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CASE REPORT
Breast

Recurrent Extreme Bilateral Gigantomastia Caused by Pseudoangiomatous Stromal Hyperplasia (PASH) Syndrome: A Case Report

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Summary: Pseudoangiomatous stromal hyperplasia (PASH) of the breast is a rare and benign medical condition in which the breast tissue is affected by an abnormal myofibroblastic proliferation, which mimics a low-grade sarcoma angiomatous proliferation. PASH usually presents itself either as a palpable mass or as an incidental diagnosis during breast specimens' histological examination. A few cases have been reported in the literature of a diffuse form of breast PASH syndrome in which the clinical presentation is a bilateral form of gigantomastia without palpable masses. In such cases, the optimal surgical management is still debated due to a significant risk of relapse after breast reduction. Mastectomy seems to be the endpoint of this condition in relapsing cases. Recent studies report a good outcome with a Tamoxifen regimen when surgery cannot be performed, supporting a hormonal component for the etiology of the condition. This study reports on an extremely rare case of bilateral, rapid, and severe PASH in a young patient, presenting as a truly disabling gigantomastia that forced the patient to use a wheelchair due to the excessive breast weights (25 kg the right breast and 21 kg the left). We describe her complicated medical history, her diagnosis, and our course of treatment. *(Plast Reconstr Surg Glob Open 2023; 11:e4571; doi: 10.1097/GOX.0000000000004571; Published online 24 January 2023.)*

Pseudoangiomatous stromal hyperplasia (PASH) of the breast is a rare and benign medical condition with a wide spectrum of clinical manifestation. Interestingly, according to Hargaden et al,[1] PASH can be detected radiologically in 69%–100% of cases. In 44% of patients with PASH, it appears as a palpable mass and rarely like a diffuse bilateral gigantomastia without palpable masses.[2]

From a histopatological point of view, PASH can be defined as a myofibroblastic proliferation of the breasts, which simulates an angiomatous one, that can be confused with a low-grade angiosarcoma.[3]

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The best management of PASH is still debated. Many authors advocate wide local excision due to the uncertain nature of the lesion.[4] Recent studies proposed a medical management with tamoxifen, which seems to be an alternative when surgery cannot be performed, supporting a hormonal etiology.[5]

A case of PASH associated with a relapsing, rapid, and significant bilateral breast enlargement causing gigantomastia is described.

CASE REPORT

A 27-year-old woman presented to our department for severe and progressive bilateral enlargement of the breast (Fig. 1) with significant osteoarticular involvement of the spine, neck pain, difficulty in walking with the need to move with the wheelchair, and important psychosocial discomfort.

The patient reported a massive and continuous growth of the breast since the age of 18, particularly during menstrual cycles, accompanied by a *calor* and *rubor* sensation. So, at the age of 20 years, she underwent a reduction mammoplasty with normal histopathological results. Later on, she developed a massive relapse with the breasts assuming their current size.

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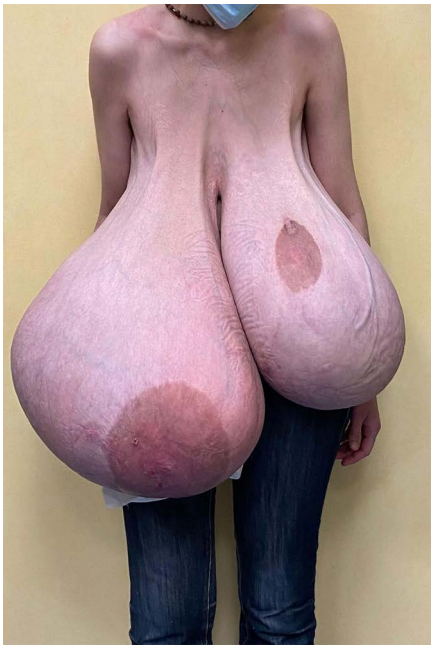

Fig. 1. Diffuse asymmetrical bilateral enlargement of the breasts due to PASH.

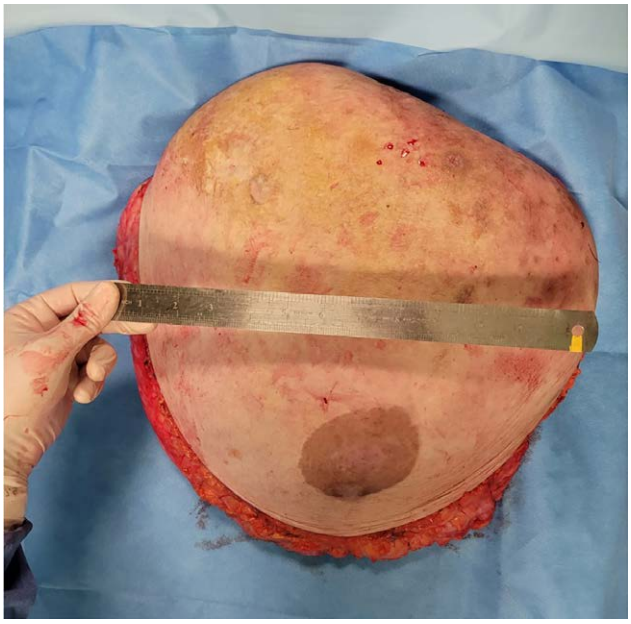

Fig. 2. Postoperative specimen.

The patient was affected by celiac disease, scalp psoriasis, polycystic ovary syndrome, myasthenia gravis, and systemic lupus erythematosus with osteoarticular and hematological involvement. She received immunosuppressive therapies based on corticosteroids and immunoglobulins over the years until the current phase of remission. All radiological findings resulted negative for adenomas in the pituitary and adrenal glands.

The examination of the breast and axilla bilaterally was negative for palpable masses. The overlying skin of the breast was severely hypotrophic and presented multiple grade 2 ulcers. The nipple-areolar complexes (NACs) were hypotrophic, asymmetric, and distorted bilaterally.

Breast ultrasonography and CT scan were performed, showing no significant alterations. It was not possible to perform a magnetic resonance imaging scan due to the absence of suitable instruments for her breast volume.

A bilateral mastectomy with free NAC grafting was performed (Fig. 2). The patient wished to delay breast reconstruction. Mastectomy specimens were 25 kg on the right and 21 kg on the left, and no masses or cysts were identified.

Histopathological examination of the excised breast tissue revealed a complex network of slit-like spaces within a dense collagenous stroma, expanding the intralobular and interlobular compartments of both breasts (Fig. 3). These optically empty spaces were lined by a population of spindle cells with no atypia and no evidence of mitotic activity (Fig. 3, insert), showing immunohistochemical positivity for cluster differentiation 34 and negativity for cluster differentiation 31 estrogen receptors, and progesterone receptors. These findings were consistent with the diagnosis of diffuse, bilateral PASH (Fig. 3).

The patient had an uneventful postoperative period, with exception of free NAC graft necrosis bilaterally and subsequent healing by secondary intention (Fig. 4). The other surgical wounds healed completely, and after 1 month, there was no recurrence of the disease. The patient resumed walking and was able to keep a standing position without discomfort and with an important improvement of the psychophysical condition.

DISCUSSION

First described by Vuitch et al in 1986,[6] PASH is a benign, mesenchymal lesion of the breast that commonly presents as an incidental finding at histology or as a palpable mass on clinical examination. Rarely, PASH can also manifest with rapid and significant enlargement of both breasts, a condition that has been reported in the context of immune-mediated diseases[7] as might happen in the present case. On clinical and radiographic evaluation, PASH can easily be confused with fibroadenoma, and the diagnosis is exclusively histological, with demonstration of the anastomosing, cleft-like spaces lined by spindle-shaped myofibroblasts simulating the appearance of vascular structures lined by endothelial cells. On immunohistochemistry, these spindle cells are positive for vimentin, cluster differentiation 34 and smooth muscle actin and negative for cytokeratin, S100, and endothelial markers such as cluster differentiation 31 allowing exclusion of a vascular lesion. Immunostains for estrogen and progesterone receptors are usually positive, with the latter often presenting stronger intensity,[8] but both tested negative in our specific case.

A diffuse, bilateral, and massive breast enlargement associated with PASH, as described in this case, is extremely rare, and a few similar cases have been reported in the literature.[9]

A literature search using the meshed terms “PASH” and “gigantomastia” gives 14 results. Only two cases presented recurrent relapsing swelling of the mammary

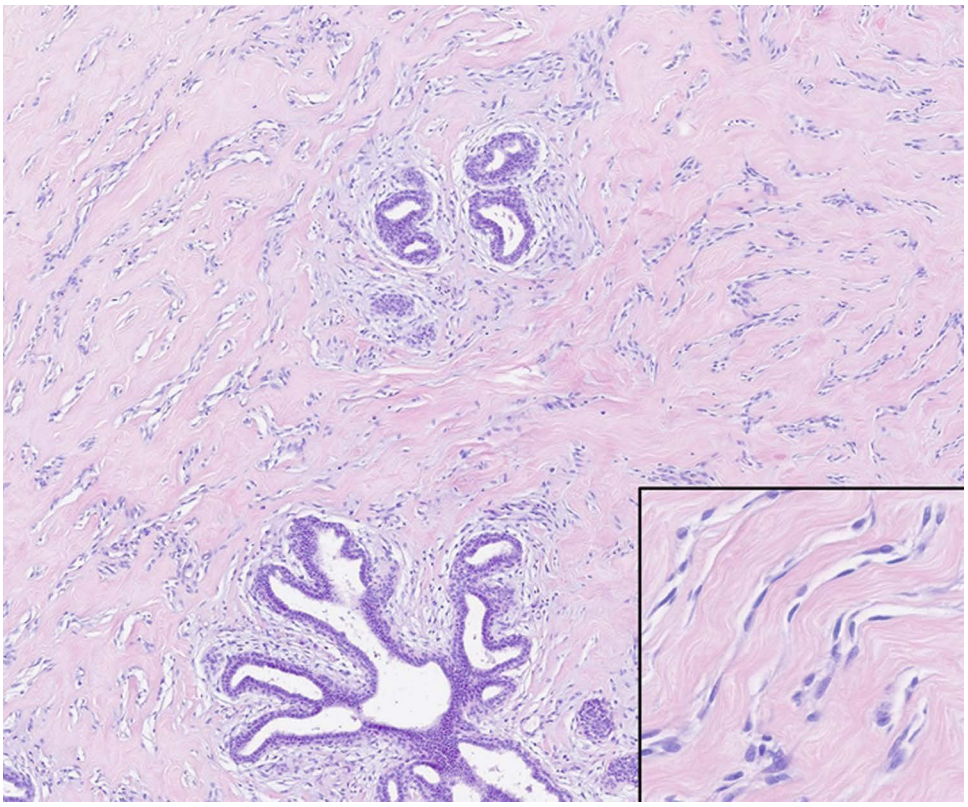

Fig. 3. The intralobular and interlobular stroma presents multiple, anastomosing, slit-like spaces lined by a single layer of spindle-shaped myofibroblasts simulating endothelial cells. There is no evidence of cytologic atypia. (Hematoxylin and eosin, 4×. Insert: hematoxylin and eosin, 20×).

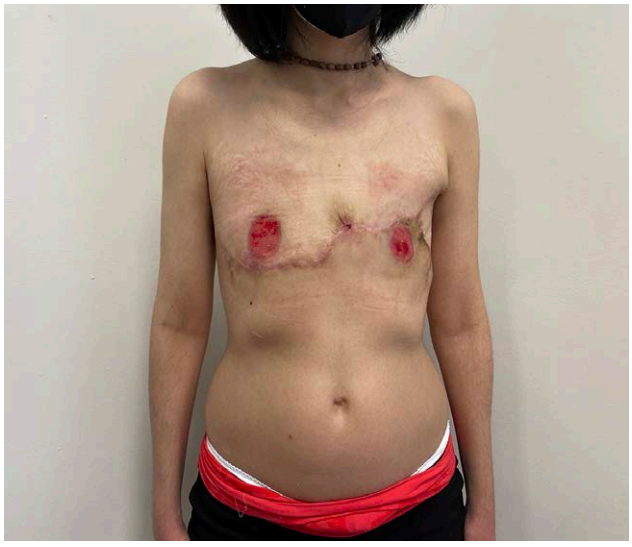

Fig. 4. Postoperative result after 2 months. Note the free NAC graft necrosis bilaterally and subsequent healing by secondary intention.

gland with gigantomastia after breast reduction as in our case.[10,11]

A weight of mastectomy specimens ranging from about 5 to 7 kg is reported in the literature.[9] In the presented case, the breast weight was 25 kg on the right and 21 kg on the left; no cases of massive breast enlargement caused by PASH have ever been described in the literature. In severe cases like this, surgery should be considered the treatment of choice with great improvements in patients' quality of life.[4] In the present case, a radical mastectomy with free NAC grafting was preferred over a breast reduction, due to the relapse and worsening of the condition after a previous breast reduction procedure. Other cases may be managed by a contextual conservative surgery and hormonal therapy. Due to the rarity of this condition, more studies are necessary to test the efficacy of a combined approach and to delineate clinical guidelines.

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STATEMENT OF CONFORMITY

The study was conducted in accordance with the Helsinki Declaration of 1964 (revised 2008).

PATIENT CONSENT

The patient provided written consent for the use of her image.

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