Surgical and Experimental Pathology

CASE REPORT

Open Access

"Intraparenchymal leiomyoma of breast with atypical features: diagnostic dilemma"

Amber Parwaiz[1*], Avinash Singh[1], Tarun Kumar[1] and Punam Bhadani[1]

Abstract

Background Breast leiomyoma is a rare neoplasm, accounting for less than 1% of all breast neoplasms. Most of the leiomyomas occur in the subareolar region. There are a few reported cases of intraparenchymal leiomyoma. Rarely reported, cases of intraparenchymal leiomyoma with atypical features are not a well-defined entity, and little is known about their clinical course.

Case presentation We present a rare case report of breast parenchymal leiomyoma in a 45-year-old woman. The clinical characteristics, imaging findings, and histology of the lesion are discussed here. Atypical morphological features observed in this case were focal atypia, increased mitosis, and Ki-67 proliferation index.

Conclusion In the absence of a well-defined diagnostic criteria, the exact behavior of parenchymal leiomyoma with atypical features is difficult to ascertain. These cases should be closely followed after wide local excision.

Keywords Leiomyoma, Atypical, Leiomyosarcoma

Background

Leiomyoma is a benign tumor composed of smooth muscle cells. It is the most common mesenchymal tumor of the uterus and fairly common in the gastrointestinal tract (Stewart et al. 2016). Leiomyoma of the breast is a rare benign non-epithelial tumor and accounts for less than 1% of all breast neoplasms. In the breast, they are commonly found in the subareolar region due to the abundance of smooth muscle cells in this location (Sampaio et al. 2016). The clinical, imaging, and pathological characteristics do not differ much from the leiomyoma of the uterus. The uterine smooth muscle tumors are classified into benign leiomyoma and its subtypes, Smooth Muscle Tumors of Uncertain Malignant Potential (STUMP) and leiomyosarcoma, based on their histological features and clinical behavior (Liu et al. 2022). However, due to its rarity in the breast, there are no definitive diagnostic criteria for atypical intraparenchymal breast leiomyoma. There are only 34 published cases of intraparenchymal leiomyoma in the English literature, and only two cases have been described as intraparenchymal leiomyoma with 'gray zone' features (Brandão et al. 2017; Kafadar et al. 2017; Long et al. 2022; Philipose et al. 2021). We present here an additional case of leiomyoma of the parenchymal breast with increased cellularity and mitosis, though not meeting the criteria for leiomyosarcoma. We summarize its imaging, histopathological, and immunohistochemical findings, highlighting its atypical features.

Case presentation

A 45-year-old female presented with vague discomfort in the left breast for 2 months. The patient did not report any nipple discharge or any constitutional symptoms. The physical examination revealed a well-defined, painless, mobile nodule in the upper outer quadrant of the left breast.

*Correspondence:
Amber Parwaiz
amberparwaiz@gmail.com
[1] Department of Pathology, All India Institute of Medical Science, Patna, Bihar, India

Imaging findings

Left breast ultrasonography (USG) scanning identified a well-defined, heterogeneously hypoechoic soft tissue lesion with lobulated margins and parallel orientation. The lesion measured approximately 8 cm in its largest dimension, exhibiting no significant internal vascularity or calcification. The lesion was 3 cm away from the areola without any overlying skin changes, nipple retraction, or axillary lymphadenopathy. It was reported as BI-RADS category 3, benign lesion likely fibroadenoma (Fig. 1).

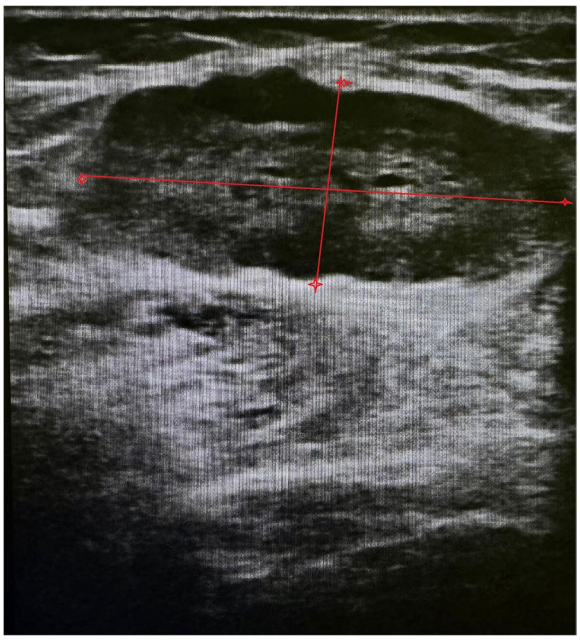

Fig. 1 Ultrasound examination of the left breast showing a heterogeneously hypoechoic oval nodule with lobulated margins and well-defined borders, located in the upper outer quadrant

Histopathology and immunohistochemistry

Ultrasound-guided percutaneous biopsy was performed. Histopathological examination revealed a spindle cell lesion. These spindle cells showed mild nuclear atypia, having delicate chromatin, small inconspicuous nucleoli, and abundant eosinophilic cytoplasm. Mitotic figures were observed 2–3/10 HPF (Fig. 2A, B). Necrosis was not observed in the core biopsy. Immunohistochemistry (IHC) for smooth muscle actin (SMA) was uniformly positive, and the Ki-67 index was about 5% (Fig. 2C, D). IHCs for CD34, S-100, and Beta-catenin were negative.

The patient underwent surgical excision of the lesion. Gross examination revealed a well-circumscribed lesion measuring 8 cm × 5 cm. The cut surface showed a white, rubbery mass with a whorled appearance. Areas of cystic change, congestion, and discoloration were also noted (Fig. 3).

Microscopy revealed a well-circumscribed spindle cell lesion forming interlacing bundles and fascicles with an entrapped gland at the periphery (Fig. 4A). The lesion showed areas of variable cellularity and nuclear atypia. Predominantly there were areas of benign leiomyoma

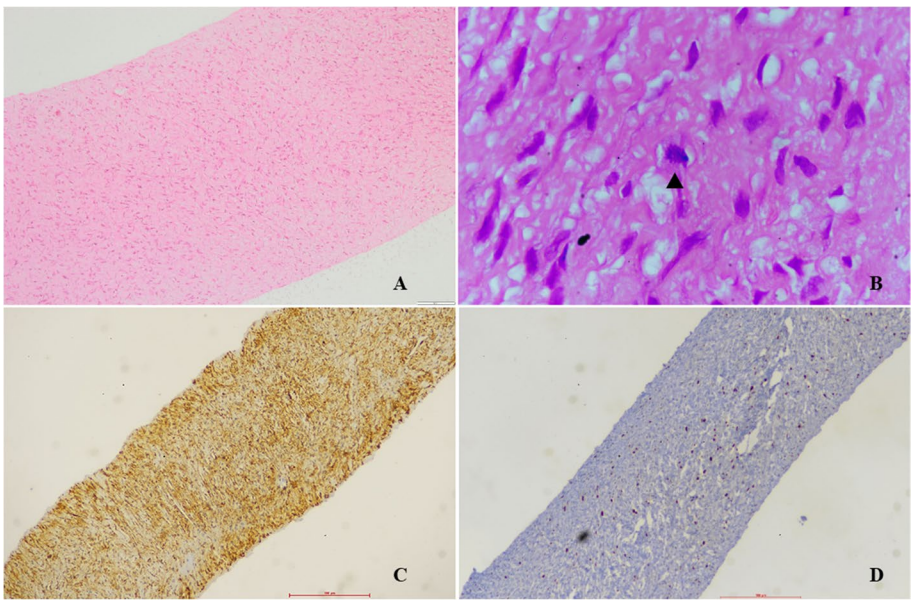

Fig. 2 Microscopic images of sections of core biopsy through histopathological (**A**, **B**) and immunohistochemical examination (**C**, **D**) **A** Tumour cells show spindle cell morphology with blunt ended nuclei and abundant eosinophilic cytoplasm characteristic of leiomyoma (H&E, × 100) **B** Higher magnification shows atypia and mitosis (H&E, × 400) **C**, **D** IHC staining for smooth muscle actin and Ki-67 (× 100)

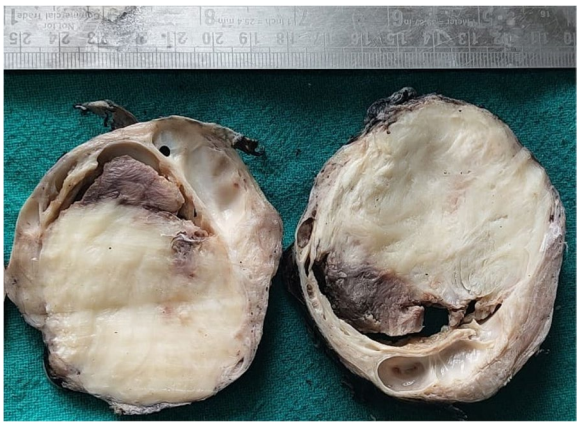

Fig. 3 Grossly lesion is well circumscribed with a white whorling cut surface having areas of cystic change and discoloration

with mild nuclear atypia and inconspicuous nucleoli (Fig. 4B). Areas of hyalinization and cystic changes were noted. Focal areas showed high cellularity and mitotic figures (4–5/10 HPF) (Fig. 4C). In addition, foci of infarct-type necrosis with granulation tissue were also observed (Fig. 4D). However, tumor-type necrosis was not observed in the multiple sections examined. We did extensive sampling from different areas, included 18 blocks for microscopic examination, and thoroughly examined all the sections. We did not find any malignant component with epithelial differentiation, ductal carcinoma in situ (DCIS), benign epithelial cells with an intracanalicular/ pericanalicular pattern suggesting a diagnosis of fibroadenoma, leaf-like architecture, or any lipomatous component. Immunohistochemical staining for SMA and caldesmon was uniformly positive in tumor cells, and desmin showed only focal positivity (Fig. 5A, B). Ki-67 on sections of the excised specimen reveals a similar pattern as observed in the core biopsy (Fig. 4E, F). Immunohistochemistry for p63, CAM 5.2, and CK 5/6 was negative (Fig. 5C, D). Given the above findings, a diagnosis of leiomyoma with atypical features was offered. Close follow-up of the patient was recommended.

Discussion

Intraparenchymal leiomyoma of the breast was first described by Strong et al. in 1913. So far, only 34 additional cases of intraparenchymal leiomyoma have been documented (Strong 1913). Previously reported cases revealed a wide age range of patients from 20 to 70 years with a mean age of 43 years (Brandão et al. 2017; Kafadar et al. 2017; Long et al. 2022). All the cases were reported in women and only one in a man (Strader et al. 2013).

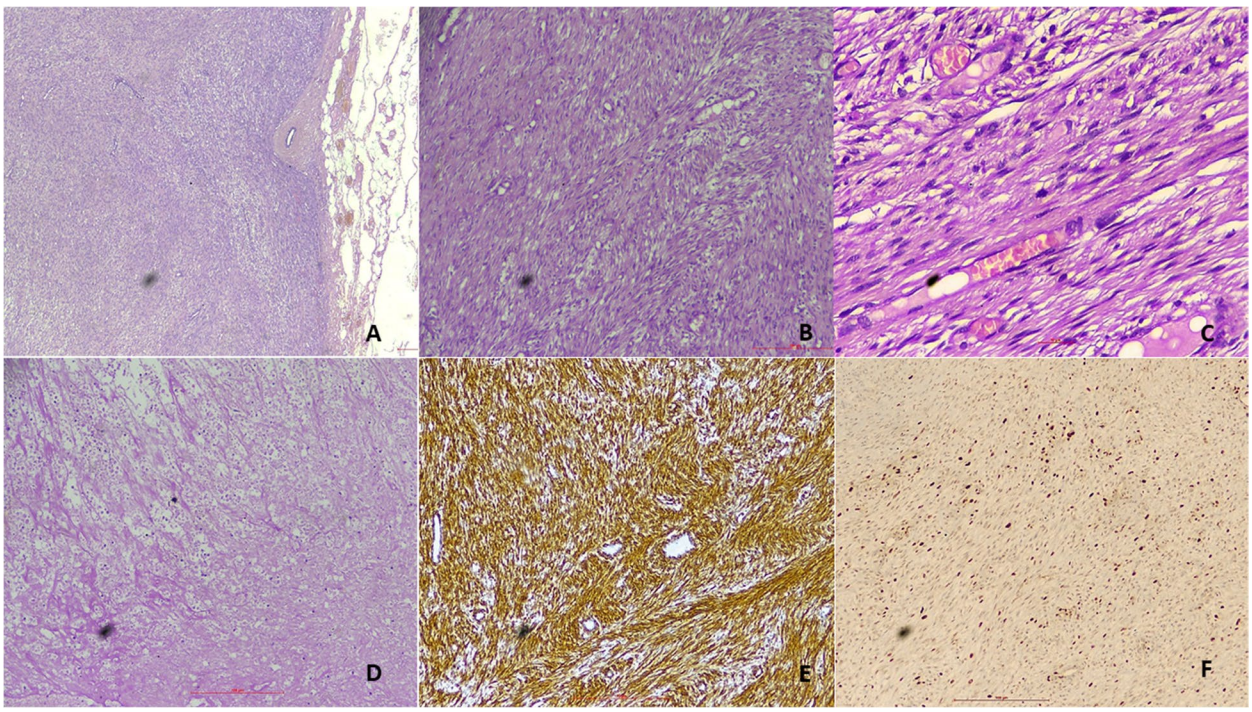

Fig. 4 **A**, **B** Histopathological examination revealed a well circumscribed spindle cell lesion with interlacing bundle and fascicles (H&E, × 20, × 100) **C** Areas with increased cellularity and mitosis (H&E, × 400). **D** Focal areas of infarct type necrosis (H&E, × 100) **E**, **F** IHC staining for smooth muscle actin and Ki-67 (× 100)

Clinically, a patient may present with pain and discomfort or a slow-growing palpable mass. Nipple discharge, skin retraction, or regional lymphadenopathy are usually not encountered (Brandão et al. 2017).

On ultrasonography, intraparenchymal leiomyoma appears as hypoechoic lesions with a homogeneous echotexture, sometimes with cystic components (Sidoni et al. 1999).

On gross examination, the lesion often appears well circumscribed and measures 0.5 cm to 13 cm with a whorled cut surface and firm consistency. The histological findings are usually typical with interlacing fascicles of smooth muscle cells showing oval nuclei with blunt ends, delicate chromatin, occasional inconspicuous nucleoli, and abundant eosinophilic cytoplasm with indistinct cell borders. The majority of the cases do not show increased cellularity, nuclear atypia, abundant mitosis, or necrosis (Ende et al. 2007). Histologically, leiomyosarcoma, which is an important differential diagnosis, has an infiltrative border and cytological atypia, with 2–16 mitotic figures per 10 high-power fields, atypical mitoses, vascular invasion, and necrosis (Oktay and Fikret 2011).

Boscaino et al. described cases with "grey zone features" in the spectrum of lesions between leiomyoma and leiomyosarcoma. They considered this group of breast lesions as a spectrum with a gradual transition from benign entity to frank malignancy and suggested a diagnosis of leiomyosarcoma in the presence of a high mitotic index (4/10 HPF) or the presence of a lower mitotic index if associated with necrosis, hypercellularity, and evident cytologic atypia. Cases with minimal but appreciable mitotic index (1–3/10 HPF) and with accessory features of malignancy might be classified as smooth muscle tumors of indeterminate prognosis (low-risk lesions) (Boscaino et al. 1994).

Long et al. described a case of atypical leiomyoma with infiltrative border, mild nuclear atypia, and mitosis up to 3/10 HPF, which exceeded the diagnostic criteria for typical benign leiomyoma but fell short of the threshold for leiomyosarcoma (Long et al. 2022).

According to Pourbagher et al., the presence of 1–3 mitotic figures might be considered to represent an intermediate category of leiomyoma with a higher risk of local recurrence (Pourbagher et al. 2005).

Due to its rarity and lack of diagnostic criteria to define atypical leiomyoma, we took a cue from smooth muscle lesions of the uterus. The spectrum of uterine smooth muscle lesions includes leiomyoma, Smooth Muscle Tumor of Uncertain Malignant Potential (STUMP) and leiomyosarcoma. According to the 2020 WHO Classification of Female Genital Tumors, the diagnostic criteria of STUMPs include focal/multifocal or diffuse nuclear atypia and 6–9 mitoses/10 HPF; more than 15 mitoses/10 HPF without cytological atypia or necrosis; tumor with diffuse nuclear atypia and uncertain mitoses which is often due to brisk karyorrhexis (Organisation mondiale de la santé, Centre international de recherche sur le cancer 2020). The index case showed focal areas of nuclear atypia with 4–5 mitosis/10HPF and a ki-67 index of 5%. Infarct-type necrosis with granulation tissue with or without hemorrhage or fibrosis may also occur in leiomyoma as observed in this case (Yang and Mutter 2015).

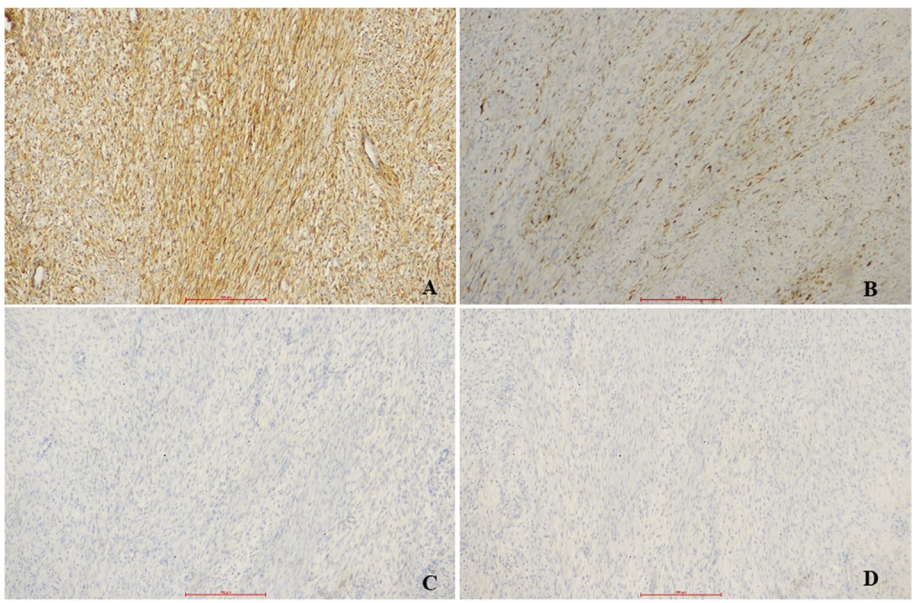

Fig. 5 IHC staining for **A** caldesmon **B** Desmin **C** CK 5/6 and **D** p63 (× 100)

This case did not have an infiltrative margin, diffuse atypia, or tumor necrosis. Increased Ki-67 expression, as observed in this case, is more compatible with STUMP than leiomyosarcoma (Mayerhofer et al. 2004). Another important differential diagnosis of spindle lesions of the breast is metaplastic carcinoma. Metaplastic carcinoma is a heterogeneous group of rare aggressive malignancies. It can be monophasic (with only one metaplastic component) or biphasic (with two or more components). Based on histological pattern, it can also be classified into 1) low-grade adenosquamous carcinoma, 2) fibromatosis-like metaplastic carcinoma, 3) squamous cell carcinoma, 4) spindle cell carcinoma, 5) metaplastic carcinoma with heterologous mesenchymal differentiation, and 6) mixed metaplastic carcinoma. Metaplastic carcinoma expresses various epithelial markers like CK 5/6, CK 14, and CAM 5.2, as well as p63 (Thomas et al. 2023). We did extensive grossing to exclude other differential diagnoses like fibroadenoma with smooth muscle metaplasia, phyllodes tumor with stromal overgrowth, and spindle cell lipoma. Pseudoangiomatous stromal hyperplasia and nodular fasciitis were excluded in this case based on histology and immunohistochemistry findings.

The treatment of choice for intraparenchymal breast leiomyoma is wide excision. In our case, the patient has no recurrence after 12 months of follow-up.

Conclusion

Intraparenchymal breast leiomyoma is a rare entity that can clinically and on imaging studies mimic other spindle cell lesions of the breast. The majority of the cases are benign; however, the exact behavior of the cases with atypical features is difficult to ascertain due to limited experience. This case emphasizes the need for long-term follow-up after wide local excision due to the potential recurrence or malignancy.

Abbreviations

IHC Immunohistochemistry
SMA Smooth muscle actin
USG Ultrasonography
DCIS Ductal carcinoma in-situ

Acknowledgements

None.

Authors' contributions

AP: Conceptualization, literature review, interpretation, writing and editing; AS: Data collection, literature review, writing initial draft; TK: Literature review, critical review, editing; PB: Feedback and supervision.

Funding

The authors declare that no financial support was received.

Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Informed and signed consent was taken.

Competing interests

None.

Received: 5 August 2024 Accepted: 25 April 2025
Published online: 20 May 2025

References

Boscaino A, Ferrara G, Orabona P, Donofrio V, Staibano S, De Rosa G. Smooth muscle tumors of the breast: clinicopathologic features of two cases. Tumori. 1994;80(3):241–5.
Brandão RG, Elias S, Pinto Nazário AC, Alcoforado Assunção MDCG, Esposito Papa CC, Facina G. Leiomyoma of the breast parenchyma: a case report and review of the literature. Sao Paulo Med J. 2017;136(2):177–81.
Ende L, Mercado C, Axelrod D, Darvishian F, Levine P, Cangiarella J. Intraparenchymal leiomyoma of the breast: a case report and review of the literature. Ann Clin Lab Sci. 2007;37(3):268–73.
Kafadar MT, Yalcin M, Gok MA, Aktas A, Yurekli TS, Isal AA. Intraparenchymal leiomyoma of the breast: a rare location for an infrequent tumor. Eur J Breast Health. 2017;13(3):156–8.
Liu HT, Wong CN, Wong CN, Liu FS. Uterine smooth muscle tumor of uncertain malignant potential: a review of current knowledge. Taiwan J Obstet Gynecol. 2022;61(6):935–40.
Long M, Hu XL, Zhao G, Liu Y, Hu T. Intraparenchymal breast leiomyoma and atypical leiomyoma. BMC Womens Health. 2022;22(1):119.
Mayerhofer K, Lozanov P, Bodner K, Bodner-Adler B, Kimberger O, Czerwenka K. Ki-67 expression in patients with uterine leiomyomas, uterine smooth muscle tumors of uncertain malignant potential (STUMP) and uterine leiomyosarcomas (LMS). Acta Obstet Gynecol Scand. 2004;83(11):1085–8.
Oktay Y, Fikret A. Leiomyosarcoma of the breast. J Surg Case Rep. 2011;2011(7):1–1.
Organisation mondiale de la santé, Centre international de recherche sur le cancer, editors. Female genital tumours. 5th ed. Lyon: International agency for research on cancer; 2020. (World health organization classification of tumours).
Philipose TR, Vishwanath M, Mulki S, Ilanthodi S. Leiomyoma of the breast- a rare case report. JCDR; 2021. Available from: https://jcdr.net/article_fulltext.asp?issn=0973709x&year=2021&volume=15&issue=6&page=ED04&issn=0973-709x&id=14992. Cited 2024 Jan 26.
Pourbagher A, Pourbagher MA, Bal N, Oguzkurt L, Ezer A. Leiomyoma of the breast parenchyma. Am J Roentgenol. 2005;185(6):1595–7.
Sampaio GP, Koch MV, Boechat M, Matos VE, Santos AASMDD. Leiomyoma of the breast: an uncommon tumor. Radiol Bras. 2016;49(5):343–4.
Sidoni A, Lüthy L, Bellezza G, Consiglio MA, Bucciarelli E. Leiomyoma of the breast: case report and review of the literature. Breast. 1999;8(5):289–90.
Stewart EA, Laughlin-Tommaso SK, Catherino WH, Lalitkumar S, Gupta D, Vollenhoven B. Uterine fibroids. Nat Rev Dis Primers. 2016;2(1):16043.
Strader LA, Galan K, Tenofsky PL. Intraparenchymal leiomyoma of the male breast. Breast J. 2013;19(6):675–6.
Strong LW. Leiomyoma of the breast. Am J Obstet Dis Women Child. 1913;68(1):53.
Thomas HR, Hu B, Boyraz B, Johnson A, Bossuyt VI, Spring L, et al. Metaplastic breast cancer: a review. Crit Rev Oncol Hematol. 2023;182:103924.
Yang EJ, Mutter GL. Biomarker resolution of uterine smooth muscle tumor necrosis as benign vs malignant. Mod Pathol. 2015;28(6):830–5.

Publisher's Note