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CASE REPORT

Case Report: a rare case of PASH mimicking a lactational adenoma [version 1; peer review: 3 approved with reservations]

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V1 First published: 09 Feb 2018, 7:169
<https://doi.org/10.12688/f1000research.13909.1>
 Latest published: 09 Feb 2018, 7:169
<https://doi.org/10.12688/f1000research.13909.1>

Abstract

Pseudoangiomatous stromal hyperplasia (PASH) is a rare, benign breast lesion that is usually discovered as an incidental finding in breast biopsies. We present a case report of a twenty three-year-old female who presented with a large central mass in the left breast 24 weeks into her pregnancy. An ultrasound-guided core biopsy was performed which was reported as a lactational adenoma and due to the significant size of the mass it was excised as a suspected giant lactational adenoma. The ultrasound appearance was of a mass with well-defined superficial and radial margins with multiple large gentle lobulations, and a thin echogenic pseudocapsule pointing towards a benign diagnosis. Multiple prominent internal vessels were visualised on doppler imaging; PASH lesions do not commonly have internal blood flow which therefore pointed away from the diagnosis in this case. It is likely the imaging features were confounded by the pregnant state. Macroscopically, the lesion consisted of a large lobulated red mass measuring 170 x 170 x 75 mm and weighing 838 g with a central area containing yellow cream-like material measuring 25 x 20 mm. Microscopically, the breast tissue showed prominent gynaecomastoid-like lobules with intervening oedematous stroma showing florid pseudoangiomatous hyperplasia. There was prominent but only patchy lactational change. PASH can often be an incidental finding and is commonly found in combination with other diagnoses. It is therefore possible for PASH to be overlooked in biopsy specimens, as in this case, and it is important to analyse the breast stroma carefully for evidence of PASH, even if the biopsy contains an alternative lesion that could account for the mass seen clinically. We feel this case highlights the potential for PASH to be overlooked in core biopsy specimens when a concurrent lesion is present and therefore not appropriately treated.

Keywords

Pseudoangiomatous stromal hyperplasia, pash, lactational adenoma, breast

Open Peer Review

Approval Status

	1	2	3
version 1
09 Feb 2018	view	view	view
<p>1. Malcolm M. Hayes, The University of British Columbia, Vancouver, Canada</p> <p>2. Josko Bezic, Clinical Hospital Center, Split, Croatia</p> <p>3. Modupeola Omotara Samaila , Ahmadu Bello University and Ahmadu Bello University Teaching Hospital Zaria, Zaria, Nigeria</p> <p>Any reports and responses or comments on the article can be found at the end of the article.</p>			

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Author roles: **Hoggard S:** Conceptualization, Project Administration, Resources, Visualization, Writing – Original Draft Preparation; **Meara N:** Conceptualization, Project Administration, Resources, Supervision, Writing – Review & Editing; **Bundred S:** Resources, Validation, Visualization, Writing – Original Draft Preparation

Competing interests: No competing interests were disclosed.

Grant information: The author(s) declared that no grants were involved in supporting this work.

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How to cite this article: Hoggard S, Meara N and Bundred S. **Case Report: a rare case of PASH mimicking a lactational adenoma [version 1; peer review: 3 approved with reservations]** F1000Research 2018, 7:169 <https://doi.org/10.12688/f1000research.13909.1>

First published: 09 Feb 2018, 7:169 <https://doi.org/10.12688/f1000research.13909.1>

Case report

Pseudoangiomatous stromal hyperplasia (PASH) is a rare, benign breast lesion that is usually discovered as an incidental finding in breast biopsies¹. Despite usually being an incidental finding, there have been many reports in the literature of PASH presenting clinically as a discrete mass, and several reports of it presenting as bilateral diffuse breast enlargement². We present a case report of PASH presenting as a large clinically-evident breast mass in a pregnant woman which was initially diagnosed as a lactational adenoma on the core biopsy. The subsequent excision specimen demonstrated a large, discrete tumour composed of PASH with a central galactocoele, as well as prominent but only patchy lactational change. Following this, PASH was retrospectively identified as being present in the initial core biopsy.

Clinically, PASH has a wide range of signs and symptoms, ranging from presenting as a large breast mass, to being an incidental finding. Indeed, non-tumour-forming PASH has been reported to be an incidental microscopic finding in 23% of breast biopsies³. Tumour-forming PASH occurs predominantly in premenopausal women and usually presents clinically as a palpable, mobile, firm, painless, intra-mammary mass⁴. Cases of tumour-forming PASH have also been described in post-menopausal women, men, adolescents and even in the paediatric age group⁵. In our case, the patient was a twenty three-year-old female who presented with a large central mass in the left breast 24 weeks into her pregnancy (Figure 1). She first noticed the mass at around week 10 of her pregnancy but it then massively increased in size around week 24. She had a history of a biopsy-proven lactational adenoma six years previously during her first pregnancy. An ultrasound-guided core biopsy was performed which was reported as a lactational adenoma, B2, and due to the significant size of the mass it was excised in week 25 of her pregnancy as a suspected giant lactational adenoma.

Several publications of case series^{6–9} show the typical ultrasound appearance of PASH to be a well-circumscribed oval or round mass encompassed by a thin echogenic capsule and usually indistinguishable from a fibroadenoma, with size ranging from 3 to 70 mm. Internal echotexture is most commonly hypoechoic, sometimes isoechoic, and occasionally complex containing cysts or

vascular channels. In this case, the 140 mm mass within a breast hypertrophied through pregnancy changes presented a challenge for imaging with conventional ultrasound due to the extremely large size. The subcutaneous breast tissue was oedematous and there was skin thickening present up to 5.5 mm in more dependant areas of the breast. The mass had well-defined superficial and radial margins with multiple large gentle lobulations, and a thin echogenic pseudocapsule pointing towards a benign diagnosis (Figure 2). The internal echotexture was predominantly bland, homogenous and hypoechoic. Multiple prominent internal vessels were visualised on doppler imaging; PASH lesions do not commonly have internal blood flow however, which therefore pointed away from the diagnosis in this case. It is likely the imaging features were confounded by the pregnant state. The differential diagnosis based on the ultrasound appearances included a fibroadenoma, a lactational adenoma and a phyllodes tumour.

The classical histological appearance of PASH is inter-anastomosing channels lined by slender spindle cells in the interlobular breast stroma¹⁰. As the name suggests, ultrastructural observations have determined that these channels are not true vascular spaces and the distinction from an angiosarcoma is obviously important¹¹. Immunohistochemistry shows the cells are positive for vimentin and CD34¹² but are negative for CD31. Macroscopically, the lesion in this case consisted of a large lobulated red mass measuring 170 x 170 x 75 mm and weighing 838 g with a central area containing yellow cream-like material measuring 25 x 20 mm (Figure 3). Histologically the breast tissue showed prominent gynaecomastoid-like lobules with intervening oedematous stroma showing florid pseudoangiomatous hyperplasia (Figure 4). There was prominent but only patchy lactational

Figure 1. Clinical appearance of left breast mass. The patient first noticed a left breast mass in week 10 of her pregnancy but it then massively increased in size around week 24.

Figure 2. Ultrasound appearance of breast mass. The mass had a thin echogenic pseudocapsule pointing towards a benign diagnosis and the internal echotexture was predominantly bland, homogenous and hypoechoic.

Figure 3. Macroscopic appearance of breast mass. The lesion consisted of a large lobulated red mass measuring 170 x 170 x 75 mm and weighing 838 g with a central area containing yellow cream-like material.

Figure 4. Microscopic high-power view of pseudoangiomatous stromal hyperplasia. The breast tissue showed prominent gynaecomastoid-like lobules, with intervening oedematous stroma showing florid pseudoangiomatous hyperplasia and prominent but only patchy lactational change.

change. The central cyst was lined by a single layer of apocrine-like cells in keeping with a galactocoele. There was no evidence of atypical hyperplasia, in-situ or invasive carcinoma. The diagnosis was given as pseudoangiomatous stromal hyperplasia with prominent but only patchy lactational change and a galactocoele.

Similar changes were seen in the initial core biopsy of this lesion and on review of the lesion cored during the first pregnancy.

PASH can often be an incidental finding and is commonly found in combination with other diagnoses. It is therefore possible for PASH to be overlooked in biopsy specimens and it is important to analyse the breast stroma carefully for evidence of PASH, even if the biopsy contains an alternative lesion that could account for the mass seen clinically. As highlighted well by this case, the presence of lactational change on its own in the core biopsy could have accounted for the mass lesion identified clinically and radiologically. This would have been further reinforced by the history of a previous biopsy-proven lactational adenoma during her last pregnancy. This highlights the potential for PASH to be overlooked in core biopsy specimens and therefore not appropriately treated. Fortunately, in this case the mass was so large and impacting upon the patient that it was excised anyway. PASH discovered incidentally does not require any specific additional treatment; however, tumour-forming PASH should be treated with local surgical excision and has an excellent prognosis with minimal risk of recurrence if adequately surgically excised according to some reports in the literature¹³. Other papers have reported recurrence rates between 15% and 22% after surgical excision¹⁴. The long-term prognosis for this patient would be expected to be excellent but we do not yet have long-term follow up data available. At her initial follow-up clinic appointment no problems were reported and her pregnancy was progressing as planned.

In summary we present a case report of tumour-forming PASH mimicking a giant lactational adenoma in a young pregnant patient. We feel it highlights the importance of looking carefully for PASH in core biopsy specimens, even if a concurrent lesion is also present which would account for the mass identified radiologically.

Consent

Written informed consent for publication of their clinical details and/or clinical images was obtained from the patient according to the Declaration of Helsinki.

Competing interests

No competing interests were disclosed.

Grant information

The author(s) declared that no grants were involved in supporting this work.

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Current Peer Review Status: ? ? ?

Version 1

Reviewer Report 19 October 2018

<https://doi.org/10.5256/f1000research.15121.r39184>

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Modupeola Omotara Samaila

Department of Pathology, Ahmadu Bello University and Ahmadu Bello University Teaching Hospital Zaria, Zaria, Nigeria

A well written manuscript with detailed ultrasound/radiological findings.

The abstract should only present the case without explanatory comments. "PASH lesions do not commonly have internal blood flow which pointed away from this diagnosis. It is likely the imaging study was confounded by the pregnant state" should be deleted from the abstract.

If there is no histological evidence of lactational adenoma in the initial core biopsy which was reviewed to PASH with lactational change and galactocoele after surgical excision, then there is no mimicry in this case. There is a difference between lactational changes and lactational adenoma which is neoplastic. Could the pregnancy have induced PASH in view of the hormonal influences which have been well documented in literature. This should be clarified appropriately in the manuscript. How this pitfall of initial misdiagnosis can be avoided will be useful to clinicians if included in the discussion.

Perhaps, the title should have reflected the radiological (ultrasound) potential of wrong diagnosis of PASH in pregnancy.

Figure 3 should have been bisected to show the central galactocoele and figure 4 shows PASH only with no areas of gynaecomastoid like changes.

Is the background of the case's history and progression described in sufficient detail?

Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

No

Is the case presented with sufficient detail to be useful for other practitioners?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Anatomic Pathologist with specialty in breast and gynaecologic pathology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 15 October 2018

<https://doi.org/10.5256/f1000research.15121.r39185>

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Josko Bezic

Institute of Pathology, Forensic Medicine and Cytology, Clinical Hospital Center, Split, Croatia

The PASH of the breast tissue is well known histological finding, firstly described by Vuitch *et al.* more than 30 years ago. However, some examples of PASH with unusual clinical, imaging, or pathohistological features may be worthy of publication. Here, Hoggard *et al.* presented the case of so-called nodular or tumorous PASH, which was associated with pregnancy and which on US guided core biopsy simulated a lactational adenoma.

The case is well presented on the clinical and radiological ground, but it is less persuasive in the histological part, mainly due to the only one presented micro-photograph of the lesion.

Major revision points:

1. There is a strong evidence that the PASH is caused by hormonal stimulation of mammary myofibroblasts, with particular role of progesterone, which well explains the rapid enlargement of the lesion during pregnancy in the presented case. Curiously, I could not find any observation about the role of hormones in pathogenesis of PASH in the manuscript.
2. The presented micro-photograph of the lesion (Figure 4) is insufficient in several ways:
 - Only the PASH is visible in the figure, and therefore the figure legend with the observations

about visible gynecomastoid-like changes, oedematous stroma and lactational changes are completely inappropriate. This may be an unintentional error related to the article technical editing after the submission.

- Related to the previous point, it would be appropriate to show micro-photographs with visible lactational changes, as well as with visible gynecomastoid hyperplasia and central galactocoele.
- One low power micro-photograph of the nodule (or at least of the part of the nodule) with visible distribution of the PASH and epithelial elements is crucial for the correct pathohistological diagnosis (see the major revision point 3).

3.The major differential diagnosis here is mammary hamartoma, and again without any notification about it in the text. The PASH is common finding in the stroma of the breast hamartoma, as well as gynecomastoid-like changes. The lactational changes are expected in the epithelium of hamartoma during pregnancy, as well as rapid enlargement of pre-existing small hamartomatous nodule. The authors must stress out in the discussion why that presented nodule better fits to the diagnosis of nodular PASH than to the diagnosis of mammary hamartoma.

Minor revision point:

1.The abstract should be more concise.

Is the background of the case's history and progression described in sufficient detail?

Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

No

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

No

Is the case presented with sufficient detail to be useful for other practitioners?

Yes

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 21 March 2018

<https://doi.org/10.5256/f1000research.15121.r31465>

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Malcolm M. Hayes

Department of Pathology and Laboratory Medicine, The University of British Columbia, Vancouver, BC, Canada

This is an interesting case that merits publication as a case report.

I think the diagnosis is sound based on the description and single photograph.

However, ideally, one would like to see a low-power picture of the lesion and a representative photograph of the epithelial elements exhibiting lactational and hyperplastic changes.

Also, the case is of interest because this lesion has a history of rapid growth - most likely induced by the pregnancy - a fact that should be stressed in the discussion to make radiologists and pathologists aware of the apparently alarming clinical evolution that may be encountered in PASH during the altered hormonal environment of pregnancy.

Is the background of the case's history and progression described in sufficient detail?

Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

Yes

Is the case presented with sufficient detail to be useful for other practitioners?

Yes

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

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