Pseudoangiomatous Stromal Hyperplasia Presenting as Gigantomastia - A Case Report and Review of Literature

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INTRODUCTION

Gigantomastia is a rare breast disease with massive bilateral enlargement of breast causing physical and psychosocial disability for the patient. Diffuse pseudoangiomatous stromal hyperplasia causing gigantomastia is a very rare presentation. We present a case of 45-year-old female with bilateral gigantomastia and cyclical mastalgia, who underwent bilateral mastectomy, postoperatively diagnosed with pseudoangiomatous hyperplasia.

Gigantomastia is a rare condition characterised by excessive breast tissue growth resulting in massive enlargement of both breast. An arbitrary definition for gigantomastia is breast size more than 1.5 kg or when the breast tissue comprises 3 % or more of patients total body weight. Gigantomastia is accompanied by skin ulceration, postural problems, back pain, traction nerve injury and social stigmata. It is physically and psychosocially disabling for the patient. The aetiopathogenesis of gigantomastia is poorly understood, but generally classified as idiopathic, drug induced (penicillamine, cyclosporine) and due to hormonal imbalance (gestational and pubertal).¹

Pseudoangiomatous stromal hyperplasia (PASH) is a benign mesenchymal proliferative disease of the breast which is usually an incidental finding accompanying other breast pathology like fibroadenoma, fibrocystic disease, breast cancer, gynaecomastia etc. It was first described by Vuitch, Erlandson and rosen (1986). Ibrahim et al. reported the occurrence of incidental microscopic PASH in breast specimens as around 23 %.² Around 200 cases of PASH presenting as a tumoral palpable mass is there in literature. Another very rare and under recognised presentation is as diffuse PASH with bilateral or unilateral massive breast enlargement. Here we report a case of diffuse PASH with gigantomastia and a review of literature.
PRESENTATION OF CASE

A 45-year-old female patient presented with complaints of gradual increase of bilateral breast size for 2 years. She has diffuse ache and heaviness of both breasts during menstruation. Her menstrual cycle is regular and she has breastfed her two kids. She is a hypertensive and on amlodipine for one month. There is no history of nipple discharge. On local examination, both breasts are massively enlarged and reaching up to the abdomen. Surface skin showed dilated veins and multiple healed ulcerations, multiple ill-defined masses are palpable. Mammogram revealed homogenously dense breast parenchyma with multiple cysts and fibro adenomas in both breast with breast imaging reporting and data system (BIRADS) grade III. Fine needle aspiration cytology (FNAC) was suggestive of benign ductal epithelial proliferative lesion. Patient underwent bilateral mastectomy. Postoperative days are uneventful.

PATHOLOGICAL DISCUSSION

Received bilateral mastectomy specimens, right measuring 27 x 25 x 5.5 cm and left measuring 27 x 22 x 5 cm. Surface skin shows multiple scars on both breasts. Cut surface shows multiple nodules, grey-white lobulated with bulging margins. Microscopically both breasts showed adenosis and the stroma between the lobules shows multiple interanastomosing slit like spaces lined by spindle cells, no atypia noted. Stromal hyalinisation was present. Immunohistochemistry showed positivity of spindle cells with CD34 and SMA, negative staining for CD31. A final diagnosis of benign proliferative breast disease associated with pseudoangiomatous stromal hyperplasia was given.

Patient is symptomatically better and recurrence free for past 5 years.

Figure 1. Right and Left Breast
Figure 2. Cut Section of Right and Left Breast
Figure 3. H & E (100x) Breast Stroma Showing Interanastomosing Slit like Spaces
Figure 4. H & E (400x) Slit Like Spaces Lined by Bland Spindle Cells
Figure 5. Immunohistochemistry (100x)-CD34 Positivity
Figure 6. Immunohistochemistry (100x)-Negative for CD31
Idiopathic gigantomastia is the term used when a patient presents with bilateral massive breast enlargement without any obvious precipitating cause (drugs or hormones). They are best treated with surgical breast reduction.

PASH is a benign breast disease characterised histologically by interanastomosing slit like spaces in the intralobular stroma to hormonal stimuli particularly progesterone. This is also supported by the fact that PASH is more common in the childbearing age group and in postmenopausal females taking hormone replacement therapy.

Clinical differentials considered for gigantomastia or a unilateral massively enlarged breast includes giant fibroadenoma, phyllodes tumour and inflammatory breast carcinoma. Histologically, PASH needs to be differentiated from low grade angiosarcoma. But in the present case, absence of cytological atypia and immunohistochemistry pattern proves otherwise.

After extensive search in world literature, we found 19 published cases of diffuse PASH with bilateral symmetric or asymmetric enlargement with no discrete mass formation (table no. 1). All these cases had bilateral breast enlargement without a discrete palpable mass and were diagnosed with PASH after biopsy. Mean age was 31.8 (range - 11 to 52 years). 2 adolescent cases were there. For 4 of the cases, symptoms started during gestational period. 2 cases reported PASH in the accessory breast tissue too.6,13 Family history of macromastia was present in one case.19 Recurrence after surgery was reported in only one case.14

| Case No | Reference | Age | Presenting Complaint | Significant Clinical Findings / History | Dimension / Size | Type of Surgery | Imaging mammography / MRI |
|---------|-----------|-----|----------------------|----------------------------------------|-----------------|-----------------|---------------------------|
| 1       | Teh et al., 2007 | 15F | Painless asymmetric breast enlargement | No distinct mass | Right > left, right - 18 cm | Right breast reduction | Extreme dense parenchyma mammoplasty right breast |
| 2       | Lanzen et al., 2009 | 37F | B/L breast enlargement for 8 years, severe back pain, difficulty in breathing | SLE for 5 years | Right - 8 kg, left - 7 kg | Reduction mammoplasty | - |
| 3       | Eummiriu et al., 2010 | 47F | B/L breast enlargement for 3 months, pain left side | Erythema skin over breast, diabetes for 15 years | - | Reduction mammoplasty | Extreme dense parenchyma both breast |
| 4       | Jordan et al., 2011 | 52F | B/L breast enlargement | Massive nodular PASH in accessory breast tissue, (axilla and groin) 7 years later | Right - 2.8 kg, left - 3.7 kg | B/L mastectomy | - |
| 5       | Dai et al., 2014 | 29F | B/L breast enlargement for 1 year, back pain | Breast tenderness | Right - 23.6 x 5.2 cm, 1 kg Left - 25 x 20 x 7.1, 1.7 kg | Bilateral mastectomy | Diffuse skin thickening and oedema throughout both breast parenchyma |
| 6       | Roy et al., 2015 | 40F | B/L breast enlargement, cystic breast swelling, localised erythema | Breast swelling | Right - 5.5 kg, left - 2.86 kg | B/L breast reduction with nipple graft | Extreme dense parenchyma both breast |
| 7       | Krawczyk et al., 2016 | 33F | Bilateral asymmetric gigantomastia, multiple skin ulcerations, back pain | Primigravida, 14 weeks pregnant with twins | Right - 7.2 kg, left - 5.15 kg | B/L skin sparing mastectomy | Increased breast density with pronounced lymphoedema without circumscribed nodular lesions |
| 8       | Oppenheimer et al., 2016 | 29F | Rapidly progressing macromastia, cystic breast swelling | - | - | Bilateral mastectomy with reconstruction | - |
| 9       | J. W. Lee et al., 2016 | 41F | Painful swelling both breasts for 2 months | Diabetic for 15 years | Volume right - 11.15 ml, left - 90 ml | Reduction mammoplasty | MRI - diffuse homogeneous persistent enhancement multiple well and ill-defined masses both breast |
| 10      | Alkhushi et al., 2016 | 45F | B/L breast enlargement for 2 years, | - | - | Core needle biopsy | - |
| 11      | Hayes et al., 2016 | 34F | Rapid B/L breast enlargement, started during pregnancy | Fascioscapulohumeral muscular dystrophy, PASH involving auxiliary breast tissue and metachronous perimal mammary type hamartoma | - | Reduction mammoplasty | MRI - marked oedema |
| 12      | Kim et al., 2018 | 33F | Recurrent gigantomastia | SLE, bilateral reduction mammoplasty before 4 years | Right - 21 x 1.5 x 13 cm, 2.79 kg, Left - 23 x 22 x 20 cm, 4.5 kg | B/L mastectomy | Extreme dense parenchyma both breast |
| 13      | S.Y. Ko et al., 2018 | 40F | B/L breast enlargement - 1 year | - | Right - 3.7 kg, left - 3.3 kg | B/L mastectomy | Extreme dense parenchyma both breast |
| 14      | Morone et al., 2018 | 11F | Exacerbatated breast growth for 8 months from menarche, | - | Right - 2.33 kg, left - 860 gm | Reduction mammoplasty | - |
| 15      | M Vijverberg et al., 2020 | 15F | Rapidly growing breasts, back pain, neck pain, mastalgia | - | Right - 324 gm, left - 381 gm | Reduction mammoplasty | MRI - BIRADS II, multiple well bounded masses with varying intensity |
| 16      | Farias et al., 2020 | 27F | B/L breast enlargement 3 years started from pregnancy | Enlargement of accessory breast (11 x 8 x 5 cm) | Right - 6.2 kg, Left - 4.3 kg | B/L mastectomy | - |
| 17      | Al Balas et al., 2020 | 21F | B/L breast enlargement, neck pain | Family history of macromastia | Right - 1.7 kg, left - 1.95 kg | Reduction mammoplasty | Heterogeneously dense breast with no mass lesion |
| 18      | Aikansha Vasishtha et al., 2020 | 37F | B/L breast enlargement for 8 years, severe back pain | - | Right - 5 kg, left - 3.5 kg | Reduction mammoplasty | Gigantomastia with no abnormal findings (BIRADS 2) |
| 19      | S. Vyas et al., 2020 | 20F | B/L breast enlargement, started during pregnancy | Implanted birth control | - | Punch biopsy | Extreme dense parenchyma both breast |
| 20      | Present case | 45F | B/L breast enlargement for 2 years, with cyclical pain and heaviness | Hypertensive (on amlodipine) | Right - 27 x 25 x 5.5 cm, left 27 x 22 x 5 cm | Bilateral mastectomy | Dense parenchyma with multiple cysts and fibro-adenomas |

Table 1. Survey of Previously Published Cases of Diffuse PASH
PASH is not a malignant or premalignant condition. There is only one reported case of malignant change in a PASH. For palpable tumoral PASH, excision with wide margins seems to be curative.22

There is no definite guideline for the management of diffuse PASH presenting with gigantomastia. Histology, risk factors, patient preference and cosmetic appearance is also considered before surgical management. Reduction mammoplasty/mastectomy/symmetrisation (in case of asymmetrical enlargement) are the usual surgical procedures considered. Pruthi et al. reports a case where tamoxifen is successfully used in the management of PASH.23

CONCLUSIONS

We report this case for its rarity. PASH should be considered in the differential diagnosis of gigantomastia. There is scope in researching the aetiopathogenesis of gigantomastia with PASH and further treatment protocol. Bilateral mastectomy seems to be the definitive management for these cases and the patients should be under follow up for recurrence.

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