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Breast Imaging

Bilateral mammary Paget disease in a young adult female

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ABSTRACT

Mammary Paget disease is an uncommon malignancy of the breast that presents with ulceration or eczema of the nipple and is almost always associated with an underlying breast carcinoma. This disease is most commonly seen in the fifth and sixth decades of life and is almost always unilateral. The diagnosis of mammary Paget disease is generally based on clinical findings, confirmed by histopathologic examination. Mammographic and ultrasonographic findings may be nonspecific for malignancy, with 50% of cases showing negative findings. Magnetic resonance imaging can be used as a diagnostic tool to detect clinically occult cancer with nonspecific findings on mammogram and ultrasonogram. In this article, we are presenting a rare case of a young woman with biopsy-proven bilateral mammary Paget disease, for which bilateral modified radical mastectomy was done, followed by adjuvant chemotherapy and radiotherapy.

Case report

Clinical history

A 27-year-old woman, P1 L1, married, was referred for ultrasound of both breasts to our department. The woman had a history of nonhealing nipple eczema for 1 year. On examination, nipple excoriation and blood-stained nipple discharge was present bilaterally (right > left) (Fig. 1A); a lump of size of 2 × 2 cm was palpable in the left breast, which was firm in consistency. Bilateral axillae were free, and there were no palpable lymph nodes.

Radiological investigations

Ultrasound examination of both breasts was performed using a high-frequency linear transducer. An irregular, ill-defined hypoechoic lesion measuring approximately 2.0 × 1.1 cm was seen at the 3-o' clock position, circle 1, zones B and C of the left breast (Fig. 1); the lesion was categorized as Breast Imaging

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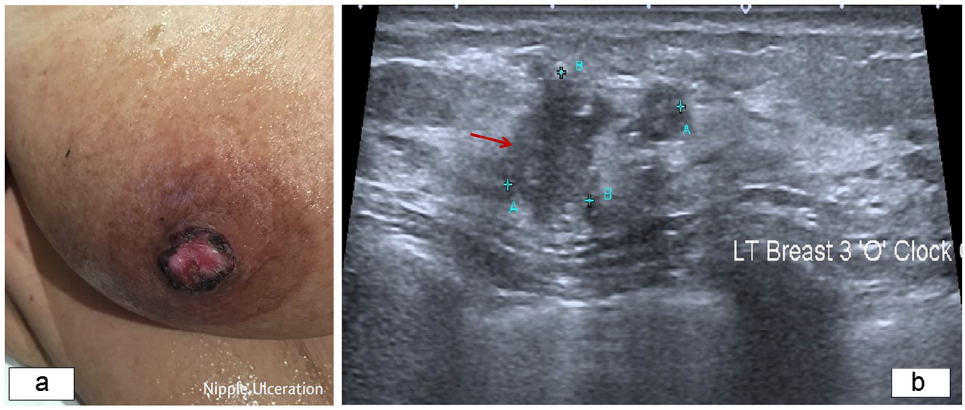

Fig. 1 – (A) Clinical image of the right breast showing nipple ulceration. (B) Ultrasound image showing an irregular, ill-defined hypoechoic lesion measuring approximately 2.0 × 1.1 cm at the 3-o' clock position, circle 1, zones B and C of the left breast (arrow).

Reporting and Data System (BIRADS) 4c, and ultrasound-guided (USG) Tru-cut biopsy was suggested.

No lesion was identified beneath the diseased superficial skin or elsewhere in the right breast. Excoriation was physically noted on and around the nipple-areolar complex.

There were few enlarged axillary lymph nodes with a nonuniformly thickened cortex measuring up to 4.7 mm involving the left axilla (Fig. 2A). The right axilla showed round lymph nodes with a lost fatty hilum (Fig. 2B and C). USG biopsy of the bilateral abnormal lymph nodes was advised.

The patient underwent dynamic contrast-enhanced magnetic resonance imaging (MRI) to evaluate the exact extent of the disease bilaterally. Dynamic contrast-enhanced MRI performed at 1.5 T showed focal skin thickening and homogenous enhancement of the bilateral nipple-areolar complex on intravenous gadolinium administration (Fig. 3A). An irregular, noncircumscribed lesion approximately measuring 4.8 × 3.6 cm, appearing isointense on T1-weighted imaging and T2-weighted fat-saturated imaging, was seen in the upper outer quadrant in the posterior half of the left breast between the 2- and 3-o' clock positions. The lesion showed clumped non–mass-like enhancement on the administration of intravenous gadolinium (Fig. 3B). Linear nodular enhancement was also noted extending from the nipple up to the mass lesion in the left breast (Fig. 3C). Diffusion restriction was also noted in the region of the lesion. The left axilla showed few nonspecific lymph nodes.

Type 2 time-kinetic curves were noted in the lesion suggestive of indeterminate lesion.

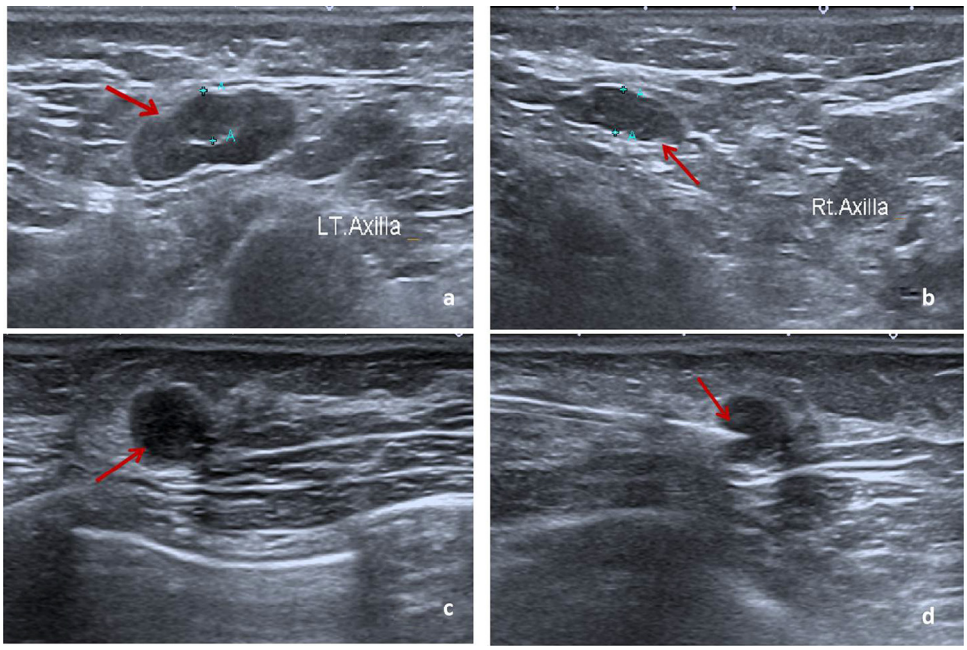

Fig. 2 – Ultrasound image showing enlarged axillary lymph nodes (arrow) with a nonuniformly thickened cortex involving the Lt axilla (A). Ultrasound image shows round lymph nodes (arrows) with a lost fatty hilum in the Rt axilla (B and C). Image shows ultrasound-guided biopsy of the round lymph node (arrow) in the Rt axilla (D). Lt, left; Rt, right.

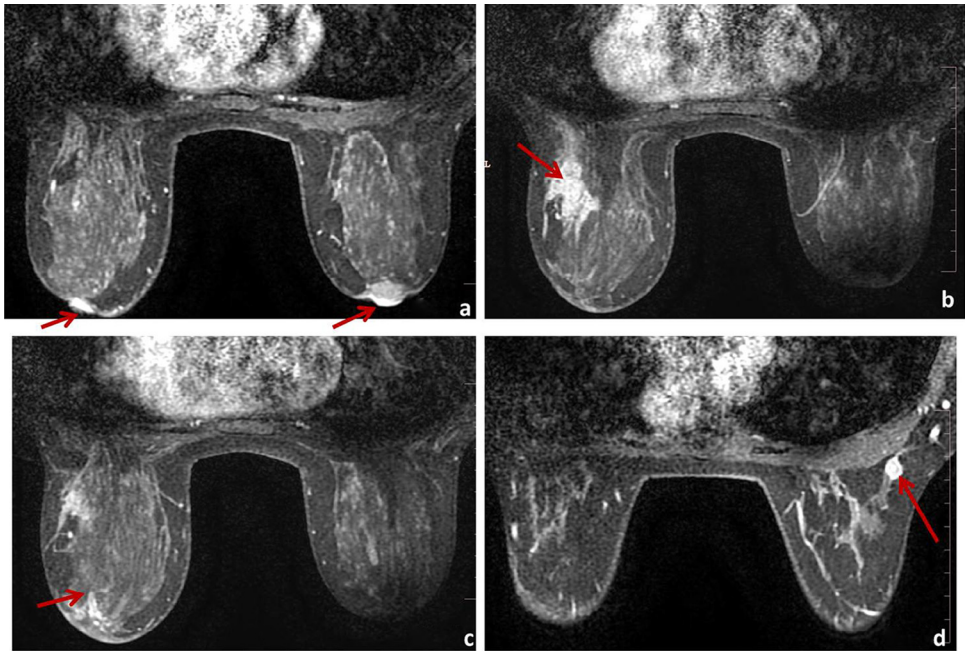

Fig. 3 – Selected images of the dynamic contrast-enhanced magnetic resonance imaging show (A) a focal skin thickening and homogenous enhancement of the bilateral nipple-areolar complex (arrows); (B) an irregular, not circumscribed lesion in the upper outer quadrant in the posterior half of the left breast between 2- and 3-o' clock positions showing a clumped, non–mass-like enhancement (arrow) on the administration of contrast; (C) a linear nodular enhancement (arrow) extending from the nipple up to the mass lesion in the left breast; and (D) enlarged, round, enhancing lymph nodes (arrow) in the right axillary tail.

The left breast lesion was categorized as BIRADS 5, and USG biopsy was advised for histopathologic evaluation.

MRI also showed round enhancing enlarged lymph nodes measuring 2.2 cm in the short axis in the right axillary tail (Fig. 3D).

Histopathologic examination

Histopathologic examination of the USG biopsy specimen from the lesion in the left breast revealed it as a ductal invasive mammary carcinoma (Fig. 4B and C).

USG biopsy of the round lymph node in the right axilla was also performed (Fig. 2D), which was positive for invasive ductal carcinoma.

Skin biopsy on the right side proved the lymph node to be a mammary Paget disease on histopathologic examination (Fig. 4A and D).

The patient underwent bilateral modified radical mastectomy (MRM).

Histopathologic examination of the left MRM showed a pathologic staging of pT1c pN2a cM0 and Paget disease of the nipple (Fig. 5).

Right MRM showed Paget disease of the nipple with an underlying ductal carcinoma in situ (DCIS)—high-grade comedo type.

Treatment

The patient underwent bilateral MRM with bilateral axillary node dissection. Seven cycles of palliative chemotherapy were followed by radiotherapy for the mass on the left side. Presently, the patient is on regular follow-up.

Discussion

Paget disease of the breast is an uncommon disease described as a "syndrome in which ulceration of the nipple is invariably associated with an underlying cancer." Most studies report the presence of concurrent malignancy in over 90% of patients. Therefore, mammary Paget disease is nearly always a sign of underlying breast malignancy [1].

Clinical findings

Mammary Paget disease is commonly seen in the fifth or the sixth decade of life, although it can also be seen in adolescents and in the elderly. It is more common in men than in women. This disease is almost always unilateral [2].

Our case is a rare presentation, as the patient is young (27 years old) and the disease was present bilaterally.

Clinically, patients may present with itching, eczema, erythema of the nipple and areola, nipple erosion or ulceration, scaly or flaky skin, nipple retraction, bloody discharge from the nipple, or a combination of these. The clinical manifestations of Paget disease may be the only signs of breast cancer [1].

Our case had a similar clinical presentation and no palpable mass lesion was found.

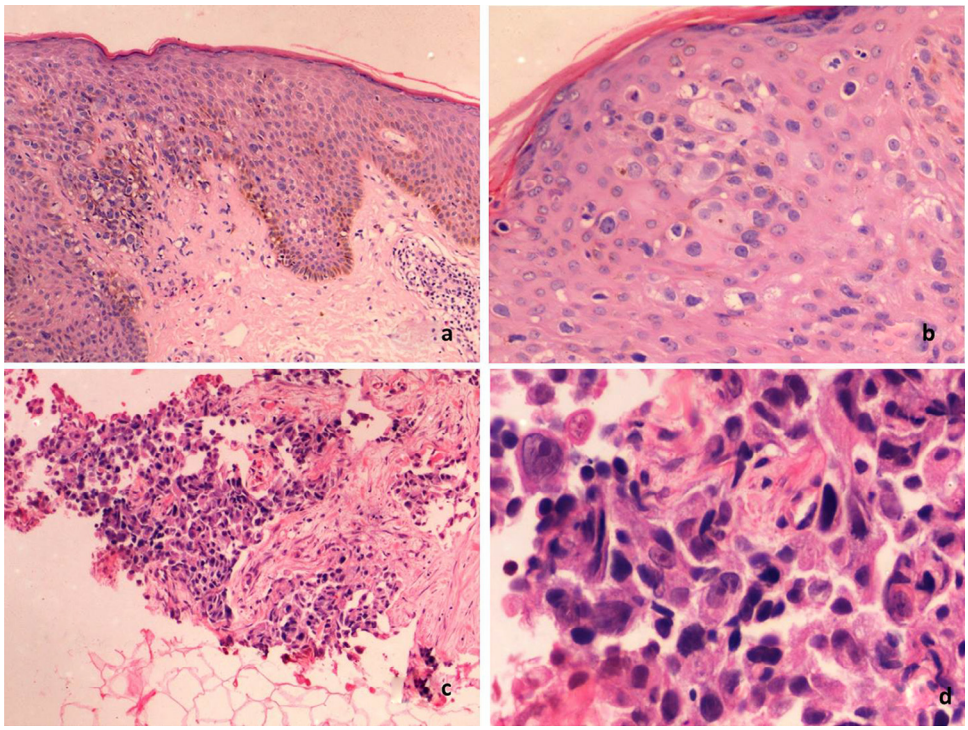

Fig. 4 – Hematoxylin and eosin-stained images of the skin biopsy specimen from the right nipple-areolar complex proved it to be mammary Paget disease (A and B). (A) Adjacent normal epithelium and epithelium infiltrated by Paget cells (100×). (B) Single cells and clusters of large cells having an abundant pale cytoplasm, an irregular nucleus with prominent nucleoli in the epidermis (200×). Hematoxylin and eosin-stained images of the ultrasound-guided biopsy specimen from the lesion in the left breast revealed it as a ductal invasive mammary carcinoma (C and D). (C) Cores of fibrocollagenous tissue infiltrated by nests of large atypical cells (100×). (D) Large atypical cells with increased nuclear-to-cytoplasmic ratio, hyperchromasia, and an irregular nuclear membrane, with some showing prominent nucleoli (400×).

Occasionally, a palpable mass or thickening of the parenchyma is detectable on physical examination. Ninety to ninety-four percent of patients presenting with palpable mass are found to have invasive disease, whereas those presenting without a palpable mass are usually associated with DCIS [1].

Temporary resolution of the eczematous changes may be seen with topical steroid therapy, but this, in turn, might cause further delay in the diagnosis of mammary Paget disease. A biopsy from the nipple-areolar region is necessary to confirm the diagnosis [1]. Mammary Paget disease must be differentiated from other conditions, such as atopic or contact dermatitis, chronic eczema, psoriasis, nipple duct adenoma, malignant melanoma, basal cell carcinoma, and Bowen disease [3].

Etiopathogenesis

The pathogenesis of mammary Paget disease was explained with 2 different theories (Fig. 6):

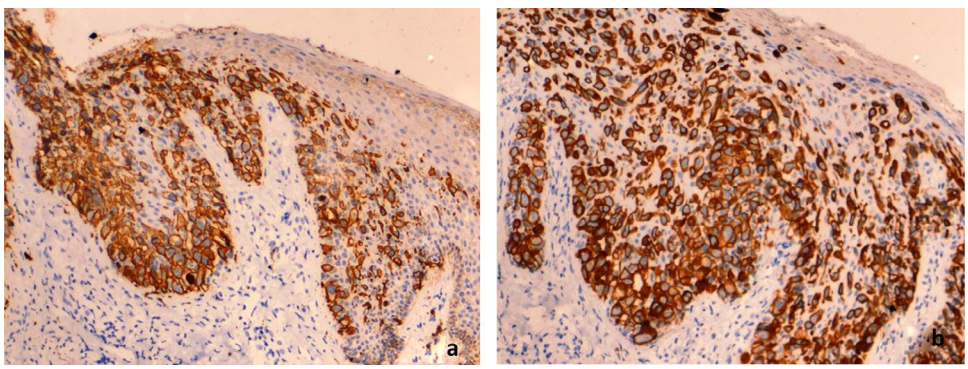

Fig. 5 – Immunohistochemistry images: ImmunoHistoChemistry for Her2neu showing membrane positivity in the Paget cells (100×) (A). ImmunoHistoChemistry for CK7 showing positivity in the large Paget cells in the epidermis (100×) (B).

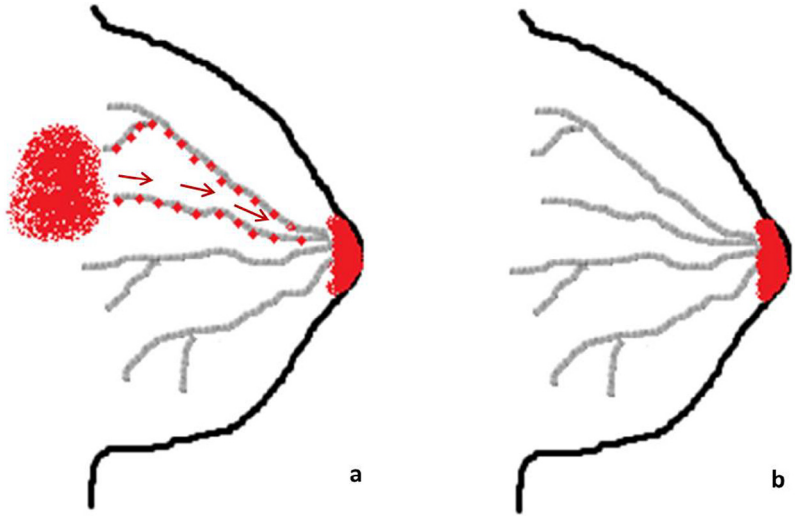

Fig. 6 – (A) Shows the migration (arrows) of malignant cells (red dots) from the primary breast carcinoma (red-colored mass in the retromammary region) through milk duct to the nipple-areolar complex region. (B) Shows Paget cells (red-mass) arising in the epidermis of the nipple.

(1) *Epidermotropic theory:* According to this theory, the malignant cells migrate from the breast carcinoma through the milk ducts along the basal membrane and enter the nipple and areola. This theory was widely accepted because of the fact that the Paget cells and the underlying associated ductal carcinoma share the same immunohistochemical profile [2].
(2) *Intraepidermal transformation theory*: According to this theory, the Paget cells arise in the epidermis of the nipple independently of the underlying carcinoma by means of in situ malignant transformation or degeneration of existing cells. This theory is supported by the fact that in few cases of mammary Paget disease, findings are confined to the nipple-areolar region with no evidence of an associated underlying carcinoma [2].

Classification

Mammary Paget disease can be divided into 3 categories (Fig. 7):

(1) Paget disease of the nipple without DCIS
(2) Paget disease of the nipple with associated DCIS in the underlying lactiferous ducts of the nipple-areolar complex
(3) Paget disease of the nipple with associated DCIS in the underlying lactiferous ducts of the nipple-areolar complex and associated DCIS or invasive breast cancer elsewhere

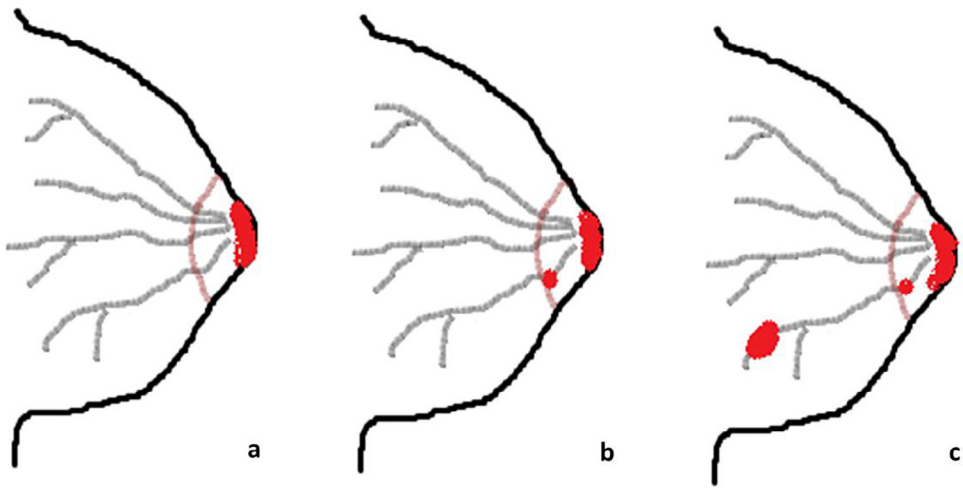

Fig. 7 – Diagrammatic representation showing the types of mammary Paget disease. Type 1—Paget disease of the nipple without DCIS (A). Type 2—Paget disease of the nipple with associated DCIS in the underlying lactiferous ducts of the nipple-areolar complex (B). Type 3—Paget disease of the nipple with associated DCIS in the underlying lactiferous ducts of the nipple-areolar complex and associated DCIS or invasive breast cancer elsewhere in the breast, at least 2 cm from the nipple-areolar complex (C). DCIS, ductal carcinoma in situ.

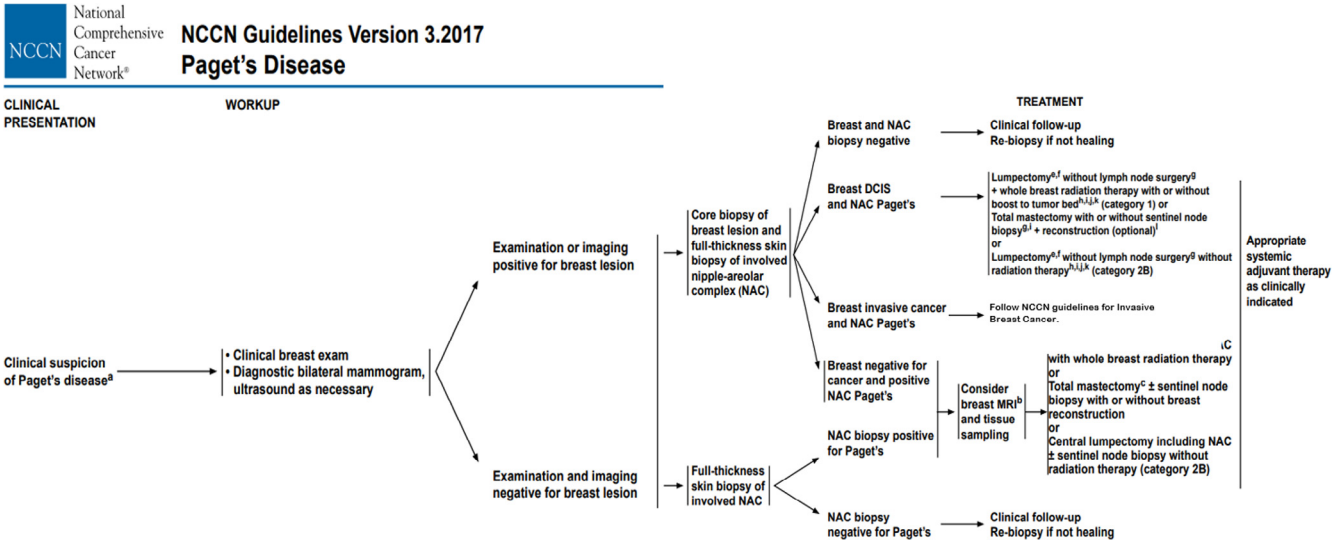

Fig. 8 – Flowchart showing the National Comprehensive Cancer Network guidelines for management of mammary Paget disease.

in the breast, at least 2 cm from the nipple-areolar complex [1].

Imaging features

In cases of clinical suspicion, radiological imaging can aid in detecting underlying conditions. The first line of radiological investigation would be *mammography*, which would show skin thickening, malignant calcification, masses at the level of the nipple, architectural distortion, and nipple retraction. However, underlying carcinoma is common even in women with benign mammogram and no palpable mass. Hence, ultrasound and MRI may be useful in detecting the lesion [3].

USG findings would include mass, ductal ectasia, flattening, asymmetry, and thickening of the nipple and the areola [3].

MRI has a sensitivity of 95% compared with 70% of mammography in the detection of breast lesions. MRI helps differentiate a normal nipple from an abnormal one and evaluates the extension of the tumor. MRI findings in mammary Paget disease include abnormal nipple enhancement, thickening and enhancement of the nipple-areolar complex, an associated enhancing DCIS or invasive tumor, or a combination of these [3].

Clinical and imaging findings are complementary and should be correlated to confirm the diagnosis of mammary Paget disease. Surgical biopsy is, however, the diagnostic standard [4].

Treatment

Mastectomy has been regarded as the standard therapy for a long time. However, recently, conservative treatment involving complete resection of the nipple-areolar complex, followed by radiation therapy, has shown good prognosis in patients with cancer confined to the central quadrant of the breast [1]. Of late, the National Comprehensive Cancer Network guidelines are being widely recognized and practiced as the standard policy in oncology by clinicians (Fig. 8).

Mammary Paget disease associated with underlying breast carcinoma should be completely resected with excision of the nipple-areolar complex and radiation therapy of the remaining breast tissue [3].

Conclusion

Mammary Paget disease is mostly unilateral and occurs in elderly women [3]. Our case stands here as rare, being a bilateral Paget disease in a young woman.

A benign-appearing mammogram and a clinically nonpalpable mass do not rule out the possibility of an underlying breast carcinoma, especially in identifying the correct type and in showing the correct extent of the disease [2]. Mammography and histopathology are the gateways for earlier diagnosis of underlying breast malignancies.

MRI is a valid diagnostic imaging modality for the diagnosis of mammary Paget disease and has better specificity and sensitivity compared with mammography and ultrasound.

REFERENCES

[1] Lim HS, Jeong SJ, Lee JS, Park MH, Kim JW, Shin SS, et al. Paget disease of the breast: mammographic, US, and MR imaging findings with pathologic correlation. Radiographics 2011;31(7):1973–87.
[2] Sripathi S, Ayachit A, Kadavigere R, Kumar S, Eleti A, Sraj A. Spectrum of imaging findings in Paget's disease of the breast-a pictorial review. Insights Imaging 2015;6(4):419–29.
[3] Gaspari E, Ricci A, Liberto V, Scarano AL, Fornari M, Simonetti G. An unusual case of mammary Paget's disease diagnosed using dynamic contrast-enhanced MRI. Case Rep Radiol 2013;2013:206235.
[4] Lourenco AP, Mainiero MB. Paget's disease of the breast. R I Med J 2013;50–1.