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# A RARE CASE OF ADULT B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA PRESENTING AS A BILATERAL BREAST MASS WITH SUBCUTANEOUS NODULE AND LEFT HUMERUS PATHOLOGICAL FRACTURE.

**Breast Surgery**

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## ABSTRACT

Acute lymphoblastic leukemia (ALL) is the most common type of malignancy in children. B-cell ALL is the most common type of ALL in both adults and children. However, mature B-cell ALL is rare in adults, comprising only 2% to 4% of the adult population. Symptoms can include fatigue, fever, night sweats, unintentional weight loss, spontaneous bleeding, infections, and shortness of breath. We report a rare case of extra-medullary leukemic infiltration of the breast by B-cell ALL presenting as a bilateral breast mass and a paraumbilical subcutaneous nodule with pathological fracture of lateral condyle of the left humerus without any bone marrow involvement or circulating blast cells. **Summary:** Leukemic infiltration of breast, though rare, can be a diagnostic dilemma and must be evaluated with imaging, histopathology and cytogenetic studies.

## KEYWORDS

Breast lump, B-cell ALL, Breast Lymphoma, leukemic infiltration of breast

## INTRODUCTION

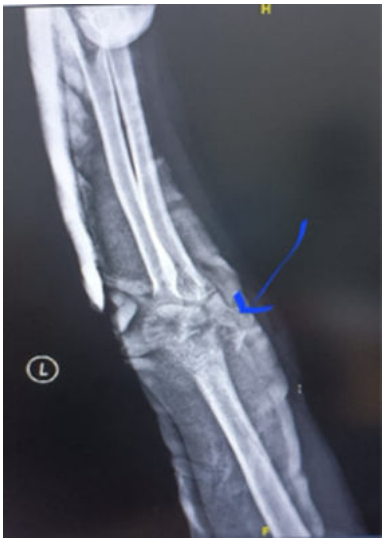
Acute lymphoblastic leukemia (ALL) is the most common type of malignancy in children, with peak incidence at 3 years of age. However, mature B-cell ALL is rare in adults, comprising only 2% to 4% of the adult population. Symptoms can include fatigue, fever, night sweats, unintentional weight loss, spontaneous bleeding or bruising, infections, and shortness of breath. On clinical examination, patients might have hepatosplenomegaly and generalised lymphadenopathy. Though there are some reports of extra-medullary leukemic infiltration of the breast [1], rarely, it may also present as a breast lump as an initial and only symptom [2].

### Case Presentation

A 29-year-old lady presented to the surgery OPD with complaints of a lump in both breasts, which was incidentally noticed 5 months ago, and a lump in the right upper abdomen for 2 months, which was insidious in onset, progressive in nature from approximately 2x2 cm to the current size of approximately 5x5 cm in size. The mass was not associated with pain or vomiting. There was no history of hematemesis, melena, bleeding per rectum or jaundice. There was no history of early satiety or weight loss. The breast lumps were not associated with pain and gradually increased in size from 2x2 cm in the right breast to the current size of 7x7 cm and from 3x3 cm in the left breast to the current size of 5x5 cm. It was not associated with any axillary swelling, fever or nipple discharge. There was no history of any known comorbidities or past surgeries. The patient also gave a history of left upper limb swelling and pain following a trivial electrical injury 15 days ago, for which she was evaluated outside and diagnosed to have a pathological fracture of the left humerus with an unknown primary. The patient has a regular menstrual cycle. She has been married for 2 years and is nulliparous. She gives a family history of right breast carcinoma in her mother, for which she had undergone a right-modified radical mastectomy and is on follow-up.

At presentation, she was well built and moderately nourished, and her vitals were stable. There was a 7x7cm firm lump in the upper outer quadrant of the right breast, which was well-defined, mobile, and non-tender. A 4x4 cm lump was palpated in the upper inner quadrant of the left breast, which was firm in consistency with well-defined borders and was mobile and non-tender. There was no axillary or cervical lymphadenopathy. The abdomen was soft with a mass of approximately 4 x 4 cm in size involving the umbilical region in the subcutaneous plane. The mass was mobile and firm in consistency, with a smooth surface and well-defined margins. It was non-tender. There was no ascites or organomegaly, and per rectal examination was normal. The patient had a left above elbow cast with a shoulder sling for a left humerus fracture (figure 1).

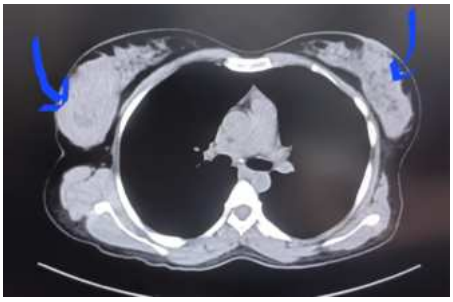
She was worked up with routine blood investigations and imaging studies. Her initial haemoglobin level was 11.7 g/dl, WBC count was 5580/µL and platelet count was 454000/µL, S. urea was 11 mg/dl, S. creatinine was 0.43 mg/dl, S. sodium was 135 mEq/L, S. potassium was 3.88 mEq/L. Her liver function tests, and coagulation profile were within the normal range.




**(Figure 1:** X ray of left upper limb - arrow showing displaced left lateral condyle fracture of humerus. L- left, F- forearm, H- hand).

Ultrasound of bilateral breasts was suggestive of a BIRADS 3 lesion of the right breast and a BIRADS 1 lesion of the left breast. Core needle biopsy of bilateral breast lump was suggestive of B-cell ALL, and FNAC of the paraumbilical lesion was suggestive of lymphoblastic lymphoma. An orthopedic opinion was taken for the pathological fracture, and an MRI of the elbow was done, which showed an epi-metaphyseal lesion with bone lysis in the lateral condyle of the left humerus. CECT thorax, abdomen and pelvis and PET CT done in view of pathological fracture revealed a well-defined heterogeneously enhancing mass lesion of 6.9x4.5x7.1 cm in size in the upper outer quadrant of the right breast with an area of central necrosis with an ill-defined heterogeneous mass in the upper inner quadrant of left breast measuring 3.2x4.8 cm in size (figure 2) and a 2.5x3.6 cm well defined homogeneous soft tissue dense cutaneous lesion extending into the subcutaneous plane in the right paraumbilical region. It also showed an ill-defined heterogeneously enhancing mass lesion in the left adnexa of 7x5.2x7 cm in size. There were a few FDG avid left level V cervical lymph nodes and an FDG avid cutaneous lesion in the flexor aspect of the left forearm of 2.6x1.5 cm size. Increased FDG uptake in a few lytic lesions involving the medial end of left clavicle, multiple sites of left scapula, manubrium sterni and supracondylar region of left humerus with pathological fracture and callous formation. PET CT suggested Lugano stage IV ALL. Bone marrow biopsy revealed normocellular reactive marrow with no lymphoma infiltration, and the CSF

examination was normal.



(**Figure 2:** CECT thorax - arrows showing bilateral breast lesions in the upper outer quadrants with central areas of necrosis)

The patient was referred to the medical oncology team and was started on chemotherapy with the BMF-95 (Berlin-Frankfurt-Munster 95) protocol. Induction chemotherapy with methotrexate, cyclophosphamide, L-asparaginase and cytarabine was given. However, follow-up PET CT suggested increased FDG uptake in bilateral cervical and mediastinal lymph nodes and hence, induction chemotherapy was continued for four months, after which it was switched over to maintenance chemotherapy with high-dose methotrexate.

A repeat PET CT obtained after one month showed low-grade uptake in bilateral level 4 lymph nodes and multiple mediastinal lymph nodes (D-score 2). However, clinically, there were no palpable breast lump or lymph nodes, and there was complete resolution of the para umbilical nodule.

## DISCUSSION

Acute lymphocytic leukemia is a malignancy of B or T lymphoblasts characterised by the uncontrolled proliferation of abnormal, immature lymphocytes and their progenitors, which ultimately replace the bone marrow elements and other lymphoid organs. In India, the incidence of ALL accounts for about 35% of all hematological malignancies and is the most common childhood malignancy. Patients typically present with symptoms related to anaemia, thrombocytopenia, and neutropenia due to the replacement of the bone marrow with the tumor. Symptoms can include fatigue, easy or spontaneous bruising and/or bleeding, and infections and B-symptoms like fever, night sweats, unintentional weight loss, and hepatomegaly, splenomegaly, and lymphadenopathy can be seen. Central nervous system involvement is common and can present as cranial neuropathies, with meningeal symptoms, or with raised intracranial pressure.

The etiology of Acute Lymphocytic Leukemia is idiopathic. However, exposure to benzene, ionising radiation, or previous exposure to chemotherapy or high-dose radiotherapy are certain environmental factors implicated as predisposing factors to ALL.

Unlike T-cell lymphoblastic leukemia, B-cell ALL rarely presents with extra-medullary infiltration. But B cells have recently become a focus in breast cancer pathology due to their effects on tumor regression, prognosis, and response to treatment, in addition to their contribution to antigen presentation, immunoglobulin production, and regulation of adaptive responses [3]. Leukemia cutis is also a rarely encountered presentation of low-grade B cell ALL, which can present as skin and subcutaneous nodules, papules, hemorrhagic spots and ulcers [4, 5, 6]. When it presents as a breast mass, the lesion usually presents as a well-defined, firm mass, most commonly in the upper outer quadrant [1,7]. It can be a part of a disseminated disease considered as secondary involvement of the breast. It can mimic a fibroadenoma or breast carcinoma with its course and clinical presentation. A tissue diagnosis (FNAC or core needle biopsy), flow cytometry, and bone marrow biopsy are required to confirm the diagnosis.

Various studies on leukemic infiltration of the breast suggest that FNAC exhibit dispersed monomorphic blast cells ranging from small, medium to large cells with a high nuclear: cytoplasmic (N: C) ratio with rounded or convoluted nuclei having dispersed chromatin, inconspicuous nucleoli and scanty cytoplasm. Mitotic figures may be present and variable in number [8].

Ultrasound breast is helpful in diagnosing patients with dense breasts, typically below 35 years of age. In USG examination, leukemic infiltration of the breast appears as homogenous and ill-defined hypoechoic masses with microlobulations with no acoustic changes [9, 10]. Mammography findings can be unremarkable, nonspecific, and variable. They may show an enlarged breast with diffusely coarse parenchyma, an ill-defined mass with irregular borders, or a solitary nodule simulating primary breast carcinoma. Micro calcifications are very rarely reported, unlike primary breast carcinoma [10].

On MRI, these lesions appear as a hyper-intense signal compared with normal breast parenchyma on T2W images, and there is a rapid ring-enhancement of the lesions due to central necrosis and peripheral angiogenesis [11].

While MDCT has low diagnostic value in the evaluation and characterization of breast lesions, in ALL, due to leukemic infiltration of surrounding glandular parenchyma, one might see indistinct margins of the mass. Even in a dense breast, a coincident mass may be better visualised than mammography. It also has the added benefit of identifying and screening the other breast. Axillary lymphadenopathy is another clue to diagnosing leukemic disorder or lymphoma, especially when bilateral, in the absence of known primary breast cancer [7]. Other ancillary findings like pleural effusion or involvement of mediastinal lymph nodes increase the value of MDCT in not only pointing to a correct diagnosis but also staging the malignancy.

In another case report presented by Gilbert T Chua et al. [12], a similar presentation of ALL was noted. The patient presented with a pathological fracture of the right distal tibia without any abnormal circulating blast cells and bone marrow involvement, and the diagnosis was confirmed with high clinical suspicion and cytogenetic study. Patients with primary or secondary breast lymphomas respond well to chemotherapy, and hence, excision biopsy should be avoided.

## CONCLUSIONS

Leukemic infiltration of the breast, though rare, should be included as a differential diagnosis for a breast lump, and an early FNAC or core needle biopsy reduces the chances of mismanagement or delay in treatment without having to undergo an excision biopsy. Patients presenting with multiple symptoms should be evaluated with tissue diagnosis of each and imaging such as PET-CT to arrive at the diagnosis with a high clinical index of suspicion.

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