Case Report Open Access

Archives Of Breast Cancer

DOI: 10.32768/abc.2403834727505

Recurrent Inflammation from Adult-Onset Lymphatic Malformation: A Management Conundrum

Audrey Tan Poh Poha[a], Wong Chow Yin[a], Ying Ching Tan*[a]

[a]Department of SingHealth Duke-NUS Breast Centre, General Surgery, Singapore General Hospital, Singapore

ARTICLE INFO

Received:
10 February 2025
Revised:
23 March 2025
Accepted:
23 March 2025

Keywords:
lymphatic abnormalities, breast, breast diseases, neoplasm, lymphatic tissue

ABSTRACT

Background: Breast lymphatic malformation is a rare condition that may pose a diagnostic dilemma and result in debilitating outcomes for the affected patient.

Case Presentation: We present a case of adult-onset breast lymphatic malformation complicated by recurrent inflammation, which posed a clinical conundrum. A 33-year-old female from Papua New Guinea, previously well, with no family history of cancer, first presented with a 6-year history of persistent left breast skin nodules and recurrent inflammation. She was previously extensively evaluated and treated overseas. However, all results were indeterminate and showed mainly inflammatory infiltrates with no infective cause. The patient notably had undergone the excision of the left chest wall lump when she was 7. She presented to our center with warty nodules and clear frogspawn-like vesicles over her left breast. She was reviewed by a multidisciplinary vascular malformation team, and multimodality imaging showed no evidence of breast cancer with possible lymphangiectasia. Excision biopsy of the left breast cutaneous nodule was performed, and histology showed lymphangiomatous proliferation of superficial dermal lymphatic vessels with PIK3CA Exon 10.c.1636C>Ap(Gln546Lys) mutation. Lymphoscintigraphy demonstrated absent left breast lymphatic channels. The patient was counselled on various management options and eventually decided on medical management with sirolimus.

Conclusion: Adult-onset breast lymphatic malformation is extremely rare, with varying clinical presentations. We present a novel case associated with PIK3CA Exon 10.c.1636C>Ap(Gln546Lys) mutation that posed a clinical perplexity and was misdiagnosed for many years. A multimodal and multidisciplinary approach may be required to aid in the diagnosis and management of this condition.

INTRODUCTION

Lymphatic malformation (LM) is an uncommon benign condition that can be congenital or acquired. Congenital LMs are a result of embryologic sequestration of lymphatic tissue with failure of communication between lymphatic channels and the rest of the lymphatic system. Up to 95% of congenital malformations of the lymphatic system occur in the head and neck region as well as the axilla, and are typically diagnosed by 2 years of age.[1] Adult-onset LM of the breast is a very rare condition that is usually associated with a triggering event such as trauma, infection, or iatrogenic causes. Oftentimes, these cases pose a diagnostic dilemma and may potentially result in debilitating outcomes for the affected patient. We present a case of LM of the breast complicated by recurrent inflammation, which posed a clinical conundrum.

***Address for correspondence:**
Dr Tan Ying Ching,
Associate Consultant,
Department of Breast Surgery, Singapore General Hospital,
Outram Road, Singapore 169608
Email: tan.ying.ching@singhealth.com.sg

CASE PRESENTATION

A 33-year-old female from Papua New Guinea, previously well, with no family history of breast or ovarian cancer, first presented with a 6-year history of persistent left breast skin nodules and recurrent inflammation. Prior to presenting to our specialist center, she was evaluated and treated overseas with multiple investigations and procedures, including a mammogram, ultrasound breast, incision and drainage of left breast abscess in 2017, and excision biopsy of left axillary nodes in 2018. However, all results were indeterminate and showed mainly inflammatory infiltrates, both acute and chronic inflammatory cells, with no infective cause. Of note, the patient had undergone the excision of the left chest wall lump when she was 7 years old. No histology report from the excision of the childhood left chest wall mass was available. She presented to our specialist center with warty saccular compressible nodules, clear frogspawn-like vesicles over her left breast, including areola, left chest wall, and left upper inner arm, with an 8cm inferior chest wall scar from the previous excision (Figure 1).

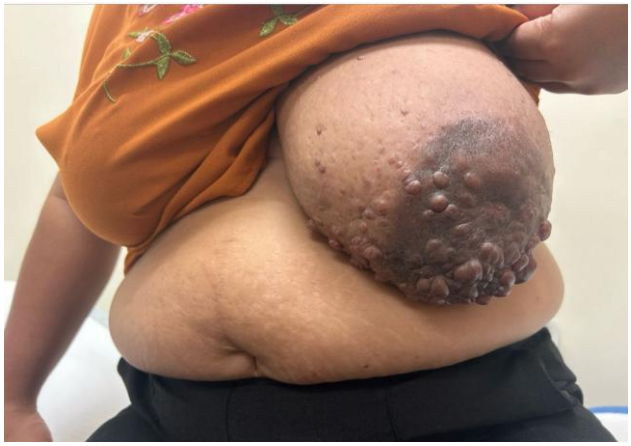

Figure 1. Left Breast with Warty Saccular Compressible Nodules and Clear Frogspawn-Like Vesicles

She was reviewed by a multidisciplinary vascular malformation team, including dermatology, hematology, radiology, breast, and plastic surgery subspecialties. Breast magnetic resonance imaging (MRI) showed no evidence of breast cancer with possible lymphangiectasia, though there were no cystic spaces normally expected in LMs (Figure 2). Targeted ultrasound only demonstrated a single blood vessel running through the subcutaneous layer with no evidence of a lymphatic or venous malformation, such as focal saccular lesions or tubular collections of dilated vessels (Figure 3).

The patient hence underwent excision biopsy of her left breast cutaneous nodule, and histology returned as lymphangiomatous proliferation of superficial dermal lymphatic vessels.

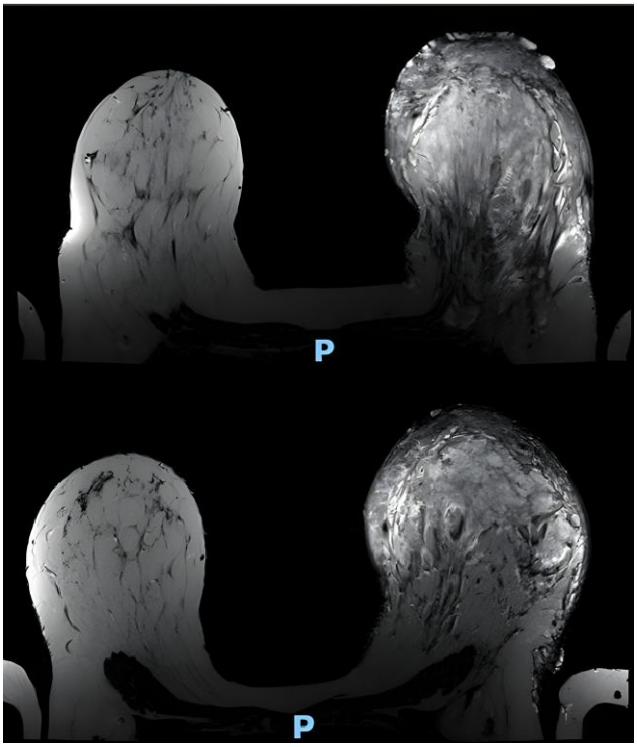

Figure 2. Magnetic Resonance Imaging of the Breast. There is no evidence of breast cancer with possible lymphangiectasia.

Figure 4A shows hematoxylin and eosin (H&E) stain demonstrating superficial dermal dilated lymphatic channels, and Figure 4B demonstrates D2-40 immunostaining positivity confirming lymphatic endothelium. Further testing of the somatic solid tumor panel also showed PIK3CA Exon 10.c.1636C>Ap(Gln546Lys) mutation.

Lymphoscintigraphy was arranged to determine lymphatic drainage and amenability for lymph node transfer or lymphatic-venous bypass. However, the study demonstrated absent lymphatic channels in the left breast with likely dermal routing due to lymphatic obstruction (Figure 4).

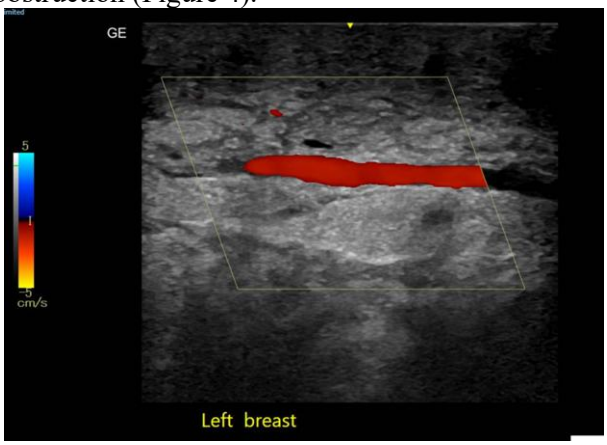

Figure 3. Targeted Left Breast Ultrasound Demonstrating a Single Blood Vessel Running Through the Subcutaneous Layer. There is no evidence of a lymphatic or venous malformation, such as focal saccular lesions or tubular collections of dilated vessels.

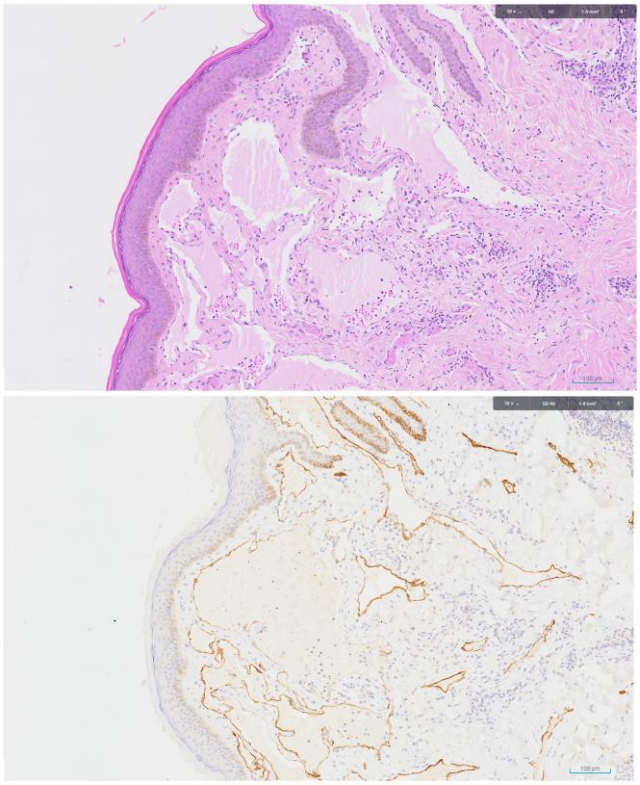

Figure 4. Left Breast Cutaneous Nodule: H&E Stain and D2-40 Immunostaining. A, Hematoxylin and eosin (H&E) stain (10x magnification) of left breast cutaneous nodule demonstrating superficial dermal dilated lymphatic channels. B, D2-40 immunostaining (10x magnification) of left breast cutaneous nodule demonstrating D2-40 immunostaining positivity confirming lymphatic endothelium.

The patient was counselled on management options, including conservative management with wrapping, symptomatic treatments to remove cutaneous nodules, breast reduction, lymphaticovenous anastomosis, and medical management with sirolimus. She eventually decided on medical management with sirolimus.

DISCUSSION

A literature review on PubMed with keywords "lymphatic", "lymphovascular", "breast", and "malformation" yielded 13 case reports and 1 case series. There are currently no studies that have described a breast LM with PIK3CA Exon 10.c.1636C>Ap(Gln546Lys) mutation, as in our case. PIK3CA activating mutations have been associated with lymphovascular overgrowth disorders in recent years[2], as well as an increased risk of breast cancer.[3] The most involved area for breast LM is in the upper outer quadrant of the breast due to lymphatic drainage of the breast, mainly following the pathway towards the axillary tail into the axillary region.[4] The studies found in the literature have varying clinical presentations. In our case, the patient was misdiagnosed and treated as per recurrent breast and axillary infections for many years.

Typical radiological features for breast LM include multiloculated, hypoechoic, cystic masses with internal septa of variable thickness. This can be appreciated on multiple imaging modalities, including breast ultrasound and breast MRI. Breast MRI has been reported to be the most informative imaging modality because lymphangiomas appear as hypointense on T1 and hyperintense on T2. However, as demonstrated in our case report, the typical radiological findings failed to diagnose LM; hence, lymphoscintigraphy and surgical excision of the lesion were performed. Surgical excision with histopathology allows for definitive diagnosis of lymphangiomas.

LMs are benign lesions that are often slow-growing and asymptomatic. Pain and discomfort may occur secondary to compressive effects, with complications such as bleeding, infection, and fistula formation.[5] Management options include conservative treatment with compression therapy, incision and drainage, sclerotherapy, laser therapy, and drug therapy for symptomatic relief. However, these treatments are associated with high recurrence rates and are ineffective, especially in larger lesions.[6] The gold standard treatment of choice is complete surgical excision of the LM. The completeness of surgical excision hinges upon the size and location of the lesion. Breast cystic lymphangiomas tend to be locally aggressive and with a predilection to infiltrate surrounding tissues. Complete excision may, hence, not be possible in such cases, and wide surgical excision can be considered instead.[7] There have been more novel approaches suggested for treating intractable LMs, such as anastomosis of the afferent lymph vessel of LM to the venous system, which allows the inflow to bypass the obstructed system.[8] The effectiveness of this technique, however, depends on pre-procedural lymph flow assessment demonstrating inflow into the LM. Further studies are required for a definitive conclusion on the efficacy of this method and feasibility in the treatment of LMs of the breast.

Limitations of our study include the lack of a histological report available from the patient's childhood excision biopsy. We cannot entirely rule out the possibility that this was a congenital LM with childhood presentation of the left chest wall mass. However, the clinical picture and timeline of the development of left breast and axillary cutaneous nodules complicated by recurrent inflammation in the patient's mid-twenties favors an adult-onset breast LM.

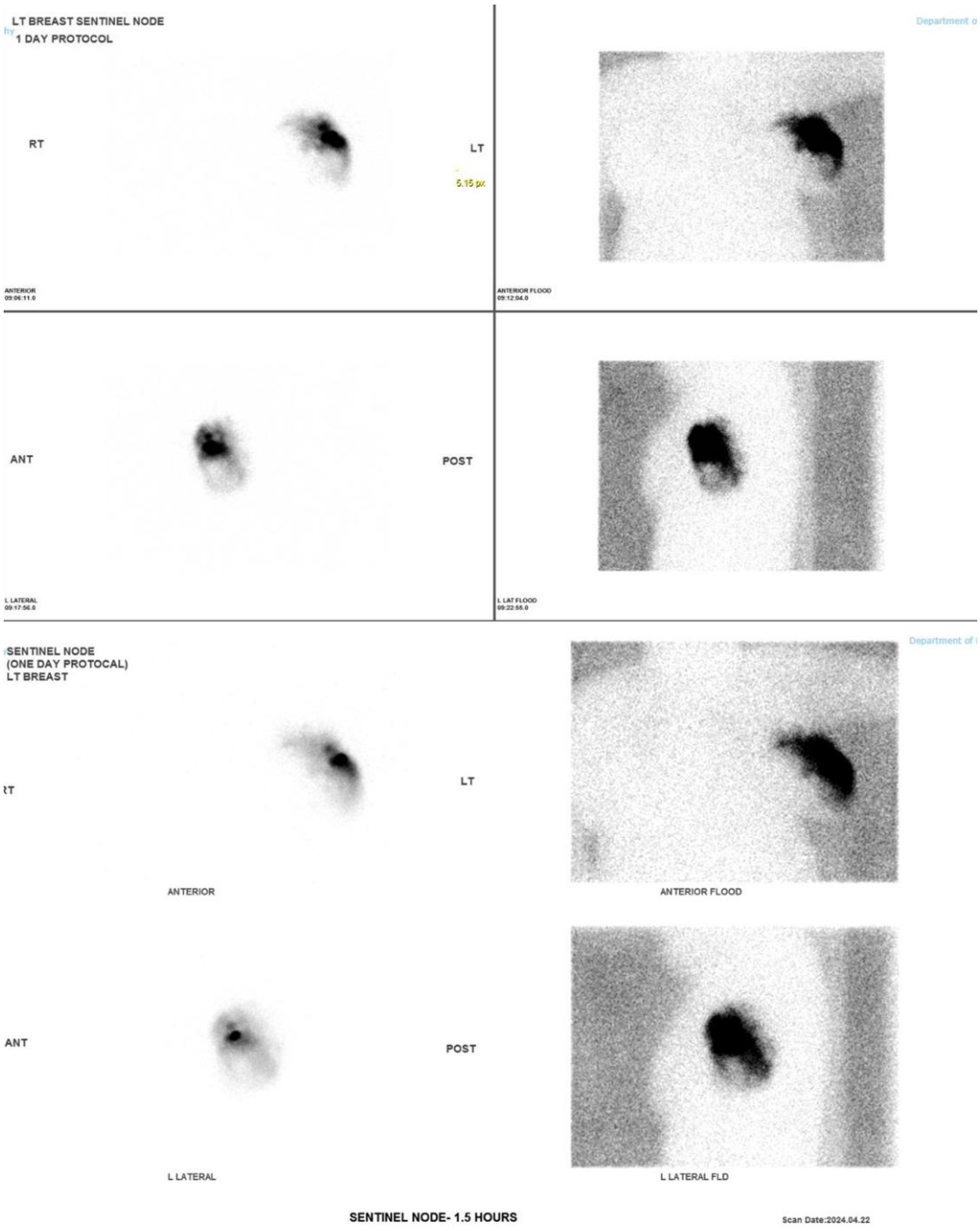

Figure 5. Lymphoscintigraphy Reveals Absent Lymphatic Channels in the Left Breast with Tracer Hold-Up in the Upper Outer Quadrant.

Further studies need to be conducted to determine if patients with breast LMs and associated PIK3CA mutations require a more vigilant breast screening surveillance, given the known association of *PIK3CA* mutations and increased risk of breast cancer.

CONCLUSION

Adult-onset breast LM is extremely rare, with varying clinical presentations. We present a novel case associated with PIK3CA Exon 10.c.1636C>Ap(Gln546Lys) mutation that posed a clinical perplexity and was misdiagnosed for many years. A multimodality and multidisciplinary approach may be required to aid in the diagnosis and management of this condition.

ACKNOWLEGMENTS

None.

ETHICAL CONSIDERATIONS

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

DATA AVAILABILITY

Not applicable.

REFERENCES

1. Kaye R, Leddy R. Pediatric breast lymphatic malformation with recurrent presentation in an adolescent female. *BJR Case Rep*. 2022;8(1):20210077. doi: 10.1259/bjrcr.20210077.
2. Blesinger H, Kaulfuß S, Aung T, Schwoch S, Prantl L, Rößler J, et al. PIK3CA mutations are specifically localized to lymphatic endothelial cells of lymphatic malformations. *PLoS One*. 2018;13(7):e0200343. doi: 10.1371/journal.pone.0200343.
3. Reinhardt K, Stückrath K, Hartung C, Kaufhold S, Uleer C, Hanf V, et al. PIK3CA-mutations in breast cancer. Breast Cancer Res Treat. 2022;196(3):483-93. doi: 10.1007/s10549-022-06637-w.
4. Gupta SS, Singh O. Cystic lymphangioma of the breast in an 8-year-old boy: report of a case with a review of the literature. *Surg Today*. 2011;41(9):1314-8. doi: 10.1007/s00595-010-4382-1.
5. Rusdianto E, Murray M, Davis J, Caveny A. Adult cystic lymphangioma in the inner quadrant of the breast-Rare location for a rare disease: A case report. Int *J Surg Case Rep*. 2016;20:123-6. doi: 10.1016/j.ijscr.2016.01.021.
6. Sasi W, Schneider C, Shah R, Ruffles T, Bhagwat P, Mokbel K, et al. Recurrent cystic lymphangioma of the breast: case report and literature review. *Breast Dis*. 2010;31(1):43-7. doi: 10.3233/BD-2009-0287.
7. Torcasio A, Veneroso S, Amabile MI, Biffoni M, Martino G, Monti M, et al. Cystic hygroma of the breast: a rare lesion. *Tumori*. 2006;92(4):347-50. doi: 10.1177/030089160609200415.
8. Kato M, Watanabe S, Watanabe A, Iida T. Flow-oriented Venous Anastomosis to Control Lymph Flow of Lymphatic Malformation. *Plast Reconstr Surg Glob Open*. 2019;7(7):e2199. doi: 10.1097/GOX.0000000000002199.

How to Cite This Article

Poha ATP, Yin WC, Tan YC. Recurrent Inflammation from Adult-Onset Lymphatic Malformation: A Management Conundrum. Arch Breast Cancer. 2025; 12(3):361-5.
Available from: https://www.archbreastcancer.com/index.php/abc/article/view/1094