

## Case Report:

### An unusual case of Essential Thrombocythemia in coexistence with Breast cancer

Charu Agarwal<sup>1</sup>, Mukta Pujani<sup>2</sup>, Novak Gupta<sup>3</sup>, Varsha Chauhan<sup>4</sup>,  
Sujata Raychaudhuri<sup>5</sup>, Ruchira Wadhwa<sup>6</sup>

#### Abstract

Essential thrombocythemia (ET) is an extremely rare myeloproliferative neoplasm (MPN) which is characterized by persistent, non-reactive thrombocytosis ( $> 450 \times 10^9/L$ ) and an increased risk for thrombotic events. These patients have an increased risk of both hematological and non-hematological malignancies however the risk of breast cancer in MPN is not increased in comparison to general population. We hereby present an extremely unusual case of ET in a 38 years old female (diagnosed with breast cancer), which came to light on routine pre-surgical work up of the patient. Diagnosis was confirmed on bone marrow aspiration clubbed with JAK 2 mutation. Patients with ET have an increased risk of thrombosis thereby it becomes challenging for the clinician to operate on a coexistent solid tumor. On extensive literary search, there was a single case of coexistent Breast Cancer and Essential Thrombocythemia and we are reporting second such coexistence to the best of our knowledge.

**Keywords:** Essential thrombocythemia; breast cancer; JAK 2 mutation; coexistence.

Bangladesh Journal of Medical Science Vol. 21 No. 02 April'22 Page : 463-466  
DOI: <http://doi.org/10.3329/bjms.v21i2.58083>

#### Introduction

Myeloproliferative neoplasms (MPN) are a clonal hematopoietic stem cell disorder comprising of ABL positive Chronic myeloid leukemia, Polychythemiavera, Essential thrombocythemia (ET) and primary myelofibrosis. Among these, ET

is an extremely rare disease and is characterized by persistent, nonreactive thrombocytosis ( $> 450 \times 10^9/L$ ) with an increased risk for thrombotic/bleeding events.<sup>1</sup>Patients of Essential Thrombocythemia have an increased risk of developing both hematological and non-hematological malignancies however there is not much increased risk of breast cancer in such

1. Dr. Charu Agarwal, MD, DNB (Pathology), MNAMS, Associate Professor, Dept. of Pathology, ESIC Medical College, aridabad, Haryana. [Dr.charu.ag@gmail.com](mailto:Dr.charu.ag@gmail.com)
2. Dr. Mukta Pujani, MD (Pathology), MAMS, Professor, Dept. of athology, ESIC Medical College, Faridabad, Haryana. [drmuktapujani@gmail.com](mailto:drmuktapujani@gmail.com)
3. Dr. Novak Gupta, MD (Medicine), DM (Medical Oncology) "Medical Oncologist, Dept. of Medicine, ESIC Medical College, Faridabad, Haryana.
4. Dr. Varsha Chauhan\*, MD (Pathology), Assistant Professor, Dept. of Pathology, ESIC Medical College, Faridabad, Haryana. [varsha.chauhan3@gmail.com](mailto:varsha.chauhan3@gmail.com)
5. Dr. Sujata Raychaudhuri, MD (Pathology), Professor, Dept. of Pathology, ESIC Medical College, Faridabad, Haryana. [sujatabulu@yahoo.co.in](mailto:sujatabulu@yahoo.co.in)
6. Dr. Ruchira Wadhwa, MD (Pathology), Senior Resident, Dept. of Pathology, ESIC Medical College, Faridabad, Haryana. [ruchirawadhwa@gmail.com](mailto:ruchirawadhwa@gmail.com)

**Correspondence:** Dr. Varsha Chauhan\*, MD (Pathology), Associate Professor, Dept. of Pathology, ESIC Medical College, Faridabad, Haryana. [varsha.chauhan3@gmail.com](mailto:varsha.chauhan3@gmail.com)

patients as compared to general population.<sup>2</sup>We hereby present an extremely unusual case of ET with coexistent breast cancer creating a therapeutic challenge for the clinicians.

### Case Report

A 38 years old female came to Surgical out-patient department with lump, left breast. The lump was present in upper outer quadrant, firm in consistency and measuring 3 X 2 cms. Fine needle aspiration cytology (FNAC) smears revealed sheets, clusters and singly scattered ductal epithelial cells with interspersed myoepithelial cells at places. Few of the clusters were loosely cohesive with nuclear pleomorphism against hemorrhagic background (Figure 1a). Cytological features were suggestive of proliferative breast disease with atypia (Category III). Clinico-radiological correlation was advised with follow-up. Complete blood counts (CBC) revealed Hemoglobin - 12gm%, Total Leucocyte count – 8000/cumm and platelet count –  $6.2 \times 10^6$ /cumm. The platelet count was elevated on two more occasions but it was considered to be reactive thrombocytosis. Viral markers including HbsAg, HIV and HCV were non-reactive. On Ultrasonography, a 4 X 5 mm hetero-echoic lesion was noted in lower inner quadrant of left breast with no evidence of vascularity. There was no evidence of left axillary lymph nodes, hepatomegaly or splenomegaly.

Wide local excision of breast lump was performed. We received a partly skin covered soft tissue piece measuring 3 X 2.5 X 2cms. Overlying skin measured 1.2 X 0.5 cms. Cut surface showed a grey-white firm area. Microscopy revealed features of Ductal Carcinoma in situ with foci of Infiltrating Duct Carcinoma (Figure 1b). On immunohistochemistry ER and PR were positive while Her2neu was negative.

Modified radical mastectomy was planned. On pre-surgical work up of the patient, all the CBC parameters were normal except platelet count which was markedly increased ( $9.5 \times 10^6$ /cumm). There was no history of thrombotic or bleeding episodes. There was no family history suggestive of thrombocytosis. On account of persistent thrombocytosis, patient

was advised bone marrow (BM) examination. BM aspiration smears showed particles which were cellular with Myeloid:Erythroid ratio – 1.04:1. Erythroid series showed a normoblastic reaction while myeloid series showed normal maturation. There was an increase in the number of megakaryocytes which were large in size with hyperlobulated nuclei (Figure 2). In view of marked thrombocytosis with megakaryocytic hyperplasia, JAK2 and BCR/ABL qualitative mutation assay was advised. JAK2 V617F mutant came out to be positive while BCR/ABL1 was negative with ABL copy number as 194900.

On whole body 18-F Fluorodeoxyglucose positron emission tomography Computed Tomography (FDG PET/CT), bilateral breasts were unremarkable. There was no discrete mass or abnormal FDG uptake in either of the breasts. Multiple sub-centimeter size bilateral axillary lymph nodes with no significant FDG uptake were seen. Patient was diagnosed as a case of Essential Thrombocythemia in the setting of breast cancer.

Patient was an intermediate risk disease as per the International Prognostic Score of thrombosis in World Health Organization essential thrombocythemia (IPSET-thrombosis) score and was started on low dose once daily aspirin. The patient received adjuvant chemotherapy for breast cancer- anthracycline and cyclophosphamide for four cycles followed by taxane. The COX-2 inhibitor was discontinued during the treatment when the platelet count decreased to less than the lower limit of normal, with a close follow up. She is now on oral Letrozole and Injection Goserlin. Patient was started on aromatase inhibitor instead of selective estrogen receptor modulator in view of the increased risk of thromboembolic phenomenon.

### Discussion

Essential thrombocythemia mostly occurs in elderly individuals with an average age of 60 years and a female preponderance (Female:Male ratio approximately 2:1).<sup>1</sup> However the present case is a much younger female in her third decade. Tefferi et al<sup>3</sup> studied ET in young females and concluded that they have long survival with a low incidence of life-

threatening thrombo-hemorrhagic complications or acute leukemia.

WHO diagnostic criteria for ET include: (1) Platelet count  $> 450 \times 10^6/\text{cumm}$ , (2) BM biopsy showing proliferation mainly of the megakaryocytic lineage with increased numbers of enlarged, mature megakaryocytes with hyperlobulated nuclei, (3) Presence of JAK2, CALR or MPL mutation (4) Not meeting WHO criteria for BCR-ABL1 + Chronic Myeloid Leukemia (CML), Polycythemia Vera (PV), Primary Myelofibrosis (PMF), Myelodysplastic syndrome (MDS) or other myeloid neoplasms with absence of any evidence for reactive thrombocytosis.<sup>4</sup>In the present case, there was isolated persistent thrombocytosis with megakaryocytic hyperplasia and enlarged hyperlobulated forms, thereby excluding other MPNs. Positive Jak2 mutation confirmed the diagnosis of Essential Thrombocythemia.

The 2016 WHO classification includes three major subcategories of JAK2/CALR/MPL related MPN - PV, ET and PMF. JAK2 mutation is the most crucial finding in myeloproliferative neoplasms accounting for 95% of PV and 60% of ET and Primary myelofibrosis patients.<sup>4</sup>JAK2 mutations have been known to be reported in the process of growth and development of mammary gland and also in breast cancer initiation and progression. JAK2 mutations have also been associated with Tumor infiltrating lymphocytes and a good prognosis in breast cancer. ET is Philadelphia chromosome negative MPN characterized by abnormal megakaryocytic morphology.<sup>1</sup>BCR-ABL1 mutation is the diagnostic hallmark of CML which was absent in the present case.

Although ET has an indolent course, but there are few solid cancers like tongue, colon and gastric cancer which have been reported in the setting of ET.<sup>5,6</sup>It is an established fact that chronic inflammation in many diseases including ET can initiate a clonal evolution resulting in secondary cancers. Platelets have a deleterious impact on cancer evolution due to their role in cancer invasiveness and metastasis.<sup>7</sup>

Barbui et al<sup>8</sup> (2012) devised a 3-tiered prognostic

model for International Prognostic Score of thrombosis in World Health Organization essential thrombocythemia (IPSET-thrombosis) score based on parameters like 1) Age  $> 60$  years (1 point), 2) Thrombosis history (2 points), 3) Cardiovascular risk factors (1 point), and 4) JAK2V617F (2 points). This was scored as low-risk =  $< 2$  points; intermediate-risk = 2 points; and high-risk =  $> 2$  points. The present case falls into intermediate risk.

On extensive literary search, we found a single case of coexistent Breast Cancer and Essential Thrombocythemia reported by Seegobin et al<sup>2</sup> in 2018. To the best of our knowledge we are reporting second such coexistence. ET and breast cancer are two malignant disorders with favorable outcome. Survival of ET patients does not substantially differ from general population however the breast cancer outcome differs depending on the stage of cancer.<sup>2</sup>

### Conclusion

Prior to diagnosing a patient as ET, it is essential to investigate and rule out all possible secondary causes of thrombocytosis. ET patients have an increased risk of thrombosis thereby it becomes challenging for the clinician to operate on a coexistent solid tumor or to initiate cytoreductive therapy. These patients should be periodically reassessed. Association of secondary malignancies with ET speculates the involvement of JAK2-STAT mechanism in its pathogenesis.

**Source of fund: (if any):** NA

**Conflict of interest:** NA

**Ethical clearance:** OBTAINED

### Authors's contribution:

Data gathering and idea owner of this study: .. DR MUKTA PUJANI DR CHARU AGARWAL

Study design: ... DR CHARU AGARWAL DR MUKTA PUJANI

Data gathering: .... DR VARSHA CHAUHAN DR NOVAL GUPTA DR RUCHIRA WADHWA

Writing and submitting manuscript: .... DR CHARU AGARWAL DR VARSHA CHAUHAN

Editing and approval of final draft: ... DR MUKTA PUJANI DR SUJATA RAYCHAUDHURI

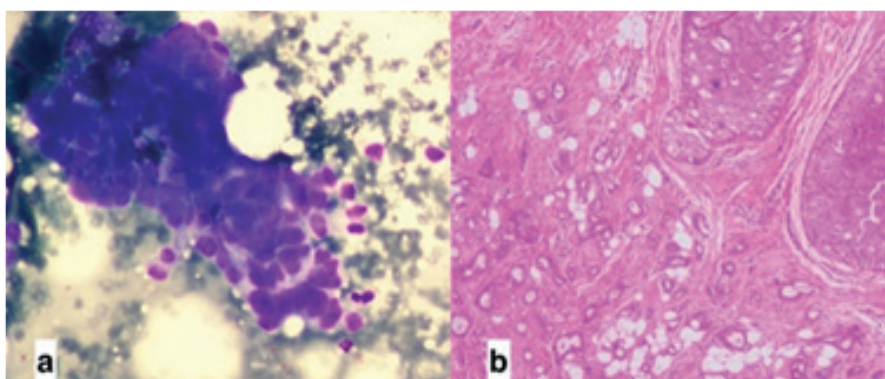


Figure:1

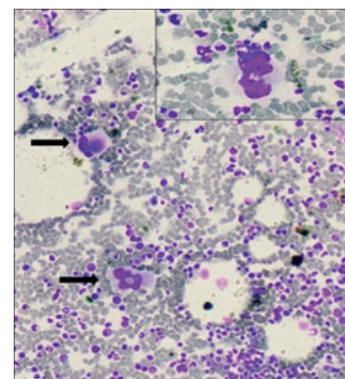


Figure:2

**Legends:**

Figure 1a) Giemsa stained smear showing loosely cohesive cluster with nuclear pleomorphism against a hemorrhagic background (200X) b) Photomicrograph showing ductal carcinoma in situ with foci of

Infiltrating Duct Carcinoma (H & E, 100X)

Figure 2 Bone Marrow Aspiration smears are cellular with increased number of megakaryocytes having cloud like nuclei (Giemsa, 200X; Inset, 400X)

**References**

1. Koshy J, Alperin J, Jana B, Markowitz A and Qian YW. A Case of Philadelphia Chromosome Positive Myeloproliferative Neoplasm in a Pregnant Woman with Unusual Primary Myelofibrosis Features . *Case Reports in Hematology* 2013; Article ID 702831,1-4. <https://doi.org/10.1155/2013/702831>
2. Seegobin K, Gharia B, Maharaj S and Zuberi L. Coexistent Breast Cancer and Essential Thrombocythemia: How We Addressed the Therapeutic Challenges. *Case Reports in Hematology*. 2018; Article ID 2080185,1-4. <https://doi.org/10.1155/2018/2080185>
3. Tefferi A, Fonseca R, Pereira DL and Hoagland HC. A long-term retrospective study of young women with essential thrombocythemia. *Mayo Clin Proc*. 2001; **76**(1):22-8. <https://doi.org/10.4065/76.1.22>
4. Barbui T, Thiele J, Gisslinger H, Kvasnicka HM, Vannucchi AM, Guglielmelli P, Orzi A and Tefferi A. The 2016 WHO classification and diagnostic criteria for myeloproliferative neoplasms: document summary and in-depth discussion *Blood Cancer Journal*. 2018; **15**:1-11. <https://doi.org/10.1038/s41408-018-0054-y>
5. H. Kondo, Y. Sakai, and T. Takaso, "Coexistence of essential thrombocythemia and gastric cancer," *Rinsho Ketsueki*. 1993; **34**(2):224-228.
6. Mihaila RG, Marchian S, and Mihaila R. A rare case of thrombocytosis with double malignant etiology-pathogenetic interrelationships and consequences. *Scholars Journal of Medical Case Reports* .2015; **3**(8),684-6.
7. Hasselbalch HC. The platelet-cancer loop in myeloproliferative cancer. Is thrombocythemia an enhancer of cancer invasiveness and metastasis in essential thrombocythemia, polycythemia vera and myelofibrosis? *Leuk Res* .2014; **38**(10):1230- 1236. <https://doi.org/10.1016/j.leukres.2014.07.006>
8. Barbui T, Finazzi G, Carobbio A, Thiele J, Passamonti F, Rumi E et al. Development and validation of an International Prognostic Score of thrombosis in World Health Organization-essential thrombocythemia (IPSET-thrombosis). *Blood* 2012; **120**(26):5128-33. <https://doi.org/10.1182/blood-2012-07-444067>