Bilateral pseudoangiomatous stromal hyperplasia in a human immunodeficiency viral-infected patient

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ABSTRACT

Pseudoangiomatous stromal hyperplasia (PASH) is an uncommon mesenchymal neoplasm of the breast demonstrating stromal myofibroblastic proliferation and having the appearance of anastomosing slit-like pseudovascular spaces lined by spindle-shaped cells. A case of nodular PASH of the bilateral breasts in a 40-year-old woman with clinically presenting with a progressive enlarged breast lump is reported. Mammographic and ultrasonographic features of the right and left breasts showed a large solid lump with well-circumscribed border measuring 4 cm × 1.7 cm × 3.4 cm and 13.8 cm × 10.9 cm × 12.1 cm, respectively. Wide excision of the right breast and quadrantectomy of the left breast were performed. The histopathological examination of the lesion showed anastomosing slit-like pseudovascular spaces. The stromal cells were immunoreactive for muscle actin (HHF35), smooth muscle actin, and progesterone receptor. Clinical and pathological findings with briefly reviewed relevant literatures are discussed. This is the first clinicopathological and radiological report of bilateral mammary nodular PASH in a human immunodeficiency virus-infected patient.

KEY WORDS: Acquired immunodeficiency syndrome, bilateral, human immunodeficiency virus, pseudoangiomatous stromal hyperplasia

INTRODUCTION

Pseudoangiomatous stromal hyperplasia (PASH) is an uncommon mesenchymal neoplasm of the breast demonstrating stromal myofibroblastic proliferation and having the appearance of anastomosing slit-like pseudovascular spaces lined by spindle-shaped cells.[1,2] Mammary PASH was first described by Vuitch et al. in 1986.[3] PASH is a rare benign proliferating breast condition commonly occurred in immunocompetent patients. There has been only one reported case of unilateral PASH occurred in a clinical setting of human immunodeficiency viral (HIV) infection. We report a rare case of bilateral PASH in an HIV-infected patient who received highly active antiretroviral therapy (HAART).

CASE REPORT

A 40-year-old Thai female HIV-infected patient presented with a huge lump in her left breast for 4 months. She also had a progressive rubbery lump in her right breast, 1-month ago. She had a history of HIV infection for 7 years. She started on a HAART including stavudine, lamivudine, and nevirapine. Her CD4 count was 330 cell/μL (15%). Mammography showed a large solid lump with well-circumscribed border measuring 4 cm × 1.7 cm × 3.4 cm and 13.8 cm × 10.9 cm × 12.1 cm in the right and left breast, respectively [Figures 1 and 2]. Wide excision of the right breast and quadrantectomy of the left breast were performed. The pathologic diagnosis was bilateral mammary nodular PASH. At the 2 years of follow-up, she was asymptomatic with no evidence of recurrence. She has been advised routinely follow-up in view of local recurrence.

The right and left mammary masses measuring 6.7 cm × 5 cm × 4 cm and 11 cm × 9 cm × 7.3 cm were obtained. The external surfaces showed well-demarcated, rubbery-firm, tan-brown appearance [Figure 3]. The cut surfaces showed uniform, solid, trabecular white appearance. The histopathology revealed anastomosing slit-like pseudovascular spaces, which are either acellular or lined by slender, spindle-shaped stromal cells [Figure 4]. There was no evidence of atypia, mitosis, and pleomorphism. The stromal cells were immunoreactive for muscle actin (HHF35), smooth muscle actin, and progesterone receptor. The stromal cells were the negative immunoreactivity for CD31, factor VIII-related antigen, Fli1, S100, desmin, sarcomeric actin, MyoD1, human herpes virus-8 (HHV-8), estrogen
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DISCUSSION

Pseudoangiomatous stromal hyperplasia is an uncommon mesenchymal neoplasm of the breast demonstrating anastomosing slit-like pseudovascular spaces.[1,2] It is hypothesized that PASH originate from myofibroblastic cells with a variable expression of myoid and fibroblastic feature.[1,2] The ages of patients range from 9-month-old to 67-year-old with a mean age of 37-year-old.[1] Its clinicopathologic spectrum ranges from incidental, microscopic foci to clinically and mammographically evident breast mass. The common presenting symptom of PASH is a palpable painless unilateral lump.[1,2,4] The sizes of PASH range from 1 to 18 cm with an average size of 6 cm in diameter.[1] Peau d’orange change and skin necrosis with clinically presented with massive breast enlargement during pregnancy has been described.[2]

The macroscopic finding of PASH is a nonencapsulated, dense, smooth, firm to rubbery, partially to completely well-demarcated receptor [Figure 4]. Epstein-Barr virus (EBV)-encoded RNA in situ hybridization was negative. The final pathologic diagnosis was bilateral mammary nodular PASH.

The histological differential diagnoses of mammary PASH include fibroadenoma, phyllodes tumor, angiosarcoma, Kaposi sarcoma, and smooth muscle tumor. Fibroadenoma is a benign, well-circumscribed stromal lesion characterized by a proliferation outer surface.[1,2,4] The cut surface is glistening with homogenous fibrous firm rubbery tan-gray-white appearance. The classical histopathologic finding shows intermixed stromal and epithelial elements. There is a complex pattern of interanastomosing empty slit-like spaces lined by slender spindle cells intersecting through a keloid-like wavy hyaline stroma (H and E, x100). (a) The spindle-shaped stromal tumor cells are immunoreactive for CD34, (b) And vimentin, (c) And the epithelial ductal and lobular cells are immunoreactive for CD117, (d) x100

The histological sections of the mammary tumor reveal slit-like spaces of pseudoangiomatous stromal hyperplasia lined by spindle stromal myofibroblastic cells intersecting through a keloid-like wavy hyaline stroma (H and E, x100). (a) The spindle-shaped stromal tumor cells are immunoreactive for CD34, (b) And vimentin, (c) And the epithelial ductal and lobular cells are immunoreactive for CD117, (d) x100

Figure 1: Mammogram in mediolateral oblique (a) And craniocaudal (b) Views show a 4-cm. Mass with partially obscured border (arrow) at the upper-outer quadrant of right breast. The 13.8-cm lobular mass with circumscribed border (asterisk) is detected at the upper-outer quadrant of left breast. Single round calcification is seen overlying the left breast lump on both mediolateral oblique and craniocaudal views

Figure 2: Target ultrasonograms reveal the oval-shaped masses with gently lobulated borders. Internal cystic spaces are shown in the right breast mass, (a) While the left breast mass shows heterogeneous echotexture. (b) Both mammary masses have posterior acoustic enhancement

Figure 3: The gross image of the right and left mammary masses shows well-demarcated, rubbery-firm, tan-brown external surface with uniform, solid, trabecular white appearance on cut surfaces

Figure 4: The histopathologic sections of the mammary tumor reveal slit-like spaces of pseudoangiomatous stromal hyperplasia lined by spindle stromal myofibroblastic cells intersecting through a keloid-like wavy hyaline stroma (H and E, x100). (a) The spindle-shaped stromal tumor cells are immunoreactive for CD34, (b) And vimentin, (c) And the epithelial ductal and lobular cells are immunoreactive for CD117, (d) x100

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of glandular and stromal elements of terminal duct-lobular unit, consisting of intracanalicular and pericanalicular growth patterns. Phyllodes tumor is a group of circumscribed biphasic tumor, characterized by a double layered epithelial component arranged in clefts surrounded by an overgrowing hypercellular mesenchymal component typically organized in leaf-like structure. Angiosarcoma is a malignant neoplasm exhibiting endothelial differentiation. Angiosarcoma and Kaposi sarcoma typically express CD31, CD34, factor VIII-related antigen, FLI1, and vimentin but does not express muscle actin (HHF35). Kaposi sarcoma is uniformly associated with HHV-8 infection. Relative affluence may increase the risk of Kaposi sarcoma and smooth muscle tumor in HIV-infected patients. In contrast to Kaposi sarcoma, smooth muscle tumor has been associated with EBV infection.

The pathogenesis of PASH remains enigmatic, although initially PASH was thought to represent a hamartoma. However, hamartoma defined as a tumor-like lesion composed of the proliferation of one or more tissues, normal to organ but abnormally mixed and overgrown. PASH is a lesion formed by myofibroblasts with a variable expression of myoid and fibroblastic feature, which is not true hamartoma. Currently, there are few reports in the literatures suggesting hormonal dependent tumor. PASHs typically show immunoreactivity for progesterone receptor and occasionally show immunoreactivity for estrogen receptor. A proliferative response of myofibroblasts to hormones is likely to be an important factor as it is most commonly observed in young premenopausal women or older women taking hormone replacement therapy. This concept is supported by a previous case report of rapid growth of PASH during pregnancy. It is believed that aberrant response of myofibroblastic stromal cells to hormones is a hypothesized pathogenesis.

Pseudoangiomatous stromal hyperplasia has been described in a renal transplant patient with cyclosporine treatment. Moreover, one previously reported case of unilateral mammary PASH in an HIV-infected patient has been documented. Impaired cellular immune response including decreased T-lymphocytic function may be part of the pathogenesis of PASH. Since the study of the relationship between PASH and HIV infection is still scarce. The role of HIV in the pathogenesis of mammary PASH should be further investigated.

Pseudoangiomatous stromal hyperplasia typically has benign nature following complete excision. Wide excision without lymphadenectomy remains the cornerstone of management of PASHs. PASHs generally behave in an indolent manner and generally do not recur after complete excision. The local recurrence rate is 13-26%. The adjunctive therapy includes selective estrogen receptor modulator, which has been reported regressing and resolving PASHs.

**CONCLUSION**

Pseudoangiomatous stromal hyperplasia is a rare benign mesenchymal neoplasm demonstrating anastomosing slit-like pseudovascular spaces and originating from myofibroblastic stromal cells. Our case report highlights the PASHs occurred in an HIV-infected patient, who received HAART. Therefore, it is noteworthy to keep PASH in mind when dealing with a breast lump in an HIV-infected patient. Clinical, radiological and pathological correlations are essential. The definitive diagnosis of PASH requires histopathological confirmation.

**REFERENCES**