



## Case Report

# A case report of coexistent carcinoma breast with chronic myeloid leukemia

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### ABSTRACT

Multiple primary cancers are gradually becoming a regular condition and frequently result in many diagnostic and therapeutic difficulties. In our case report we present a 68-year female with breast lump who was incidentally diagnosed with chronic myeloid leukemia. The fine needle aspiration biopsy (FNAC) of the breast lump lead to the diagnosis of Invasive ductal carcinoma.

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## 1. Introduction

The incidence of breast carcinoma is briskly increasing in Indian scenario rapidly surpassing the incidence of cervical cancer. The prevalence of breast cancer according to 2017 registry is as high as 25.8 per 100,000 women and mortality 12.7 per 100,000 women.<sup>1</sup> The incidence of chronic myeloid leukemia is reported to be 0.8 to 2.2 per 100,000 population.<sup>2</sup> The incidence of synchronous occurrence of breast carcinoma with chronic myeloid leukemia devoid of any inciting factors like chemotherapy is not vividly documented.

## 2. Case Report

A 68 year-old woman came with complaints of lump in the left breast since 4 years. Ultrasound of breast showed heterogenous echotexture with BIRADS 5. Investigation and with routine examination revealed Complete blood count with high white blood cell count of 60,790 cells/cumm. Peripheral smear report of the patient exhibited Myeloproliferative disorder- Chronic myeloid

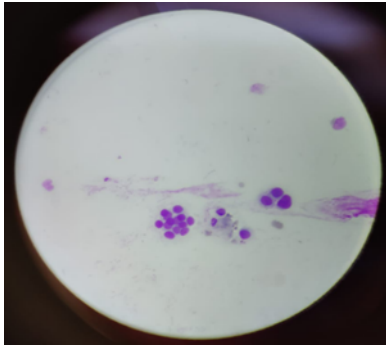
leukemia. The patient underwent a bone marrow biopsy showing Hypercellular marrow with predominance of myeloid precursor, Blast cells 2% and basophils 2% and morphology of Chronic myeloid leukemia- chronic phase. Cytogenetics of the patient showed 46 xx, t(9;22)(q34;q11.2), positive for Philadelphia chromosome. A fine needle aspiration cytology (FNAC) was done for breast lump, showing pleomorphic cells arranged in discohesive clusters, individual tumour cells show pleomorphism with moderate cytoplasm, high nuclear cytoplasmic ratio and irregular chromatin. Few binucleate cells and mitotic figures also noted. Lymphocytes and plasmacytoid cells noted in a haemorrhagic background, suggesting features of Invasive ductal carcinoma. The patient was sent to a higher cancer facility for treatment of invasive ductal carcinoma and CML.

## 3. Discussion

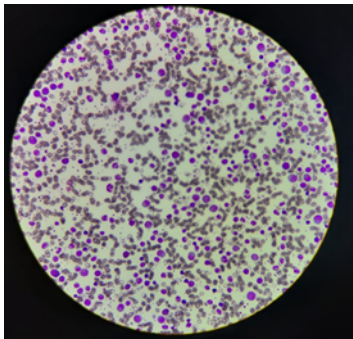
Carcinoma of the breast is the most frequent solid epithelial malignant tumor in women. It occurs at a higher incidence in developed countries. The etiological factors are high caloric diet, reduced physical activity, early menarche, nulliparity, lack of breastfeeding and a small risk is associated with

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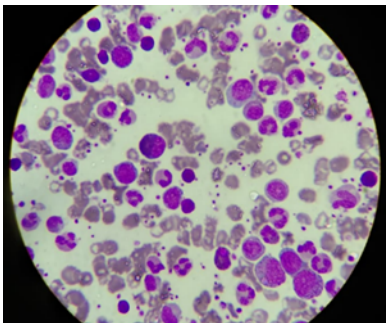
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**Fig. 1:** FNAC slide showing discohesive clusters(100x Pap stain)  
Inset: individual cells with high N:C ratio (400 x pap stain)



**Fig. 2:** Peripheral smear of the patient showing features of CML (400x, leishman stain)



**Fig. 3:** Peripheral smear (1000x, leishmann stain), Blue arrow: Basophil Orange arrow: blast cell

usage of oral contraceptive pills. Familial predisposition is seen, with the common genes identified being BRCA1 and BRCA2. It can occur at any age but rare in patients younger to 25 years or older than 80 years with peak incidence between 45-60 years. Invasive carcinoma of breast patients usually present with varying sized palpable lump in the breast associated with nipple discharge. Overlying skin dimpling, fixity to the deep fascia can also occur in patients presenting at a later stage. The advent of radiographic imaging and fine needle aspiration cytology has helped in early diagnosis of breast carcinoma.<sup>3</sup>

Invasive ductal carcinomas are derived from the mammary ductal epithelium, particularly terminal duct lobular unit (TDLU). The invasive ductal carcinoma is of various types- the most common being the invasive ductal carcinoma (NOS) type, the other types being the mixed type carcinoma, pleomorphic carcinoma, carcinoma with osteoclastic giant cells, carcinoma with choriocarcinomatous features and carcinoma with melanotic features.

FNAC breast is the initial investigation of choice in any patient presenting with palpable breast lump. It is safe, economical, does not require anesthesia, can be done in outpatient setting and provides rapid results with reporting time less than biopsy with low false negative rate (<5%). FNAC results help the surgeon to decide about further management.

FNAC smears of malignant neoplasm generally yield a more cellular smear than a non malignant lesion. The smear pattern of with cellularity, presence or absence of a bimodal cell population, cell cohesion, size and shape of cell aggregates, stromal components all partake an important role in reaching to the accurate diagnosis. Aggregates of malignant cells are irregular, often with an angular or tubular shape. Reduced cell cohesion results in the presence of small clusters of cells, cells in single files, and single cells with intact cytoplasm, whereas single bare bipolar nuclei typical of non-neoplastic breast tissue are absent.<sup>4</sup>

FNAC smear of Invasive ductal carcinoma has Cytological smear showing Moderately to highly cellular smears, poorly cohesive malignant epithelial cell with nuclear enlargement and pleomorphism singly and in clusters.

Myoepithelial cells and single bare bipolar nuclei are absent.

The individual cells show irregular nuclear membrane and chromatin. The smears show variable amounts of fibroblasts and fragments of collagen (stromal desmoplasia) with scant amount of necrosis associated with the atypical cells, Intracytoplasmic neolumina is seen in some cases.<sup>5</sup>

Chronic myeloid leukemia belongs to the myeloproliferative group of disorders. The myeloproliferative disorders are clonal neoplasms with typical increased marrow cellularity, maturation of cell lineages and organomegaly. The underlying disorder is aberrant activation of tyrosine kinase signalling pathways which forms the basis for treatment with tyrosine kinase. Chronic myeloid leukemia is the most common myeloproliferative disorder with peak incidence at 50-60 years and slight male preponderance.<sup>6</sup>

Chronic myeloid leukemia is represented by neoplastic increase of primarily myeloid cells in the bone marrow with an intense elevation of these cells in the peripheral blood. The disease progresses through 3 phases- chronic phase, accelerated transition and blast crisis. In chronic

phase, the leukaemia cells are minimally invasive and can be sometimes appreciated in the blood, bone marrow, spleen, and liver. In Blast crises, the presence of blasts can be seen in any extramedullary site, with a preference for spleen, liver, lymph nodes, skin, and soft tissue.<sup>7</sup>

Chronic myeloid leukemia arises in a haematopoietic stem cell and is marked by the chromosomal translocation t(9;22)(q34.1;q11.2), resulting in the constitution of the Philadelphia (Ph) chromosome, containing the BCR-ABL1 fusion gene. The Philadelphia chromosome (Ph) was first acknowledged in 1960 in a patient with CML. Translocation of the proto-oncogene tyrosine-protein kinase (ABL1) gene located on chromosome 9 to the breakpoint cluster region (BCR) gene located on chromosome 22 results in a BCR-ABL1 fusion gene on the Ph. Three BCR-ABL1 fusion gene hybrids encode BCR-ABL1 protein isoforms p210, p190, and p230, which have continually enhanced tyrosine kinase (TK) activity. These aberrantly activated kinases disturb downstream signalling pathways, causing enhanced proliferation, differentiation arrest, and resistance to cell death.<sup>8</sup>

In CML, BCR-ABL1 is located in all myeloid lineages and in some lymphoid and endothelial cells. The detection of the Ph chromosome and/or BCR-ABL1 in the proper clinical and laboratory settings confirms diagnosis of Chronic myeloid leukemia.

Patients diagnosed with chronic myeloid leukemia (CML) have a 30% higher risk of developing a secondary solid organ cancer compared to general population. Studies indicate to have repetitive signs of cancer within the first year of diagnosis. The common malignancies reported are of gastrointestinal (GI), nose and throat, melanoma, kidney, endocrine and non-Hodgkin's lymphoma (NHL) and rare cases in female breast.<sup>9</sup>

Treatment for CML by tyrosine kinase is a risk factor for development of various malignancies. However, CML itself has been discussed as a risk factor for solid cancers and hematologic malignancies. The acquired translocation t(9;22) at diagnosis of CML and additional chromosomal changes/mutations as a sign of clonal evolution during the course of disease show the potential of genetic instability in CML.<sup>10</sup>

Furthermore, mutation at stem cell level of Philadelphia chromosome in CML, occurs around 6 years prior to the presentation of the symptoms, but carcinoma breast occurs many years prior to this presentation.<sup>11</sup>

#### 4. Conclusion

The occurrence of incidental synchronous carcinoma validates that careful investigation of each and every patient will help in identifying hidden symptoms and increasing patient outcome. In our case report the synchronous

presentation appears more as a coincidence than as any association.

#### 5. Source of Funding

None.

#### 6. Conflict of Interest

The authors declare no conflict of interest.

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