

Pseudoangiomatous stromal hyperplasia (PASH) presenting as axillary lump: case report and review of the literature

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SUMMARY: Pseudoangiomatous stromal hyperplasia (PASH) presenting as axillary lump: case report and review of the literature.

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Pseudoangiomatous stromal hyperplasia (PASH) is an uncommon benign mesenchymal breast lesion. There are extremely rare reports of PASH arising in accessory breast tissue. To date, in literature, fewer than 10 cases of PASH occurring in axillary region have been descri-

bed. We report a case presenting as axillary lump in a young woman.

A 20-year-old female presented to our surgical unit for a progressively growing and painful palpable mass of the right axilla for about a year. Before surgery an ultrasound was performed. The patient underwent local excision of the lesion under local anaesthesia. Through histological and immunohistochemical examination a pseudoangiomatous stromal hyperplasia (PASH) was diagnosed. At 6 months of follow-up the patient is free of disease.

It is important to include PASH also in the differential diagnosis of axillary lumps. Histological examination of the surgical specimen and surgery represent, respectively, the mainstay for diagnosis and therapy.

KEY WORDS: Pseudoangiomatous stromal hyperplasia - PASH - Benign breast lesions - Axillary lumps - Accessory breast tissue.

Introduction

Pseudoangiomatous stromal hyperplasia (PASH) is an uncommon benign proliferative lesion of the mesenchymal breast tissue. Its etiopathogenesis is still unclear but its onset seems to be strongly linked to hormonal stimuli (1-5). Typically it occurs in premenopausal women but it has also been reported in females of different ages and in men (6-8). It is usually diagnosed incidentally in breast tissue removed for other reasons (9). There are extremely rare reports of PASH arising in accessory breast tissue, in the axillae but also in the anogenital region (10-18). To date, in literature, fewer than 10 cases of PASH occurring in axillary region have been described (10-12, 14-18).

Preoperative diagnosis is very difficult, thus histological examination of the surgical specimen is essential for the definitive diagnosis (19).

Surgery represents the mainstay of treatment (10, 19). The prognosis is good and it does not seem to be a premalignant lesion (20). It has a recurrence rate up to 26% following surgery (1, 12, 21-23). In this paper, we report a case of PASH arising in the right axilla of a young female and presenting as a palpable mass.

Case report

A 20-year-old Caucasian female presented to our surgical unit for a progressively growing and painful mass in the right axilla for about a year. Her past medical history was unremarkable and she did not have a family history of breast disease. She was taking oral contraceptives.

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Physical examination revealed a well-defined oval lump with a maximum diameter of about 2 cm in the right axilla, without any skin change. Moreover, the mass resulted firm, mobile and tenderness. No other lesions were found in the contralateral axilla and in breast.

Ultrasound showed a hypoechoic oval mass, measuring 2,62 x 0,51 cm. No other examination was performed preoperatively.

The patient underwent local excision of the lesion under local anaesthesia. Postoperative course was uneventful and the young woman was discharged 5 hours after surgery in good condition.

On histological examination a complex pattern of empty slit-like spaces lined by myofibroblasts, resembling vascular structures, were observed (Figure 1). On immunohistochemical evaluation cells showed positive staining for CD34, actin and vimentin, and negative staining for Factor VIII-related antigen, CD31 and cytokeratins (Figures 2, 3). The final diagnosis was pseudoangiomatous stromal hyperplasia (PASH).

At 6 months of follow-up the patient is free of disease.

Discussion

Pseudoangiomatous stromal hyperplasia (PASH)

was first described in 1986 by Vuitch et al. (21). It is a rare benign proliferative mesenchymal lesion of the breast.

Histologically, it is characterized by a complex pattern of slit-like spaces, in a dense collagenous stroma, that resembles vascular structures. However, these spaces are lined by myofibroblasts rather than endothelial cells and red blood cells are missing. From this histological feature derives the term "pseudoangiomatous".

PASH, as in our case, typically affects premenopausal women (6). However, some cases occurring in adolescent girls, postmenopausal women and men have also been reported. In male this disease has always been described in association with gynecomastia (7, 8).

Its etiopathogenesis is still unclear. However, its onset seems to result from an abnormal proliferative response of myofibroblasts to hormonal stimuli. This theory is supported by its higher occurrence in females of reproductive age. Furthermore, this hypothesis is corroborated by some other reasons, as the evidence that more than half of postmenopausal women with PASH received hormone replacement therapy, a case of rapid growing PASH during pregnancy and a case of PASH in a transgender male receiving exogenous hormones (1-3, 5). According to this theory, it has also been hypothesized that the use of contraceptives, also taken by our patient, may

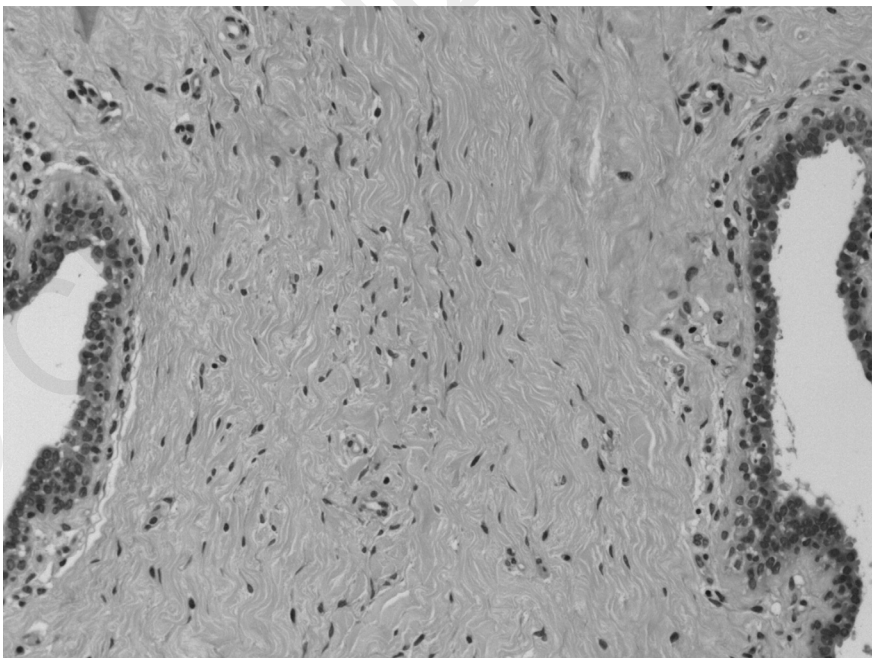


Figure 1 - Complex pattern of empty slit-like spaces lined by myofibroblasts resembling vascular structures (H&E, 200x).

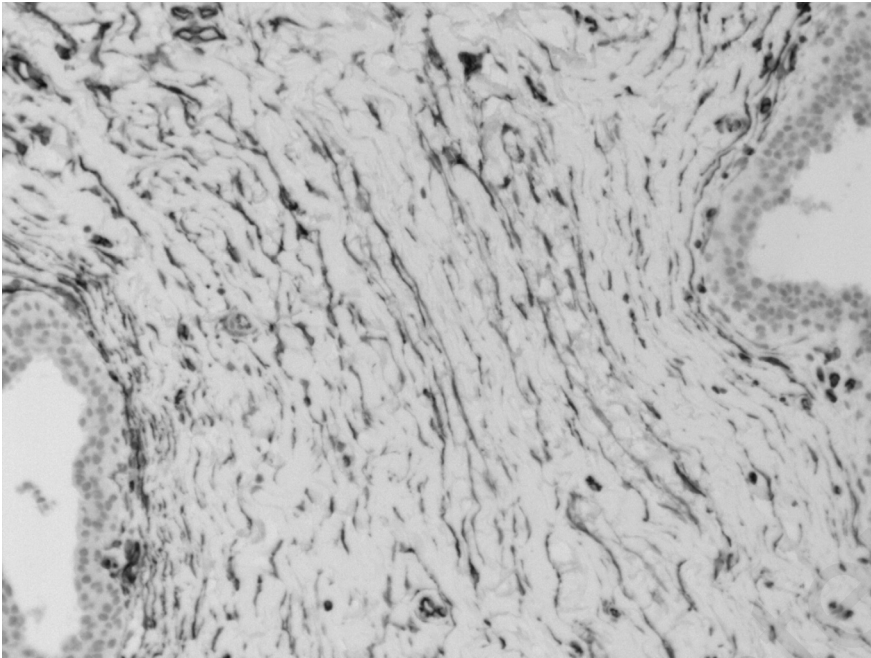


Figure 2 - Myofibroblasts lining the empty slit-like spaces show positive staining for CD34 (200x).

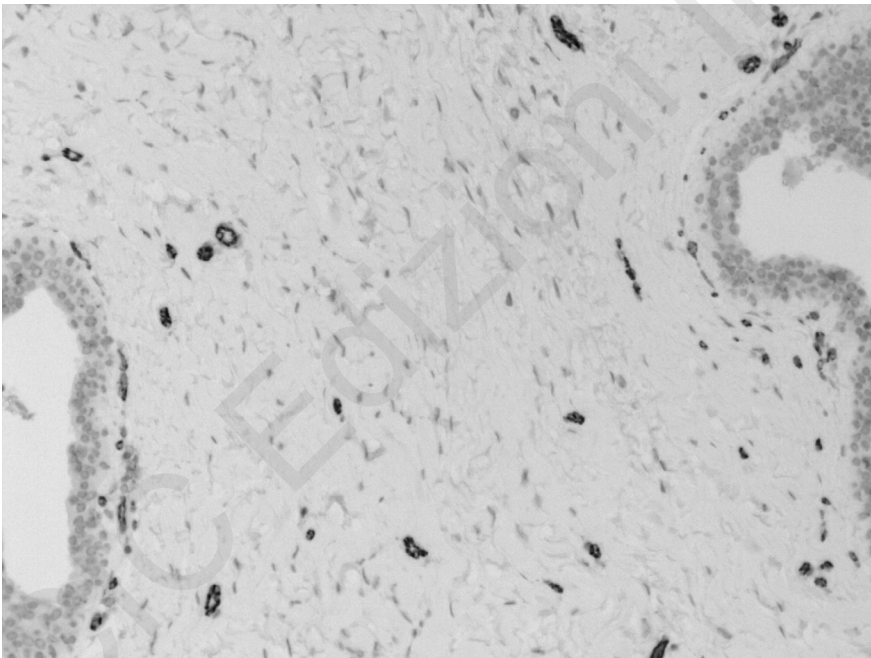


Figure 3 - Myofibroblasts lining the empty slit-like spaces show negative staining for CD31 (200x).

play a role in the onset of this disease (4).

PASH is usually an incidental microscopic finding in breast tissue removed for other reasons (9). It is indeed commonly associated with other concomitant breast diseases, both benign and malignant (1, 3, 7, 9, 21, 22, 24, 25). Besides appearing as a microscopic finding only, it can also present as a clinically

manifest lesion, with extremely variable clinical scenarios (20).

This disease can arise in other locations outside its usual site in breast, it has indeed been described in accessory breast tissue. Incomplete regression of portions of the milk line explains the persistence of accessory breast tissue. This tissue can be identified

anywhere along the milk line but it is mostly located in the axillary region. It is detected more frequently in females, but it can also be found in males. Accessory breast tissue is functionally identical to normal breast tissue and it is subjects to all physiological and pathological changes that occur in normal mammary gland (26, 27). Extremely rare cases of PASH arising in axillary and anogenital regions have indeed been described (10-18). We report a case of PASH occurring in the right axilla of a young woman and presenting as a lump. In literature, we found only 8 other cases of PASH arising in axillary region, 6 occurred in women (10, 12, 15-18) and 2 in men (11, 14).

Preoperative diagnosis is very difficult. On imaging, it has no characteristic features that may be useful for diagnostic aims. Ultrasound typically shows an oval, well-circumscribed and hypoechoic mass, however it can also document a heterogeneous lesion with cystic areas (28). Mammography most commonly shows a well-defined and uncalcified lesion with regular margins and borders (28). On MRI, it is isointense on T1-weighted images and can appear reticular on T2-weighted images. This last exam can provide a precise determination of the extent of disease, including the presence of multicentric or multifocal disease (6, 9, 29). About microscopical examination, FNAC is often inconclusive and the sensitivity of core-needle biopsy is equal to 83% only (9, 19). However, these two exams are useful for determining whether the lesion is benign or malignant (9, 10, 30). Ultimately, PASH definitive diagnosis requires histological examination of the surgical specimen (19). On immunohistochemical evaluation cells show positive staining for CD34, actin and vimentin, and negative staining for Factor VIII-related antigen, CD31 and cytokeratins (1, 31).

When PASH is localized in its usual site, in

breast, differential diagnosis mainly includes fibroadenoma, phyllodes tumor and angiosarcoma (24). Otherwise, when PASH is located in axillary region, differential diagnosis includes lymphadenopathy secondary to infection, lymphoma, metastatic carcinoma, benign lymphoid hyperplasia, hidradenitis suppurativa and accessory breast tissue with other pathological changes (15).

Surgery represents the mainstay of treatment (10, 19). The specific approach depends on the clinical presentation of this disease, in fact, it can range from local excision, as in our case, to mastectomy (1, 9, 25, 30). In literature, we found a case refractory to surgical therapy (32). On the other hand, some authors suggested a non-surgical management. Given the possible role of hormones in its onset, a pharmaceutical treatment with antihormonal drugs has been proposed. Successful cases responding at least partially to tamoxifen have been reported (33, 34). Otherwise, other authors, suggested a regular follow-up only (6, 9). It is important to specify that when PASH is diagnosed incidentally it does not require any additional specific treatment (25).

The prognosis is good and it does not seem to be a premalignant lesion (20). Its recurrence rate after surgery ranges from 7% to 26% (1, 12, 21-23). Our patient at 6 months of follow-up is free of disease.

Conclusion

A new rare case of pseudoangiomatous stromal hyperplasia (PASH) localized in axillary region has just been described. Thus, it is important to include PASH also in the differential diagnosis of axillary lumps, even in male patients. To date, histological examination of the surgical specimen and surgery represent, respectively, the mainstay for diagnosis and therapy.

References

1. Powell CM, Cranor ML, Rosen PP. Pseudoangiomatous stromal hyperplasia (PASH). A mammary stromal tumor with myofibroblastic differentiation. *Am J Surg Pathol.* 1995;19:270-7.
2. Ferreira M, Albarracín CT, Resetkova E. Pseudoangiomatous stromal hyperplasia tumor: a clinical, radiologic and pathologic study of 26 cases. *Mod Pathol.* 2008;21:201-7.
3. Bowman E, Oprea G, Okoli J, Gundry K, Rizzo M, Gabram-Mendola S, Manne U, Smith G, Pambuccian S, Bumpers HL. Pseudoangiomatous stromal hyperplasia (PASH) of the breast: a series of 24 patients. *Breast J.* 2012;18:242-7.
4. Sollozo-Dupont I, Domínguez-Hernández HA, Pavón-Hernández C, Villaseñor-Navarro Y, Shaw-Dulin R, Pérez-Sánchez VM, España-Ferrufino AJ, Álvarez-Guadarrama LM, Porrás-Reyes FI, Pérez-Badillo MP. An Uncommon Case of Bilateral Breast Enlargement Diagnosed as Tumoral Pseudoangiomatous Stromal Hyperplasia: Imaging and Pathological Findings. *Case Rep Radiol.* 2017. *Case Rep Radiol.* 2017;2017:7603603. doi: 10.1155/2017/7603603. Epub 2017 Dec 3.
5. Prichard RS, O'Neill CJ, O'Hara JL, Atmore BB, Hassall M. Pseudoangiomatous stromal hyperplasia of the breast: an unusual pathology necessitating bilateral mastectomy during pregnancy. *ANZ J Surg.* 2011;81:304-5.

6. Jaunoo SS, Thrush S, Dunn P. Pseudoangiomatous stromal hyperplasia (PASH): A brief review. *Int J Surg*. 2011;9:20-2.
7. Badve S, Sloane JP. Pseudoangiomatous hyperplasia of male breast. *Histopathology*. 1995;26:463-6.
8. Milanezi MF, Saggioro FP, Zanati SG, Bazan R, Schmitt FC. Pseudoangiomatous hyperplasia of mammary stroma associated with gynaecomastia. *J Clin Pathol*. 1998;51:204-6.
9. Virk RK, Khan A. Pseudoangiomatous stromal hyperplasia: an overview. *Arch Pathol Lab Med*. 2010;134:1070-4.
10. Johnson HM, Reisler T. Pseudoangiomatous stromal hyperplasia presenting as accessory axillary breast tissue. *Eplasty*. 2017;17:ic19.
11. Seidman JD, Borkowski A, Aisner SC, Sun CC. Rapid growth of pseudoangiomatous hyperplasia of mammary stroma in axillary gynecomastia in an immunosuppressed patient. *Arch Pathol Lab Med*. 1993;117:736-8.
12. Lee JS, Oh HS, Min KW. Mammary pseudoangiomatous stromal hyperplasia presenting as an axillary mass. *Breast*. 2005;14:61-4.
13. Kazakov DV, Bisceglia M, Mukensnabl P, Michal M. Pseudoangiomatous stromal hyperplasia in lesions involving anogenital mammary-like glands. *Am J Surg Pathol*. 2005;29:1243-6.
14. Vega RM, Pechman D, Ergonul B, Gomez C, Moller MG. Bilateral pseudoangiomatous stromal hyperplasia tumors in axillary male gynecomastia: report of a case. *Surg Today*. 2015;45:105-9.
15. Jordan AC, Jaffer S, Mercer SE. Massive nodular pseudoangiomatous stromal hyperplasia (PASH) of the breast arising simultaneously in the axilla and vulva. *Int J Surg Pathol*. 2011;19:113-6.
16. Alikhassi A, Ensani F, Omranipour R, Abdollahi A. Bilateral Simultaneous Pseudoangiomatous Stromal Hyperplasia of the Breasts and Axillae: Imaging Findings with Pathological and Clinical Correlation. *Case Rep Radiol*. 2016. *Case Rep Radiol*. 2016;2016:9084820. Epub 2016 Oct 27.
17. Hayes MM, Konstantinova AM, Kacerovska D, Michal M, Kreuzberg B, Suvova B, Kazakov DV. Bilateral Gigantomastia, Multiple Synchronous Nodular Pseudoangiomatous Stromal Hyperplasia Involving Breast and Bilateral Axillary Accessory Breast Tissue, and Perianal Mammary-Type Hamartoma of Anogenital Mammary-Like Glands: A Case Report. *Am J Dermatopathol*. 2016;38:374-83.
18. Shimpi TR, Baska Reynolds V, Shikhare S, Srinivasan S, Clarke MJ, Peh WCG. Synchronous large tumoral pseudoangiomatous stromal hyperplasia (PASH) in the breast and axilla with subsequent carcinoma in the contralateral breast: routine and strain imaging with histopathological correlation. *BJR Case Rep*. 2015;1:20150017.
19. Kareem Z, Iyer S, Singh M. Pseudoangiomatous Stromal Hyperplasia: A Rare Cause of Breast Lump in a Premenopausal Female. *J Clin Diagn Res*. 2017;11:PD02-PD03.
20. Degnim AC, Frost MH, Radisky DC, Anderson SS, Vierkant RA, Boughey JC, Pankratz VS, Ghosh K, Hartmann LC, Visscher DW. Pseudoangiomatous stromal hyperplasia and breast cancer risk. *Ann Surg Oncol*. 2010;17:3269-77.
21. Vuitch MF, Rosen PP, Erlandson RA. Pseudoangiomatous hyperplasia of mammary stroma. *Hum Pathol*. 1986;17:185-91.
22. Gresik CM, Godellas C, Aranha GV, Rajan P, Shoup M. Pseudoangiomatous stromal hyperplasia of the breast: a contemporary approach to its clinical and radiologic features and ideal management. *Surgery*. 2010;148:752-7.
23. Singh KA, Lewis MM, Runge RL, Carlson GW. Pseudoangiomatous stromal hyperplasia. A case for bilateral mastectomy in a 12-year-old girl. *Breast J*. 2007;13:603-6.
24. Bayramoglu Z, Yilmaz R, Caliskan E, Onder S, Akkavak G, Adaletli I. Unilateral rapid enlargement of an adolescent breast: pseudoangiomatous stromal hyperplasia in a giant juvenile fibroadenoma. *Breast J*. 2018 Jul;24(4):648-649. doi: 10.1111/tbj.13030. Epub 2018 Mar 8.
25. Testori A, Alloisio M, Errico V, Bottoni E, Voulaz E, Fernandez B, Meroni S, De Simone M, Cioffi U. Pseudoangiomatous stromal hyperplasia - a benign and rare tumor of the breast in an adolescent: a case report. *J Med Case Rep*. 2017;11:284.
26. Routiot T, Marchal C, Verhaeghe JL, Depardieu C, Netter E, Weber B, Carolus JM. Breast carcinoma located in ectopic breast tissue: a case report and review of the literature. *Oncol Rep*. 1998;5:413-7.
27. Das DK, Gupta SK, Mathew SV, Sheikh ZA, al-Rabah NA. Fine needle aspiration cytologic diagnosis of axillary accessory breast tissue, including its physiologic changes and pathologic lesions. *Acta Cytol*. 1994;38:130-5.
28. Vo QD, Koch G, Girard JM, Zamora L, Bouquet de Jolinière J, Khomsy F, Feki A, Hoogewoud HM. A Case Report: Pseudoangiomatous Stromal Hyperplasia Tumor Presenting as a Palpable Mass. *Front Surg*. 2016;2:73.
29. Mai C, Rombaut B, Hertveldt K, Claikens B, Van Wettene P. Diffuse pseudoangiomatous stromal hyperplasia of the breast: a case report and a review of the radiological characteristics. *JBR-BTR*. 2014;97:81-3.
30. Samaila MO, Aliyu HO, Yusufu LM, Abdullahi S. Concurrent giant tumoral pseudoangiomatous stromal hyperplasia necessitating bilateral mastectomy. *Ann Afr Med*. 2018;17:82-85.
31. Zanella M, Falconieri G, Lamovec J, Bittesini L. Pseudoangiomatous hyperplasia of the mammary stroma: true entity or phenotype? *Pathol Res Pract*. 1998;194:535-40.
32. Lee JW, Jung GS, Kim JB, Choi KY, Chung HY, Cho BC, Park JY, Kim HJ, Park HY, Yang JD. Pseudoangiomatous Stromal Hyperplasia Presenting as Rapidly Growing Bilateral Breast Enlargement Refractory to Surgical Excision. *Arch Plast Surg*. 2016;43:218-21.
33. Seltzer MH, Kintiroglou M. Pseudoangiomatous hyperplasia and response to tamoxifen therapy. *Breast J*. 2003;9:344.
34. Pruthi S, Reynolds C, Johnson RE, Gisvold JJ. Tamoxifen in the management of pseudoangiomatous stromal hyperplasia. *Breast J*. 2001;7:434-9.