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Intralymphatic Blood Flow in Secondary Lymphedema: A Novel Finding and Its Clinical Implications – A Case Report

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Case Report

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Abstract

Background

Intact lymphatic vessels maintain strict blood-lymphatic segregation. While pathological blood-lymphatic mixing occurs in genetic animal models, spontaneous intralymphatic blood filling has not been clinically documented.

Methods

A 55-year-old woman with secondary upper-extremity lymphedema following mastectomy presented with abnormal blood flow signals within lymphatic lumina on preoperative high-frequency ultrasound. She had chronic aspirin use and developed acute severe hypertension (220/100 mmHg) with extensive cutaneous ecchymosis preoperatively. Six lymphaticovenous anastomoses were performed under microscopy.

Results

Intraoperative visualization confirmed blood-filled lymphatic vessels, corroborating ultrasound findings. At 3-month follow-up, the corrected edema reduction rate reached 33.68%, with clinically meaningful improvements in body image, symptom, and mood subdomains of the LYMQOL-Arm scale.

Conclusions

This represents the first clinical evidence of intralymphatic blood filling. We hypothesize acute hypertension exacerbated venous reflux through latent lymphovenous communications, while aspirin disrupted physiological platelet-mediated blood-lymphatic segregation. LVA remains feasible when intraoperative assessment confirms higher intralymphatic pressure and favorable flow directionality, though single-case limitations apply.

Introduction

Lymphedema is a chronic disorder characterized by the buildup of interstitial fluid resulting from lymphatic impairment (1). The majority of lymphedema arises as secondary sequelae of breast or gynecologic malignancy, with a marked female predominance (2). Typical manifestations include limb heaviness, fatigue, and progressive swelling, however, recurrent cellulitis present a notable complication (3).

Accurate imaging evaluation is essential for timely diagnosis and evaluation of disease staging. Common modalities consist of lymphoscintigraphy (4), SPECT-CT (5) and indocyanine green

fluorescence lymphangiography (ICG-FL) (6). High-frequency enhanced ultrasound has emerged as a reliable preoperative localization tool with considerable clinical significance (7).

Current management employs multi-modal strategies focused on limb volume reduction and the prevention of consequences. Complex decongestive therapy (CDT), considered the primary physical treatment, efficiently alleviates edema and mitigates the likelihood of cellulitis (8); yet, it fails to restore injured lymphatic tissue. Surgical alternatives include lymphaticovenous anastomosis (LVA), which establishes bypass pathways by linking lymphatic vessels to venules, and vascularized lymph node transplantation (VLNT) for lymphatic restoration (9).

From an anatomical perspective, lymphovenous junction occur primarily at the thoracic duct and right lymphatic trunk, where it drains into veins at the subclavian-jugular venous system (10). Pathological lymphovenous shunts may arise in three circumstances: expanded latent pathways caused by elevated intra-lymphatic pressure in lymphedema, neoplastic growths signifying advanced stages of tumors, and congenital anomalies stemming from developmental irregularities (11).

Under normal conditions, blood is absent from lymphatic vessels as red blood cells are too large to pass through the walls of normal blood capillaries into the tissue fluid. Molecular research has demonstrated that platelet activation within the lymphatic endothelial cells is mediated by intracellular signalling pathway. Disruption of these pathways may result in abnormal blood-lymphatic intermingling, a condition similarly observed in embryos lacking platelets (12).

We present a case of secondary upper extremity lymphedema with high-frequency ultrasound demonstrating blood flow within lymphatic vessels—a finding not previously reported in the literature. Following comprehensive preoperative evaluation, successful LVA achieved effective resolution of upper limb lymphedema.

Case Report

A 55-year-old woman developed left upper extremity lymphedema with recurrent cellulitis 6 years after left radical mastectomy with axillary lymph node dissection for breast cancer. Subsequently, she completed one month of radiotherapy and followed by10 years of standardized oncologic therapy. Other notable medical history included hypertension, lacunar cerebral infarction and chronic kidney dysfunction. Patient received no prior complex decongestive therapy (CDT). Physical examination revealed diffuse soft-tissue swelling with thickened skin, elevated temperature, and visible skin folds on the wrist and forearm without breakdown. Both pitting and Stemmer signs were positive. Limb function remained intact.Preoperative high-frequency ultrasound (HFU) using 18–24 MHz transducer probe on Aplio i900 system (CanonMedical Systems, Otawara, Japan) detected abnormal blood flow signals within lymphatic lumens (Fig. 1), in which the mean diameter of isolated veins and lymphatic vessels were measured to be 0.77mm and 0.89mm respectively. Indocyanine green (ICG) lymphography showed diffuse dermal backflow without linear lymphatic distribution patterns (stage 5) whereas International Society of Lymphology (ISL) was categorised as stage 2. Baseline circumferential measurements were

obtained at 5-cm intervals from the radial-ulnar styloid baseline (Fig. 2). Quality of life was assessed using the Lymphedema Quality of Life Questionnaire (LYMQOL-Arm). Six end-to-end lymphaticovenous anastomoses (LVA) were performed in end-to-end approach under microscope (MITAKA MM51) using 11 – 0 and 12 – 0 sutures. Intraoperative findings confirmed blood-filled lymphatic vessels in all cases. Following successful anastomosis, mixed lymphatic fluid and blood drained into recipient veins (Fig. 3).During 3-month follow-up, left limb volumetric analysis showed 17.6% reduction, from 4160.28 mL to 3426.46 mL (Table 1, Fig. 4). After adjusting for contralateral limb variation, which decreased 2540.79 mL to 2352.43 mL, the corrected lymphedema volume reduction was 545.46 mL, representing a 33.68% improvement rate (Table 2). LYMQOL-Arm scores showed clinically meaningful improvements: body image (− 0.80), symptoms (− 0.50), and mood (− 0.50), with a 1-point increase in overall quality of life. Functional scores remained unchanged due to preoperative ceiling effect. Postoperative management included two months of CDT followed by elastic compression garment use. No cellulitis episodes occurred during follow-up.

Discussion

Physiologically, intact lymphatic vasculature maintains complete segregation between blood and lymphatic circulations, preventing blood cells from entering lymphatic lumina. We report an extremely rare phenomenon of blood flow within lymphatic vessels in a patient with secondary lymphedema undergoing LVA.

Beyond hemostasis, platelets play a critical developmental role in separating embryonic blood and lymphatic vasculatures (12). This process depends on binding between platelet C-type lectin-like receptor 2 (CLEC-2) and podoplanin (PDPN), a transmembrane protein selectively expressed by lymphatic endothelial cells. This interaction activates the SYK–SLP-76–PLCγ2 signaling cascade, triggering platelet activation and aggregation at lymphovenous junctions. Genetic disruption of any pathway component causes severe developmental defects, including blood-filled lymphatics and perinatal lethality (13–15).

Platelets maintain blood-lymphatic segregation through two distinct mechanisms. First, at the thoracic duct–subclavian vein junction, PDPN-stimulated platelet microthrombi form physical barriers preventing retrograde blood reflux (16–18). Second, during embryonic mesenteric vascular remodeling, CLEC-2 signaling enables platelets to seal transient venous endothelial defects while primitive lymphatics clear extravasated erythrocytes (19).

The CLEC-2-dependent activation pathway suggests potential susceptibility to antiplatelet agents. Aspirin inhibits cyclooxygenase-1, reducing thromboxane A_2 synthesis and suppressing secondary platelet aggregation. We hypothesize that aspirin may elevate the platelet activation threshold required for CLEC-2-mediated responses during vascular remodeling. In patients with compromised lymphovenous valves or surgical vascular stress, chronic aspirin therapy could impair physiological microthrombus formation at lymphovenous junctions, recapitulating the blood-lymphatic mixing

observed in CLEC-2 knockout models. Our patient's prolonged aspirin therapy supports this hypothesis, though clinical validation studies are needed.

The patient exhibited unusual clinical findings. Despite unremarkable cutaneous appearance and well-controlled hypertension on admission, her blood pressure spiked to 220/100 mmHg preoperatively, necessitating surgical cancellation. Massive cutaneous ecchymoses developed simultaneously (Fig. 5)—a presentation typically seen when venous hypertension causes retrograde blood flow into lymphatics following LVA. We propose that acute hypertension exacerbated venous reflux through pre-existing abnormal lymphovenous communications, with chronic aspirin use as a contributory factor.

High-frequency ultrasound revealed blood flow signals within lymphatic lumina—an extremely rare finding. Our radiologists, with experience exceeding 2,000 lymphatic ultrasound examinations, confirmed these tubular structures as lymphatic rather than venous vessels. Intraoperative findings corroborated this observation, providing dual verification. Successful surgical intervention and favorable outcomes further validated our diagnostic approach.

This represents the first documented case of intralymphatic blood flow confirmed by clinical evidence. Despite single-case limitations and short follow-up, the extreme rarity and favorable outcomes warrant prompt publication to inform the lymphatic surgery community. Critically, LVA remains feasible in such patients when intraoperative measurements confirm higher intralymphatic pressure relative to venous pressure and verify appropriate flow directionality. This case expands our understanding of blood-lymphatic interactions and demonstrates that intralymphatic blood flow does not preclude successful surgical intervention when proper physiological criteria are met.

Declarations

Ethics Statement

Written informed consent was obtained from the patient for the publication of this case report and the use of associated clinical images.

The study protocol was approved by the Institutional Review Board and Ethics Committee of Peking University Shenzhen Hospital and registered with the Chinese Clinical Trial Registry (ChiCTR), with the registration number: ChiCTR2600117183.

Conflict of Interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Declaration on Generative Artificial Intelligence in Scientific Writing

The authors declare that no generative artificial intelligence (AI) or AI-assisted technologies were used in the writing process of this work.

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Author Contributions

All authors contributed to the preparation of this manuscript and approved the final submitted version.

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Tables

Tables 1 to 3 are available in the Supplementary Files section.

Figures

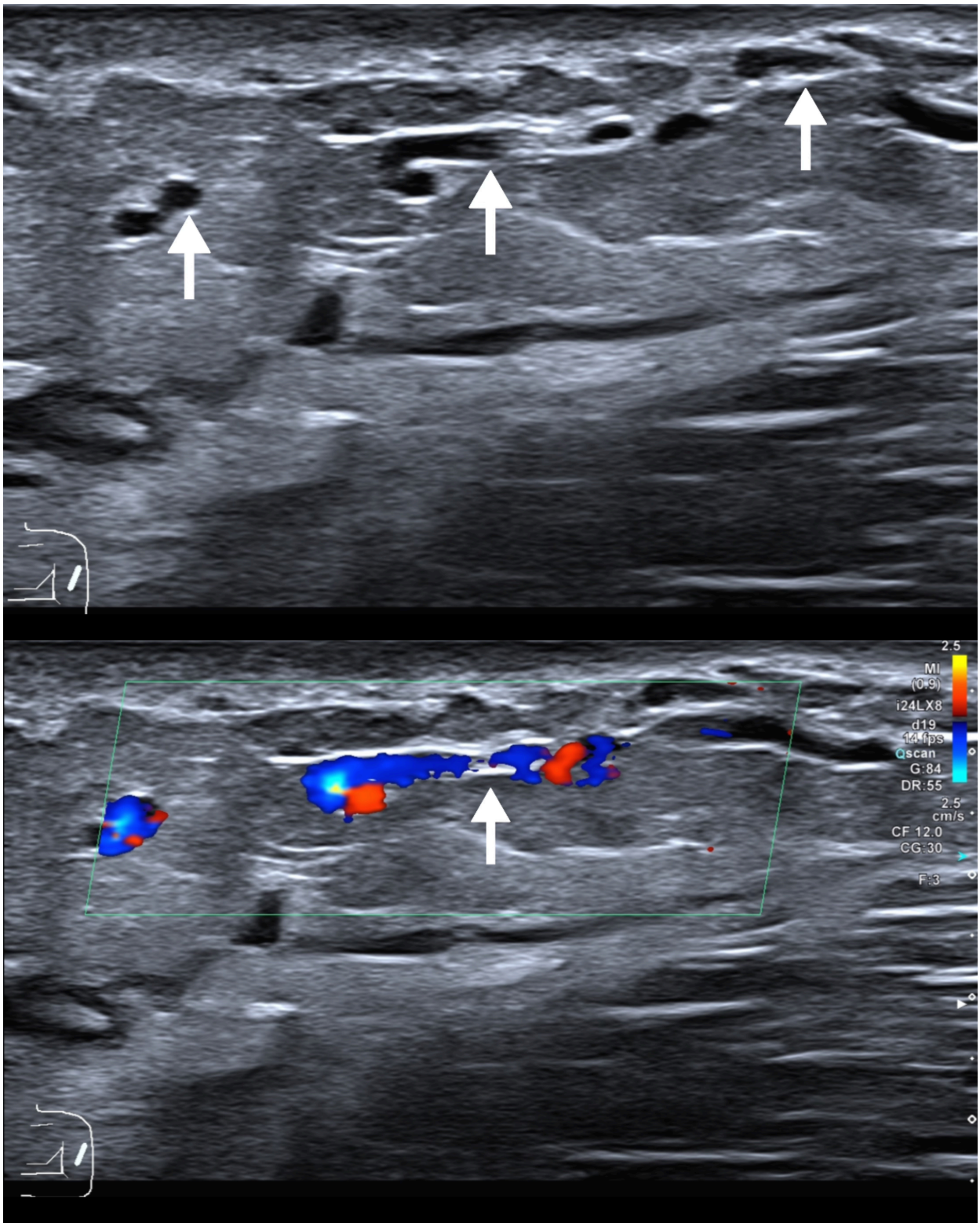


Figure 1

Color Doppler signals can be visualized within the lymphatic lumens on the image.



Figure 2

Preoperative upper-extremity circumference measurements and clinical swelling appearance, including views in forearm pronation and supination positions.

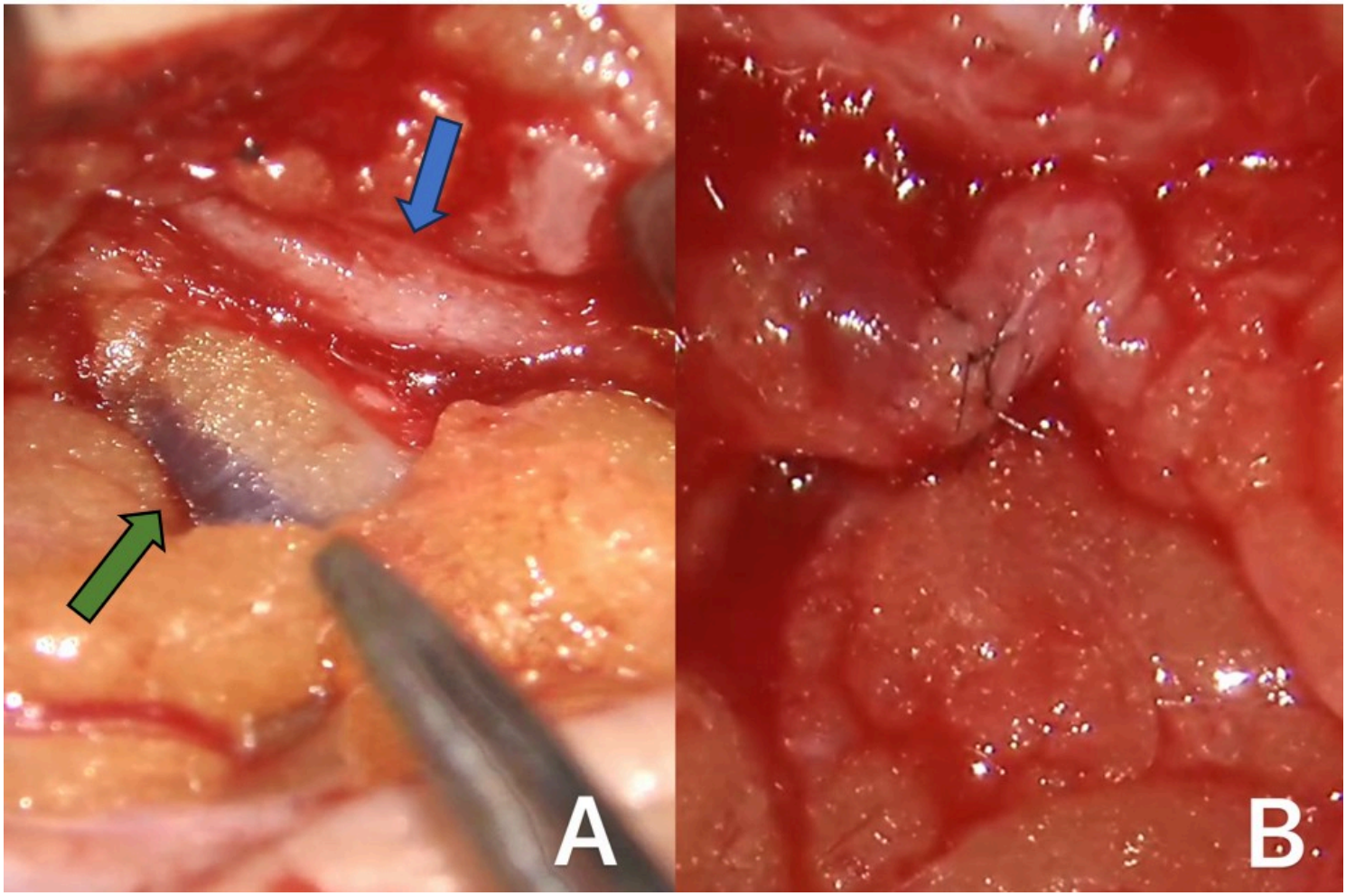


Figure 3

A: Green arrows mark blood-filled lymphatic vessel, and blue arrows indicate superficial veins. B: After successful LVA, the recipient vein is distended by the inflow of blood-tinged lymphatic fluid.



Figure 4

Post-operative 3 months follow up.



Figure 5

Extensive cutaneous ecchymoses appeared, distributed along the anatomical course of lymphatic vessels. We hypothesize venous reflux into lymphatic vessels.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Tables.docx