascular proliferation. A cellular hemangioma was favored, but the possibility of low-grade angiosarcoma could not be entirely excluded. The patient subsequently underwent lumpectomy for complete excision of the lesion.

Gross examination of the lumpectomy specimen showed the biopsy clip with no grossly distinct mass or nodule identified. Microscopic examination around the previous biopsy site revealed a small residual lesion composed of a generally well-demarcated (but not encapsulated) lobulated cellular proliferation of capillary-sized anastomosing vascular channels with intravascular fibrin thrombi and focal larger feeder type vessels with associated fibrous bands (**Figure 2A**). The endothelial cells were small, uniform, and bland, and exhibited a focal hobnailing pattern (**Figure 2B**). No mitotic activity, high-grade nuclear pleomorphism, or necrosis was identified. No extramedullary hematopoiesis was observed. Overall, these morphologic changes were similar to those seen in the previous core biopsies. Immunohistochemical studies demonstrated that the lesional cells expressed CD34 and ERG1, and had an overall low Ki-67 proliferation index of 5% (**Figure 2C**).

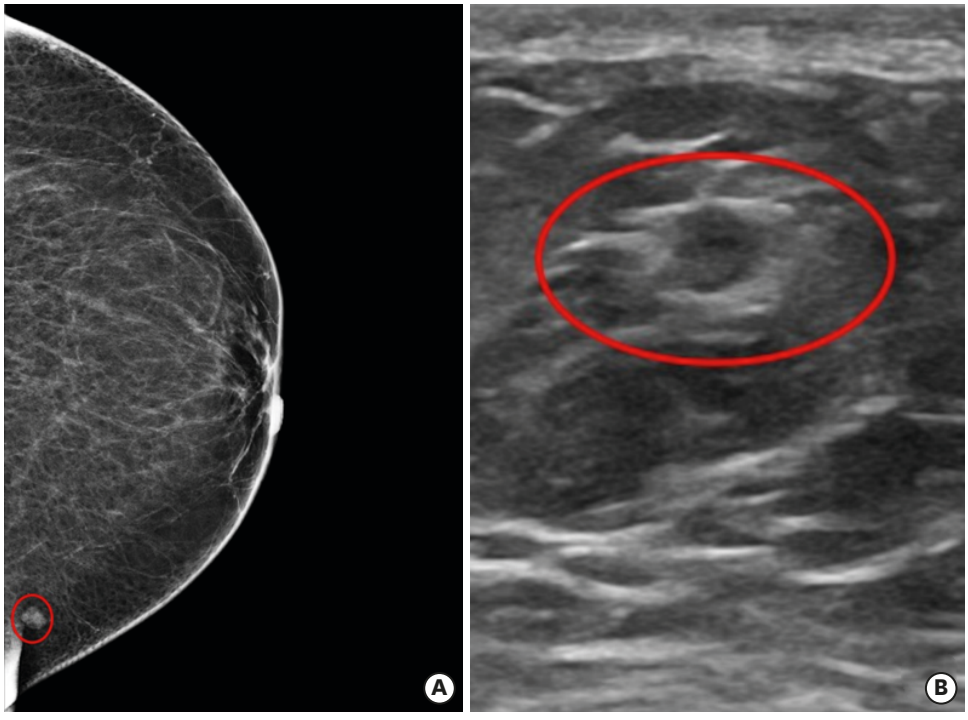

Figure 1. Diagnostic mammogram (A) showing a 7-mm lobulated mass in the posterior medial left breast, and high-resolution ultrasound (B) showing an irregular hypoechoic mass in the 9-o'clock position of the left breast, 7 cm from the nipple.

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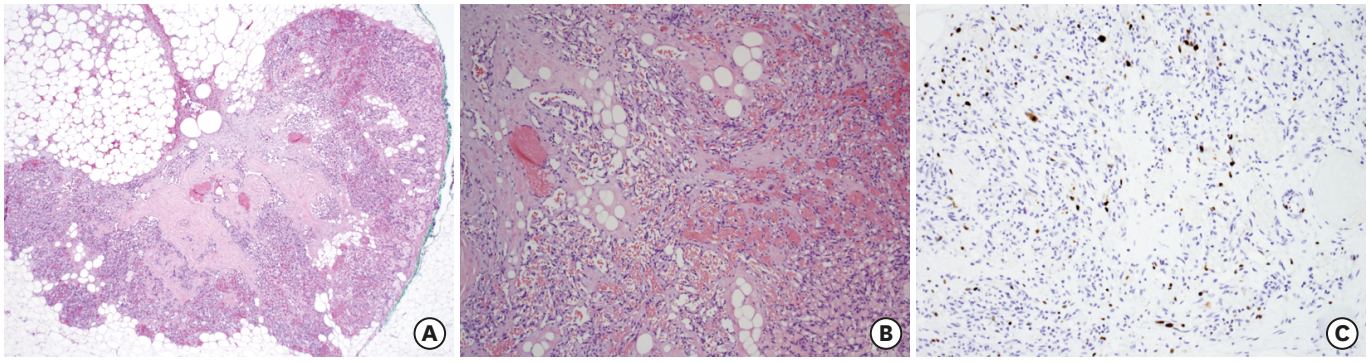

Figure 2. Low-power view of the lesion (A) showing a well-demarcated mass composed of capillary-sized anastomosing vascular channels (H&E stain, ×20). (B) High-power view showing the vascular spaces containing focal intraluminal fibrin thrombi and lined by uniform, bland endothelial cells with areas of hobnailing (H&E stain, ×100). (C) Immunohistochemical staining with Ki-67 showing an overall proliferation index of 5% (Ki-67 stain, ×100).
H&E = hematoxylin and eosin.

The surrounding breast parenchyma showed fibrocystic changes with focal usual ductal hyperplasia, dilated ducts, microcysts, and apocrine metaplasia with stromal fibrosis. No atypical hyperplasia or malignancy was seen. The patient is currently doing well with no evidence of recurrence 5 months post-operatively.

DISCUSSION

AH is a rare vascular tumor that may resemble low-grade angiosarcoma histologically but follows a benign clinical course. First described by Montgomery and Epstein [1] in 2009, over 100 cases have now been reported [2]. While the kidney is the most commonly affected organ, cases of AH have been documented in a wide variety of anatomical sites, including the testis, ovary, uterus, adrenal gland, liver, gastrointestinal tract, soft tissue (particularly in the paravertebral region), bones, and one case in the male breast [2-6]. To the best of our knowledge, this is the first case of AH of the female breast to be reported in the literature.

Clinically, AH is often asymptomatic and detected as an incidental imaging finding. If symptomatic, AH may present with hematuria and back pain in cases arising from the kidney, or with local pain in some extrarenal tumors [2]. On gross examination, AH usually appears as a well-circumscribed tan-red lesion with a spongy surface; the average reported size is 2 cm [2,5]. Microscopically, a relatively well-circumscribed proliferation of anastomosing vascular channels displaying a lobular or diffuse growth pattern is typically seen [1,2,5]. The endothelial cells lining the vascular spaces often show hobnailing, with minimal to no cytologic atypia and low mitotic activity. Frequently, intravascular fibrin thrombi and foci of extramedullary hematopoiesis are observed [1,2,5]. Hyaline globules which stain positively for periodic acid Schiff with diastase digestion may also be seen within the endothelial cells [1,2]. On immunohistochemistry, AH shows diffuse immunoreactivity for vascular markers (including CD34, CD31, ERG, and FLI-1) and a low Ki-67 proliferation index [2,5]. Recent studies have found GNAQ activating mutations in AH. These mutations have also been discovered in other benign and congenital vascular neoplasms but not in angiosarcoma [2,7]. Overall, AH has an excellent prognosis, with no reports of recurrence or metastasis following complete excision [2,5].

Vascular neoplasms are relatively uncommon occurrences in the breast, with a spectrum of entities described ranging in clinical behavior and histopathology from benign to overtly

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malignant [8,9]. One case of an AH in the male breast was previously reported in a German journal, in a 49-year-old male with a 2-cm palpable mass in the left breast [6]. This case, similar to our case, was also radiographically interpreted as BI-RADS 4, and histopathologic examination showed a well-encapsulated vascular tumor with anastomosing morphology and no overt features of malignancy [6]. The patient underwent complete excision with sentinel lymph node biopsy, and remained free of disease 6 months post-operatively. To the best of our knowledge, no other reports of AH of the breast exist in the current literature.

The most important differential diagnostic consideration in this context is a low-grade angiosarcoma of the breast. AH and low-grade angiosarcoma exhibit significant overlap in morphologic features, including anastomosing channels and hobnailing endothelial cells with mild cytologic atypia and low mitotic rate, and thus can be very difficult to distinguish [10,11]. However, while AH tends to display a well-demarcated border, low-grade angiosarcoma often shows infiltrative growth with dissection of the breast stroma and destruction of the normal lobular architecture [11,12]. While angiosarcoma tends to be larger (over 2 cm) and have a higher Ki-67 proliferation index (usually over 20%), cases of low-grade angiosarcoma under 2 cm, with lower Ki-67 indices, and relatively well-defined borders have been reported [12-14]. In these cases, the distinction of AH from angiosarcoma may be impossible and we believe that some cases diagnosed as low-grade angiosarcoma may actually represent AH, misinterpreted as angiosarcoma.

In addition to angiosarcoma, numerous benign vascular entities of the breast can also display anastomosing architecture and should therefore be considered in the differential diagnosis with AH. These include mammary hemangiomas, which are characterized by a well-circumscribed proliferation of either capillary-sized vessels (capillary hemangiomas) or dilated cavernous vessels (cavernous hemangiomas) [8,9]. A recent study of vascular neoplasms of the breast conducted by Mantilla et al. [12] found anastomosing architecture in 2 of 6 capillary hemangiomas and 2 of 4 cavernous hemangiomas of the breast; however, this was a focal finding with the majority of the lesions displaying well-formed discrete vascular channels. In addition, Hoda et al. [13] in 1992 described a series of "atypical" hemangiomas characterized by variably prominent anastomosing architecture, fibrin thrombi, and foci of endothelial hyperplasia. However, these "atypical" hemangiomas were also small in size, had well-demarcated margins, and lacked necrosis or destructive invasion. In our opinion, at least some of these cases may be retrospectively re-categorized as cases of AH. Papillary endothelial hyperplasia (Masson's tumor) can also occur in the breast, often arising from a pre-existing hemangioma, and displays complex papillary architecture which may resemble anastomoses [8,9,12]. However, the exclusively intravascular location and the morphology of hyalinized, fibrinous papillary cores lined by endothelial cells can facilitate distinction from an AH [8,9]. Finally, angiolipoma, while not a true vascular tumor, may be considered in the differential diagnosis, as it characteristically contains intravascular fibrin thrombi and often also shows prominent anastomosing architecture, as seen in AH [8,9,15]. The presence of mature adipose tissue within the lesion distinguishes angiolipoma from AH; however, it may be difficult to evaluate whether fibroadipose tissue observed in a limited biopsy specimen represents perilesional tissue or a true component of the tumor [15].

In conclusion, we describe the first reported case of AH of the female breast. It is vital that AH be differentiated from low-grade angiosarcoma, and while subtle differences do exist, there is considerable morphologic overlap between these 2 entities. Therefore, when vascular tumors composed of anastomosing channels are encountered in the breast and are of small

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size, showing circumscription, and with no significantly atypical cytology, a conservative diagnosis of AH is recommended with complete excision and close clinical follow-up.

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