Case Report

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# Pseudoangiomatous Hyperplasia of Mammary Stroma: Insights from Two Cases, Data Update and Management Algorithm

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**ABSTRACT**

Pseudoangiomatous stromal hyperplasia (PASH) is a benign breast lesion frequently discovered incidentally during imaging or biopsy for other conditions. We present two cases of PASH associated with fibroadenomas in premenopausal women, both presenting as palpable, symptomatic breast masses. In the first case, a 26-year-old woman exhibited a 5.2 cm hypoechoic lesion, initially diagnosed as PASH on core biopsy, later confirmed as fibroadenoma with PASH components post-excision. The second case involved a 37-year-old woman with a painful 5.6 cm mass, diagnosed similarly via biopsy, and later confirmed as fibroadenoma fully colonized by PASH after surgical removal. Both cases highlight the diagnostic challenge in distinguishing PASH from fibroadenomas, given overlapping clinical and imaging features. Hormonal factors, particularly contraceptive use, may contribute to PASH development. Management remains controversial, with surgery indicated for symptomatic lesions, while conservative approaches may suffice for smaller, asymptomatic cases. Based on our findings and current literature, we propose a management algorithm to guide clinicians in differentiating cases warranting surgical intervention from those suitable for monitoring. Further studies are needed to validate this approach.

**Keywords:** Breast lesion; hormonal influence; pseudoangiomatous stromal hyperplasia; surgical management

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**Key Points**

- Pseudoangiomatous stromal hyperplasia (PASH) often coexists with other lesion, complicating preoperative diagnosis.
- Hormone therapy appears to influence PASH development.
- Symptomatic PASH lesions typically require surgical excision, while conservative management may be appropriate for asymptomatic cases.
- We propose an algorithm to optimize PASH management and avoid unnecessary surgeries.

## Introduction

Pseudoangiomatous stromal hyperplasia (PASH) is a benign breast condition identified in approximately 6% of biopsies performed for other benign lesions (1). First described by Vuitch et al. (2) in 1986, PASH is predominantly detected incidentally (3). A 23% incidence was reported in a series of 200 consecutive breast biopsies for benign and malignant lesions (4).

Histologically, PASH consists of a benign proliferation of myofibroblasts arranged in slit-like spaces mimicking vascular channels within the interlobular and intralobular connective tissue. PASH predominantly affects premenopausal women and is often associated with estrogen and progesterone receptor positivity (95%) (1, 3).

Immunohistochemistry typically shows positivity for fibroblast markers ($CD34^+$) and negativity for endothelial markers ($CD31^-$) (3).

Currently, there are no specific management guidelines for PASH. It can present as a microscopic finding, a palpable nodule, or in association with another lesion (4).

A retrospective study of 66 PASH cases observed progression, defined as an increase in lesion volume, in 16.6% of cases after a median follow-up of 26 months (5). PASH has been reported alongside other benign or malignant lesions, including apocrine metaplasia, fibroadenoma, hamartoma, intraductal papilloma, atypical ductal hyperplasia, and lobular carcinoma *in situ*, occurring in 1–26% of cases (5). Another study of 70 cases of PASH found that 60.4% were associated with

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benign epithelial lesions, 25.6% with atypical hyperplasia, and 11% ($n$ = 9/79) with infiltrating carcinoma ($p$<0.001), including one case of non-invasive ductal carcinoma *in situ* (6).

Interestingly, Degnim et al. (1) found that women with PASH had a lower breast cancer risk compared to women without PASH ($p$ = 0.01), in a large cohort with a mean follow-up of 18.5 years. Esmer et al. (7) similarly reported no cases of malignant transformation after a mean follow-up of 55 months. Moreover, among 335 phyllodes tumors, PASH was present in 70% of cases and correlated with lower tumor grade, reduced malignancy risk, and lower recurrence rates (8). The mechanism behind the observed reduced breast cancer risk in PASH remains unclear.

The aim of this study was to better define which cases of PASH require surgical excision and to propose a decision-making algorithm, based on two cases managed at the Senology Department of the Institut de Cancérologie de Strasbourg, Europe.

**Case Presentations**

**Case 1 (Figure 1)**

A 26-year-old woman presented after detecting a lump in her right breast. She had no relevant medical history, was nulligravid, and had been on hormonal contraception for three years. On examination, a mobile, 4 cm mass was palpated in the inner quadrants of the right breast, with no skin abnormalities or palpable nodes.

Ultrasound revealed a hypoechoic, oval-shaped mass measuring 5.2 cm, with multilobulated contours, minimal vascularization, and benign elastographic features. No adenopathy was noted.

Core biopsy demonstrated a fibrous, hyaline collagenous lesion with multiple pseudo-vascular slit-like spaces, consistent with PASH, with no features suggestive of phyllodes tumor. The fibrotic architecture favored a diagnosis of PASH.

Due to the lesion's size and discomfort, a lumpectomy via a periareolar incision was performed. Intraoperative radiography confirmed complete excision. The pathological examination described a 4.8×3.7 cm nodular, fibrous, whitish lesion with multilobulated contours. Histology revealed a fibroadenoma with a low-cellularity stroma partially replaced by PASH, without malignancy.

Postoperative follow-up at 13 days showed good cosmetic results and complete wound healing. Clinical and imaging follow-up was scheduled at six months.

**Case 2 (Figure 2)**

A 37-year-old woman presented with a self-palpated, painful 5 cm mass in the upper outer quadrant of her right breast. Her history included two pregnancies, progestin-only contraception, and prior treatment of an Arnold nerve schwannoma with radiotherapy.

On clinical examination, a painful 5 cm mass was found. Mammography revealed a rounded central opacity measuring 5.6 cm, corresponding on ultrasound to a strongly hypoechoic mass. Imaging was classified as breast imaging reporting and data system (BI-RADS) 3 (right) and BI-RADS 1 (left).

Core biopsy showed a fibro-epithelial lesion with non-compressed glandular elements, without epithelial hyperplasia or atypia. The collagen-rich stroma contained a dense network of anastomotic cavities lined by fusiform cells without atypia or mitoses, highly suggestive of nodular PASH.

Surgical excision was performed for symptomatic relief. Intraoperative radiography confirmed complete removal. Histological analysis revised the diagnosis to a fibroadenoma entirely colonized by PASH. Histology demonstrated a hypercellular connective tissue component with abundant anastomotic, optically empty slits surrounded by hyalinized fibrocollagenous CD34⁺ stroma, without endothelial marker (e.g., ERG) expression.

At 12-day follow-up, wound healing and cosmetic outcomes were satisfactory. Surveillance was scheduled for six months.

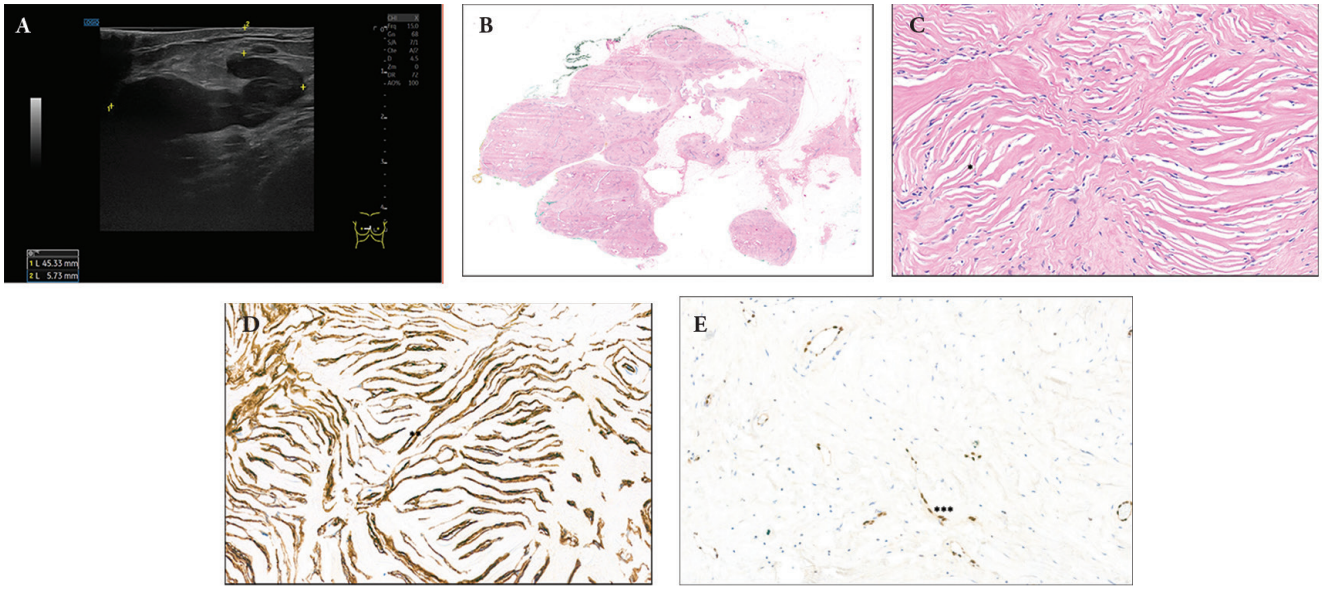


**Figure 1.** Case 1. Ultrasonography (A), low-power magnification showing a circumscribed but lobulated biphasic fibroepithelial lesion (B), with area exhibiting features of PASH at higher magnification (C), characterized by dense collagenic stroma shaping anastomosing slit-like channels (*) with CD34 immunoreactivity (**) (D) and without endothelial marker immunoreactivity (e.g., ERG) despite internal control positivity (***) (E)

## Discussion and Conclusion

These two cases highlight the frequent association of PASH with fibroadenomas. Despite biopsy results favoring a diagnosis of PASH, the palpable nature of the lesions was ultimately attributable to the fibroadenoma components.

Both patients were premenopausal and on hormonal contraception, consistent with known risk factors for PASH. Hormonal influence is supported by Vuitch et al. (2), who found similarities between PASH stroma and physiological changes during the luteal phase. In postmenopausal women, PASH is often linked to hormone replacement therapy (9), while in men, it is frequently associated with gynecomastia (10, 11). In addition, cytochrome P450-mediated drug metabolism may influence PASH development by altering estrogen and progesterone pathways (12). This is further supported by a retrospective study showing reduced PASH incidence among transgender individuals undergoing prolonged testosterone therapy (median follow-up: 17 months, $p<0.001$) (13).

Some reports suggest tamoxifen therapy (off-label) as a non-surgical treatment option for symptomatic PASH, given its presumed hormonal etiology. Two case reports described rapid symptom relief and breast volume reduction with tamoxifen, although efficacy waned in one case after three months (14, 15).

Currently, no formal PASH management guidelines exist. Based on our cases and literature review, we propose a management algorithm (Figure 3). According to this algorithm, symptomatic and palpable lesions warrant surgical excision. In contrast, for smaller lesions, withdrawal of hormonal contraception followed by re-evaluation after six months may be considered. Validation of this approach in larger cohorts is necessary to avoid unnecessary surgeries in benign cases.

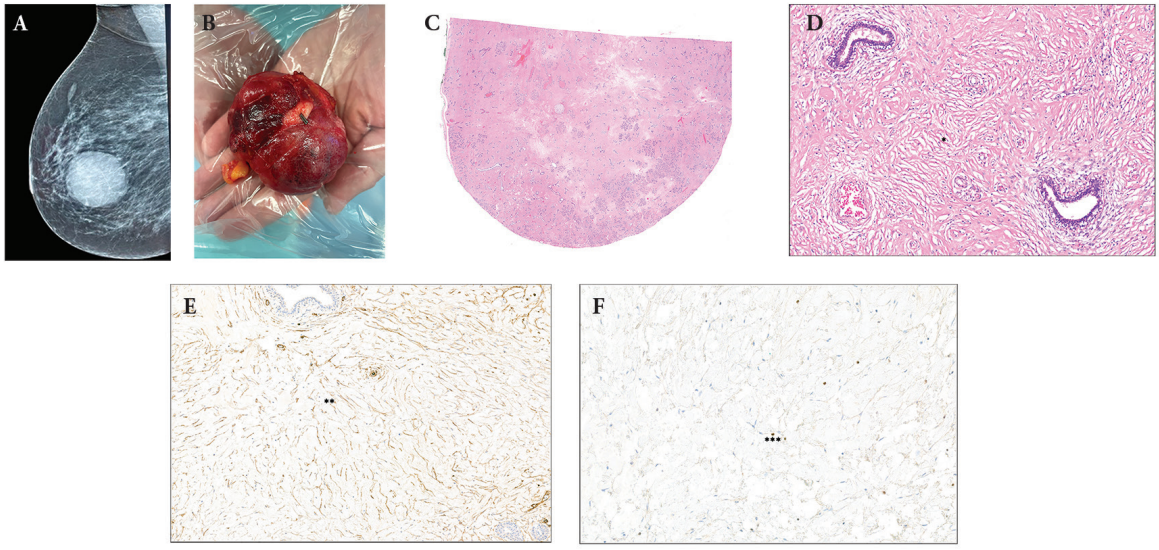


**Figure 2.** Case 2. Mammography (A), surgical specimen (B), low-power magnification showing a circumscribed biphasic fibroepithelial lesion with leaf-like pattern (C), comprising area exhibiting features of PASH at higher magnification (D), characterized by anastomosing slit-like channels (*) with weak CD34 immunoreactivity (**) (E) and without endothelial marker immunoreactivity (e.g., ERG) despite internal control (***) (F)

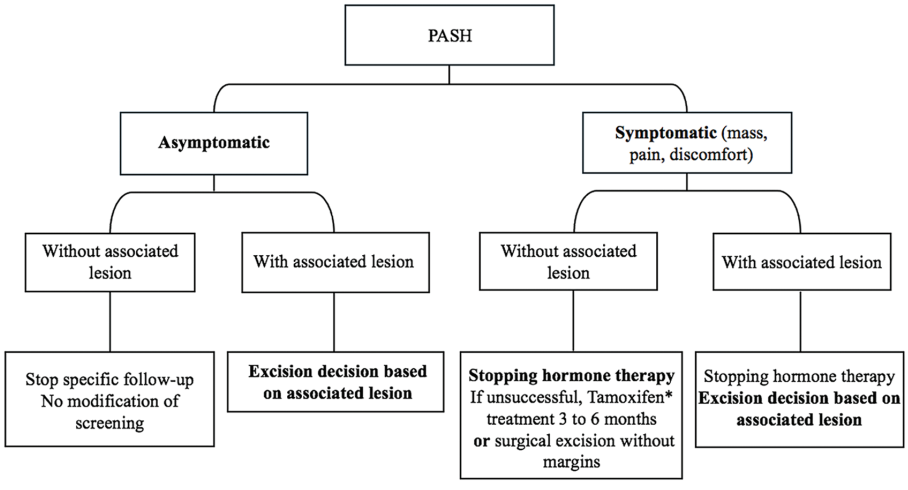


**Figure 3.** Algorithm for PASH management

*PASH: Pseudoangiomatous stromal hyperplasia; *: Off-label prescription*

## Ethics

**Informed Consent:** Retrospective study.

## Footnotes

### Authorship Contributions

Surgical and Medical Practices: C.B., T.W., M.B., C.M.; Concept: C.M.; Design: C.M.; Data Collection or Processing: C.B., T.W.; Analysis or Interpretation: C.B., T.W.; Literature Search: C.B.; Writing: C.B., T.W.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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