Pseudoangiomatous stromal hyperplasia presenting as an axillary mass in a postmenopausal woman undergoing in vitro fertilization

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Pseudoangiomatous stromal hyperplasia (PASH) is a rare, benign, tumor-like condition of the breast. Between its initial descriptions in 1986 and 2007, fewer than 150 clinically apparent cases were reported.[1] PASH presents clinically as a palpable, painless breast mass or as an incidental mass found on screening mammography.[2] Incidental PASH accounts for most cases, with ≤23% of breast biopsy specimens showing characteristic changes focally.[1,3]

CASE REPORT

A 52-year-old woman presented to our clinic with 2 nontender nodules in the left axilla of 3 months' duration within the setting of 2 years of ongoing treatment with estradiol in anticipation of in vitro fertilization (IVF) with donor oocyte. The nodules varied in size with her hormone cycle but were otherwise asymptomatic. A punch biopsy specimen was obtained and revealed hyalinized stroma with slit-like clefts, some of which were lined by flattened spindle cells, mimicking vascular channels (Fig 1). Immunohistochemistry for CD34 revealed faint staining of the spindle cells compared to intense staining observed in the true vessels (Fig 2). The findings were those of PASH. Immunohistochemistry was negative for both estrogen receptor and progesterone receptor (Fig 3). Mammography was obtained, partially visualizing the mass in the left axilla (Fig 4). A follow-up ultrasound-guided needle core biopsy specimen was obtained and supported the diagnosis of PASH. The patient's case was discussed among a multidisciplinary tumor board with consensus that there was no need for surgical excision or cessation of fertility assistance. The patient discontinued estradiol and reported a decrease in the size of the nodules. She continues taking progesterone in anticipation of IVF.

DISCUSSION

PASH presenting as a palpable nodule is rare. Although PASH is considered a benign entity, it must be differentiated histologically from low-grade angiosarcoma.[1] PASH is histologically characterized by anastomosing "slit-like" channels variably lined by thin spindle-like myofibroblasts. These channels can easily be mistaken for vascular spaces. However, they do not contain red blood cells and are not lined by endothelial cells. The clefts are thought to represent fixation artifact caused by the separation of myofibroblasts from the surrounding collagen fibers.[1,4] Moreover, the myofibroblasts in PASH will not stain positively for other endothelial markers (such as CD31 or erythroblast transformation-specific related gene), unlike angiosarcoma.[4] If elected, simple excision is often adequate to treat PASH. Rarely, it may lead to excessive breast enlargement that necessitates additional treatment.[5]

The pathophysiology of PASH is not fully understood, but is thought to represent aberrant stromal reactivity to sex hormones. It is most commonly reported in premenopausal women treated with hormone therapy.[2] In a study of 46 cases, the average age was 40 years.[3] However, it has also been reported in postmenopausal patients with hormone replacement therapy and in men with gynecomastia.[1,2]

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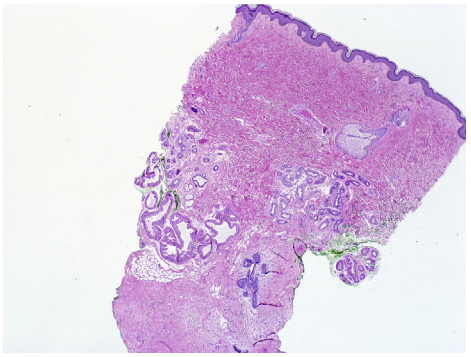

Fig 1. Pseudoangiomatous stromal hyperplasia (PASH). Low-magnification view discloses skin with eccrine and apocrine sweat apparatus and breast glandular units. The surrounding stroma appears hyalinized with slit-like clefts. (Original magnification: ×20.)

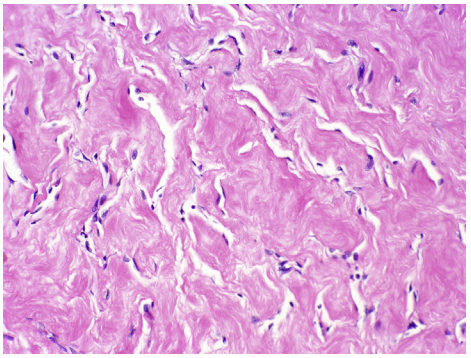

Fig 2. Pseudoangiomatous stromal hyperplasia (PASH). Examination at higher magnification reveals that the slit-like clefts are lined by flattened spindle cells, mimicking vascular channels. (Original magnification: ×200.)

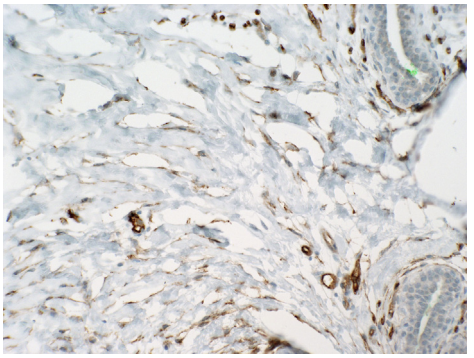

Fig 3. Pseudoangiomatous stromal hyperplasia (PASH). CD34 immunohistochemistry revealed faint staining of the spindle cells lining the stromal clefts, compared to the intense staining observed in true vessels. (Original magnification: ×200.)

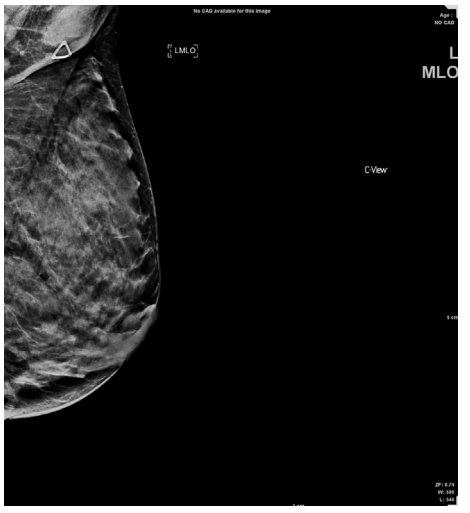

Fig 4. Pseudoangiomatous stromal hyperplasia (PASH). Medial lateral oblique view of the left breast shows a partially visualized mass over the region of the patient's palpable abnormality (triangular skin marker).

Our finding of PASH in a postmenopausal woman undergoing hormone therapy in anticipation of IVF is relevant in light of the steadily increasing popularity of IVF. In 2014, 169,602 cases of assisted reproductive technology were reported, 5.8% of which were in patients who were >44 years of age.[6] IVF in older patients presents certain challenges that are worth considering clinically. Older IVF patients typically receive hormone therapy to increase endometrial receptivity, as in this case. They may therefore be subject to sequelae associated with hormone therapy, such as PASH. As in other cases of advanced maternal age, older IVF patients are subject to higher rates of adverse pregnancy outcomes.[7]

Other characteristics of this case are also unique. One study focusing on hormone receptor staining of 19 PASH samples found that 18 of them (95%) were positive for estrogen receptor or progesterone receptor.[1] Interestingly, immunohistochemistry for estrogen receptor and progesterone receptor was negative in our patient, which is surprising given the fluctuation in size while on estradiol. The axillary location of the nodules in this case is also somewhat unusual and is not frequently reported in the literature. The first report of an axillary PASH nodule was in 2005.[8] A more recent report in 2011 noted simultaneous massive lesions in the axillae and vulva.[9] An axillary lesion is not entirely unexpected given the extension of breast tissue into the axilla. These cases and ours indicate that PASH is a rare but possible consideration in the differential diagnosis of an axillary mass, especially in a woman exposed to hormone therapy.

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