



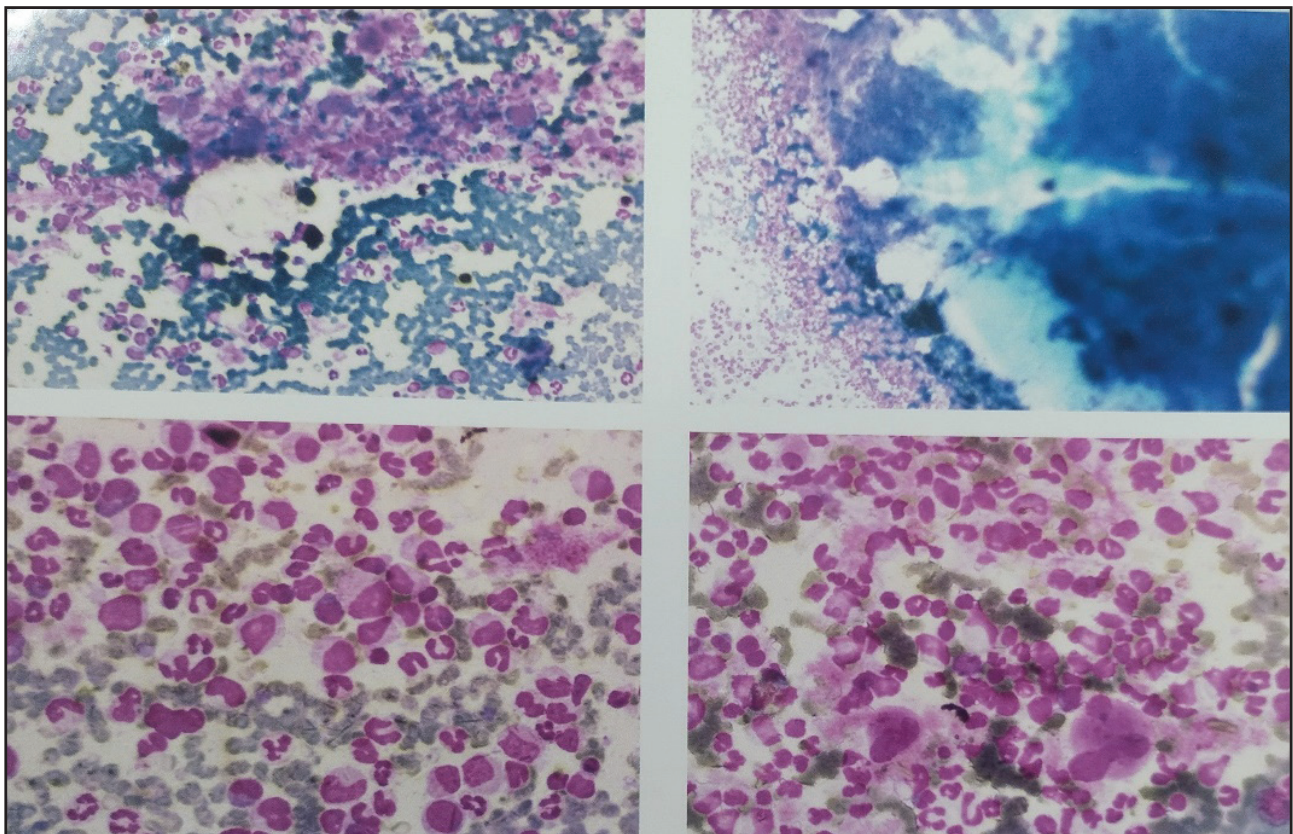
intermittent low-grade fever and generalized weakness for the past 2 months. The trucut biopsy of the mass revealed invasive breast cancer with a focal lobular growth pattern (grade 2) with E-cadherin expression and immunohistochemistry showed tumor cells to be ER-/ PR- and Human epidermal growth factor receptor-2 (HER2) 3+. A contrast-enhanced CT scan of the chest demonstrated multiple lesions in the upper outer quadrant of the left breast, consistent with multifocal disease, the largest measuring 2 cm. Ipsilateral axillary lymphadenopathy was present. Additionally, pleural-based lesions were observed in the right upper and lower lobes, raising suspicion for metastatic involvement. Although the lesions were too small for biopsy, radiologic assessment and multidisciplinary team consensus suggested metastasis, and the disease was staged as stage IV. The remainder of the imaging workup was unremarkable. Laboratory investigations showed anemia (Hemoglobin level of 12.6 g/dl), thrombocytosis (platelets  $644 \times 10^9/l$ ), and leukocytosis ( $55.1 \times 10^9/l$ ) with a left shift. Differential leukocyte count revealed: neutrophils (polymorphs) 64%, lymphocytes 13%, eosinophils 6%, basophils 2%, myelocytes 7%, metamyelocytes 3%, and monocytes 5%. Peripheral blood smear demonstrated normochromic, normocytic red blood cells, a higher number of platelets, and elevated neutrophils with young myeloid cells. Bone marrow aspiration showed myeloid and

megakaryocytic hyperplasia, with no evidence of metastatic deposits (Figure 1). Molecular testing confirmed the diagnosis of CML through BCR-ABL quantification (BCR-ABL1/ABL1 ratio of 55.8%). The patient tolerated the treatment well. Cardiac function was closely monitored with serial echocardiography during therapy, and a mild reduction in chemotherapy dosage was required in subsequent cycles. Overall, no significant adverse effects or toxicities were noted.

### Discussion

A synchronous tumor is defined as the occurrence of two distinct primary malignancies within a 6-month period in the same individual, a phenomenon considered rare in clinical oncology. The development of SPMs in cancer patients is increasingly recognized, particularly with improved survival rates. The etiology of SPMs appears to be multifactorial, involving underlying immune dysregulation, shared genetic or environmental risk factors, and possible detection bias due to increased medical surveillance following the initial cancer diagnosis [3].

Epidemiological data indicate that cancer patients have a higher incidence of secondary neoplasms compared to the general population. In women, breast cancer is frequently associated with other malignancies such as ovarian, endometrial, soft tissue sarcomas, salivary gland



**Figure 1.** Myeloid and megakaryocytic hyperplasia on bone marrow aspiration. The marrow is markedly hypercellular with predominance of myeloid precursors, resulting in an increased myeloid-to-erythroid ratio. Numerous small megakaryocytes are seen, consistent with megakaryocytic hyperplasia typical of CML

tumors, and lung cancers [4]. While therapy-related acute myeloid leukemia and myelodysplastic syndromes are well-recognized complications of breast cancer treatment [3], the synchronous occurrence of CML with breast cancer is exceedingly rare [5]. Although leukocytosis in a known cancer patient often suggests bone marrow metastasis, a thorough evaluation may reveal a second hematological malignancy such as CML, which should be considered in the differential diagnosis, as early detection enables timely treatment and may improve outcomes [6].

CML is a rare myeloproliferative neoplasm, with an incidence of 1-2 per 100,000 annually, characterized by uncontrolled proliferation of myeloid precursors and the presence of the Philadelphia chromosome (BCR-ABL fusion gene) [7,8]. This oncogene drives leukemic growth via constitutive tyrosine kinase activity and is effectively targeted by agents like imatinib. While CML has been reported following adjuvant therapy for cancers such as breast, lymphoma, and testicular cancer, with a latency of around 4.7 years, its synchronous occurrence with breast cancer, prior to cytotoxic treatment, is extremely rare [6]. These cases may suggest an underlying genetic predisposition, warranting further genomic evaluation, as BRCA1 and BRCA2 mutations have been linked to an increased risk of both breast cancer and myeloid neoplasms [9]. BRCA1 and BRCA2 mutations impair homologous recombination repair, leading to chromosomal instability and accumulation of somatic mutations. This not only increases lifetime risk of breast cancer but also predisposes carriers to therapy-related or synchronous myeloid neoplasms [10] and a positive BCR-ABL test confirm.

Howard et al. [11] conducted a study using data from four nationwide, population-based cancer registries in Sweden, Denmark, Finland, and Norway to assess the risk of secondary leukemia in breast cancer survivors. They identified 687 cases of non-chronic lymphocytic leukemia, with an excess absolute risk of 9.05 (95% CI: 7.5-10.7). The risk of developing secondary leukemia, particularly CML and acute lymphoblastic leukemia, was significantly elevated and persisted for more than 25 years after the initial breast cancer diagnosis [11]. A similar case was reported by Bhal et al. involving a 45-year-old woman diagnosed with synchronous CML and breast cancer. She presented with a lump in the left breast, confirmed as infiltrating ductal carcinoma. Investigations showed marked leukocytosis with 5% blasts; bone marrow examination and a positive BCR-ABL test confirmed CML [12].

The rare synchronous occurrence of breast cancer and CML presents a significant diagnostic challenge. The persistent markedly elevated leukocyte counts in patients with an existing malignancy should prompt suspicion for a concurrent hematologic malignancy rather than being attributed solely to bone marrow metastasis [13] or reactive changes [14]. A few important red flags raising suspicion of CML in breast cancer include:

- Unexplained marked leukocytosis
- Left-shifted myeloid series
- Basophilia and eosinophilia
- Lack of response to steroids or antibiotics

The patient's management posed significant challenges due to the complex interplay between the two malignancies and the risk of treatment-related complications. In the current case, the concurrent use of chemotherapy and imatinib was a pragmatic approach to address both advanced breast carcinoma and CML simultaneously. Currently, there are no established clinical guidelines for the management of synchronous primary cancers [15]. Limited evidence from case reports suggests that a multimodal treatment strategy may be both feasible and effective. Close coordination between oncology and hematology teams is essential to optimize care and minimize toxicity. Regular assessment of the patient's clinical status, treatment response, and emerging complications is critical to guide future therapeutic decisions and ensure appropriate management.

## Conclusion

Synchronous occurrence of breast cancer and CML is exceptionally rare but clinically significant. With increasing cancer survival, the risk of second primary malignancies, including hematological ones, must be carefully considered. Vigilant assessment of unexplained hematologic abnormalities can lead to early diagnosis, enabling timely intervention and improved outcomes. These cases underscore the potential role of genetic predisposition, the need for individualized long-term surveillance strategies, and the importance of multidisciplinary discussions in their management.

## What is new

This is the first case from Pakistan reporting the synchronous occurrence of breast cancer and CML, diagnosed during initial staging workup following incidental detection of leukocytosis. Subsequent detailed evaluation and BCR-ABL fusion testing confirmed the presence of CML in this patient. The persistent markedly elevated leukocyte counts in patients with an existing malignancy should prompt suspicion for a concurrent hematologic malignancy rather than being attributed solely to bone marrow metastasis or reactive changes.

## List of abbreviations

CML: Chronic myeloid leukemia  
SPM: Second primary malignancies

## Acknowledgment

The authors are thankful to their colleagues for their valuable support.

## Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

**Funding**

None.

**Consent for publication**

Written informed consent was obtained from the patient for publishing this case report.

**Ethical approval**

Ethical approval is not required at our institution to publish an anonymous case report.

**Author details**

Qamar Javed<sup>1</sup>, Warda Ahmad<sup>2</sup>, Saira Zafar<sup>1</sup>, Muhammad Babar Imran<sup>2</sup>

1. Department of Oncology, PINUM Cancer Hospital, Faisalabad, Pakistan
2. Department of Nuclear Medicine, PINUM Cancer Hospital, Faisalabad, Pakistan

**References**

1. Abid S, Khan AU, Sarwar N, Hamid R. Breast cancer: early detection initiative in Pakistan. *Khyber Med Univ J*. 2022;14(3):145–6.
2. Ammad Ud Din M, Shahzad M, Ashraf A, Liaqat H, Jaan A, et al. Clinical Research in Chronic Lymphocytic Leukemia in Pakistan; a systematic review. *Medicina (Kaunas)*. 2023;59(8):1483. <https://doi.org/10.3390/medicina59081483>
3. Khandeparkar SG, Bhatt NC, Deshmukh SV, Joshi A. A rare case of chronic lymphocytic leukemia in a patient with recurrent metastatic breast carcinoma. *Med J Dr DY Patil Univ*. 2015;8(1):108–10. <https://doi.org/10.4103/0975-2870.148871>
4. Kishtagari A, Bowman IA, Tallman MS, Douer D, Berman E, Maslak PG, et al. Chronic myeloid leukemia after adjuvant treatment for breast cancer: is it therapy related? *Blood*. 2013;122(21):2740. <https://doi.org/10.1182/blood.V122.21.2740.2740>
5. El-Badrawy A. MDCT evaluation of synchronous breast carcinoma and other solid malignancies. *Breast Dis*. 2021;40(4):275–81. <https://doi.org/10.3233/BD-201065>
6. Elm'hadi C, Khmamouche MR, Tanz R, Toreis M, Mahtat E, Allaoui M, et al. Successful management of synchronous

- recurrent breast carcinoma with chronic myelogenous leukemia: a case report. *J Med Case Rep*. 2017 Jan;11(1):10. <https://doi.org/10.1186/s13256-016-1180-4>
7. Pamuk GE, Ehrlich LA. An overview of myeloid blast-phase chronic myeloid leukemia. *Cancers (Basel)*. 2024 Oct;16(21):3615. <https://doi.org/10.3390/cancers16213615>
8. Khan S, Sabar MF, Akbar M, Waris A. Dilemmas in the diagnosis and management of CML in Pakistan. *Turk J Haematol*. 2024 Dec;41(4):286–7. <https://doi.org/10.4274/tjh.galenos.2024.2024.0280>
9. Churpek JE, Marquez R, Neistadt B, Claussen K, Lee MK, Churpek MM, et al. Inherited mutations in cancer susceptibility genes are common among survivors of breast cancer who develop therapy-related leukemia. *Cancer*. 2016;122(2):304–11. <https://doi.org/10.1002/cncr.29615>
10. Franco S, Godley LA. Myeloid neoplasms in individuals with breast and ovarian cancer and the association with deleterious germline variants. *Gynecol Oncol*. 2024;187:235–40. <https://doi.org/10.1016/j.ygyno.2024.05.026>
11. Howard RA, Gilbert ES, Chen BE, Hall P, Storm H, Pukkala E, et al. Leukemia following breast cancer: an international population-based study of 376,825 women. *Breast Cancer Res Treat*. 2007;105(3):359–68. <https://doi.org/10.1007/s10549-006-9460-0>
12. Bahl A, Dhiman A, Talwar V, Doval DC. Synchronous carcinoma breast with chronic myelogenous leukemia: a rare presentation. *Indian J Cancer*. 2010;47(4):477-9. <https://doi.org/10.4103/0019-509X.73558>
13. Harvey Y, Bleakley S, Blombery P, Bain BJ. Marked leukemoid reaction in a patient with metastatic breast carcinoma. *Am J Hematol*. 2018;93(2):306–7. <https://doi.org/10.1002/ajh.24849>
14. Liu Y, Liu J. Male Breast cancer complicated with leukocytosis resembling leukemia reaction after chemotherapy: a case report. *Cancer Rep (Hoboken)*. 2025;8(7):e70280. <https://doi.org/10.1002/cnr2.70280>
15. Feizi I, Sedigh-Namin A, Kani A, Namin SS, Toularoud AB. A rare case report of triple primary malignancies: synchronous breast ductal invasive carcinoma and lung neuroendocrine tumor, followed by chronic myeloid leukemia. *Int J Surg Case Rep*. 2025;130:111305. <https://doi.org/10.1016/j.ijscr.2025.111305>

**Summary of the Case**

1	Patient (gender, age)	67 years, female
2	Final diagnosis	Invasive breast cancer and chronic myeloid leukemia
3	Symptoms	Palpable breast mass, low-grade fever and generalized weakness
4	Medications	Doxorubicin and cyclophosphamide for breast malignancy, along with imatinib (400 mg OD) for CML
5	Clinical procedure	Chemotherapy, tyrosine kinase inhibitor
6	Specialty	Oncology