Polycythemia Vera With Metastatic Adenocarcinoma In Bone Marrow of A 68-Year-Old Male

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Abstract

The co-occurrence of polycythemia vera (PV) and metastatic adenocarcinoma in bone marrow is rare. The present case study describes a case of PV in association with metastatic carcinoma in the bone marrow. Magnetic resonance imaging (MRI) pelvis (for hip joints) revealed suspicious bone marrow changes in the lumbosacral spine. The bone marrow biopsy indicated hyperplastic trilineage hematopoiesis along with non-hemopoietic cells. The findings of immunohistochemistry on the trephine biopsy sample indicated the gastrointestinal origin of metastatic non-hematopoietic cells. The present study may help in the future management of patients with polycythemia vera and metastatic adenocarcinoma.

Keywords: myeloproliferative neoplasms (MPN), polycythemia vera (PV), solid cancer, metastatic adenocarcinoma

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Introduction

Polycythemia vera (PV), a myeloproliferative neoplasm (MPN), is associated with increased RBC production, panmyelosis and JAK2V617F or JAK2 exon 12 mutation.[1] It has a prevalence of 22 cases per 100,000 population.[2] Recent studies have shown that MPN patients have almost double the chance of developing solid tumours such as lung, GIT, kidney, prostate, ovary and bladder as compared to the general population.[3]

We present a case study of a 68-year-old man suffering simultaneously from PV and metastatic adenocarcinoma. We believe it may be the first case report of PV, diagnosed using World Health Organization (WHO) criteria,[1] that has been linked to metastatic adenocarcinoma. Future diagnosis and treatment of patients with metastatic adenocarcinoma and PV may benefit from the results of the current report.

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Case study

A 68-year-old man presented in medicine outdoor with a history of backache and left leg pain for 1.5 months. There was no fever, shortness of breath, chest pain, dyspepsia, melena, cough, abdominal or urinary symptoms. He had a transient ischemic attack 20 years ago but didn't take any treatment. The patient gave the history of one episode of per rectal bleeding a few years back, but it was not investigated and resolved without any treatment. The patient was a non-smoker and had no chronic respiratory illness. General physical examination revealed facial flushing and palmar erythema, and a single left inguinal lymph node 2×2 cm. The neck was supple, and the thyroid was non-palpable. On examination, the prostate was mildly enlarged with no palpable nodularity. Systemic examination was unremarkable. His CBC showed RBC Count= 8.26×1012/L, Hb=21.2 g/dL, HCT=67.1 %, MCV=81.2 fL, MCH=25.7 pg, MCHC=31.6 g/dL, TLC=10.1×103/µL, Neutrophils = 82 %, Lymphocytes=12 %, Monocytes=04 %, Eosinophils = 02 %, Retics= 2.8%, Platelets=339×103/ µL.

Peripheral smear showed polycythemia and target cells, neutrophilic predominance and platelet anisocytosis with few giant platelets (Figure#1).

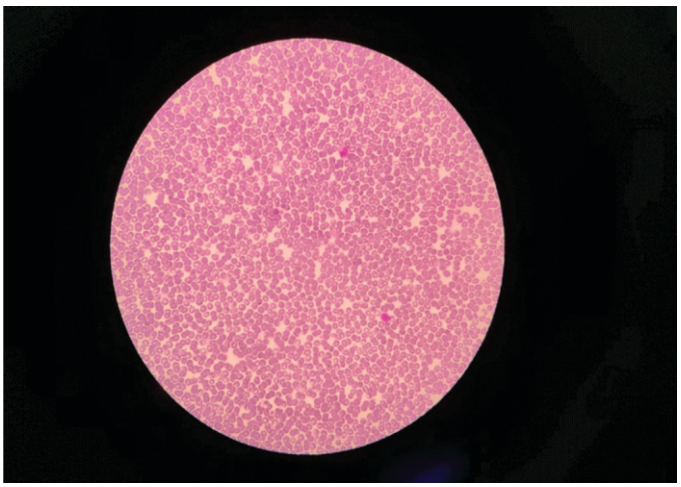

Figure 1: *Peripheral Smear Showing Polycythemia and Target Cells*

Coagulation profile, random blood glucose and renal parameters were normal. Serum potassium was 6.4 mmol/L, and serum sodium was 131mmol/L. Liver function tests revealed AST=92U/L, but total bilirubin, ALT, and alkaline phosphatase were normal. Viral markers were negative. USG abdomen showed bilateral renal parenchymal echogenicity (Grade I) and moderately enlarged prostate. X-ray lumber spine and pelvis were normal. Serum PSA was 2.8 ng/ml. Serum CRP was 1.3mg/dL and ESR was 4mm/1st hr.

MRI pelvis revealed no abnormal findings in pelvic viscera, but degenerative changes in hip and sacroiliac joints along with suspicious signals in the lumbosacral spine, were noted. Mild inflammatory changes were noted in the soft tissue around the left iliac bone. Bone marrow biopsy revealed hypercellular fragments and cell trails with panmyelosis and 2% blasts. Trephine biopsy revealed panmyelosis with pleomorphic megakaryocytes. (Figure#2)

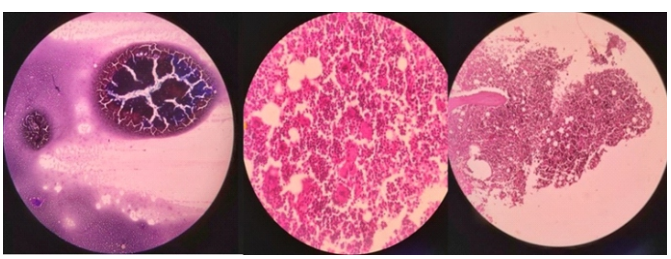

Figure 2: *Hypercellular Aspirate and Trephine Showing Panmyelosis*

Touch imprints and trephine revealed focal clusters of non-hemopoietic cells, which were large in size with hyperchromatic nuclei and prominent nucleoli (Figure # 3)

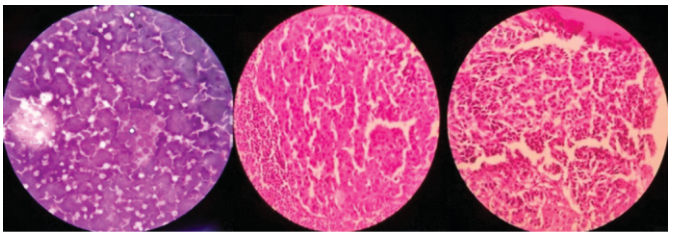

Figure 3: *Metastatic Cells in Touch Imprints and Trephine Biopsy*

The detection of JAK2 V617F mutation by PCR was positive. The serum erythropoietin level was 2.15 IU/L (reference range: 4.3 to 29 IU/L). Immunohistochemistry revealed CD45, PSA, TTF1 and Napsin-A negative in infiltrating cells. However, cytokeratin and CDX2 were positive in infiltrating cells. A diagnosis of PV with metastatic adenocarcinoma was made. Further investigations were planned, including radiological workup (CT chest and abdomen), biopsy of inguinal lymph node and upper/lower GI endoscopy to determine the site of the primary tumour. But before further workup could be done, the patient suddenly collapsed and died. We couldn't find the primary site of cancer as the attendants of the patient refused autopsy.

Discussion

Polycythemia vera is a clonal disorder that is typically associated with JAK2 mutations (V617F or exon 12).[1] Primary polycythemia is caused by bone marrow disorders, and secondary polycythemia develops as a result of other conditions, such as solid malignan-cies.[4] Malignancies of the prostate, breast, lung and gastrointestinal system commonly metastasize to the bone marrow but can be missed due to their cryptic presentation. Early detection of bone marrow metastasis is crucial as most cases exhibit bone marrow metastasis before the detection of primary tumour.[5] Patients with MPNs are more prone to having second primary solid tumours such as lung, thyroid, GIT, kidney and melanoma.[3] The identification is important as co-occurrence might affect long-term survival. The underlying mechanism might be genomic instability, cytotoxic medications, chronic inflammation and immune dysregulation.[6] Literature search shows that, especially for colorectal malignancies, the JAK-STAT pathway is proposed to play a critical role in the systemic inflammatory response.[7] Metastatic carcinoma from an unidentified primary

site presents a clinical problem. The metastatic cells of our patient were positive for cytokeratin, which points to epithelial origin. PSA, Napsin-A and TTF1 were negative, ruling out possibilities of prostate, lung and thyroid tumours. CDX2 was positive in our patient's metastatic cells. Therefore, we infer that our patient most likely had bone marrow infiltration by colorectal malignancy in addition to PV. We believe that it may be the first case report showing PV along with metastatic carcinoma in the bone marrow that is of gastrointestinal origin. The literature search revealed a 73-year-old male who developed carcinoma stomach eight years after diagnosis of PV.8 Another case was reported in which a 59-year-old man having PV was found to have ascending colon cancer.[9] But none of these cases reported marrow infiltration by metastatic carcinoma in association with MPN, while our patient presented with bone marrow infiltration. Few case studies have been published showing the relationship of PV and prostatic adenocarcinoma. In these patients, localized malignancy has been reported.[10] Our patient didn't have any symptoms, signs or radiological evidence of CA prostate and his serum PSA was also normal. From our study and literature review, we conclude that patients with PV have a high incidence of solid tumours, especially adenocarcinoma. But we are currently unsure if this relationship is merely coincidental or causal. Additional studies are required in this regard, as it can jeopardize the long-term survival of patients with PV. In order to prevent missing or delayed diagnosis, the doctor should be aware of the potential link between PV and metastatic adenocarcinoma. Our case may be the first instance of metastatic cancer in the bone marrow with a confirmed PV diagnosis.

Conclusion

Several mechanisms underlie the pathogenesis of secondary malignancy in patients with PV. Future studies are needed to evaluate these pathways. Careful examination of bone marrow and other diagnostic modalities is pivotal to identify such unusual presentations so as not to miss the diagnosis.

Conflict of Interest None

Funding Source None

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