Myelophthic Anemia in a Patient with Lobular Breast Carcinoma Metastasized to the Bone Marrow

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Abstract

Breast tumors have a predilection for metastasizing to the bone leading to cells being displaced by the cancer cells subsequently producing immature leukocytes and erythrocytes in the peripheral blood. We present a case of a 57-year-old female who was found to have myelophthic anemia secondary to stage four lobular breast carcinoma metastasized to the bone marrow after being misdiagnosed as having thrombotic thrombocytopenia purpura. Diagnosis of myelophthic anemia requires a thorough workup and treatment is based upon secondary management of the malignancy.

Categories: Internal Medicine, Medical Education, Oncology

Keywords: ttp, thrombotic thrombocytopenic purpura, adams13, a disintegrin and metalloproteinase with a thrombospondin type 1 motif (member 15), er, estrogen receptor, pr, progesterone receptor, her2, human epidermal growth factor receptor 2

Introduction

Approximately 252,710 new cases of invasive breast cancer were predicted to occur in the United States in 2017. From 2005 to 2014, the incidence of breast cancer among non-Hispanic blacks increased by 0.4% per year [1]. Breast tumors have a predilection for metastasizing to the bone. When metastasis to the bone marrow occurs, cells are displaced by the space-occupying cancer cells and this leads to immature leukocytes and erythrocytes in the peripheral blood [2-5]. Appearance of immature cells in the blood smear and evidence of bone marrow infiltration are sufficient for diagnosis of myelophthic anemia [3-5].

Case Presentation

A 57-year-old African American female with a history of diabetes presented to the hospital with severe anemia and acute change in mental status. On physical examination, the patient was noted to be lethargic and had right-sided facial drooping, right-sided tongue deviation, right-sided gaze preference, with right-sided body strength significantly diminished compared to the left. Initial laboratory results, reported in Table 1, showed severe anemia and thrombocytopenia (Hb 2.5 g/dL, Hct 8 %, Plt 15,000/cmm), and mild acute kidney injury (CrCl 101 mL/min). Numerous fragmented red blood cells (RBCs) (schistocytes) were noted in the peripheral blood smear (Figure 1). Repeated peripheral blood smears persistently showed poikilocytosis, nucleated RBCs, immature myeloid cells, and teardrop cells. Thrombotic thrombocytopenic

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purpura (TTP) was suspected due to classic presentation: microangiopathic hemolytic anemia, thrombocytopenia, acute kidney injury, altered mental status, and a low grade fever.

| Laboratory  | Value      |
|------------|------------|
| Na         | 133 mmol/L |
| K          | 4.7 mmol/L |
| Cl         | 102 mmol/L |
| CO₂        | 13 mmol/L  |
| BUN        | 33 mg/dL   |
| Cr         | 0.7 mg/dL  |
| Total Bili | 1.3 mg/dL  |
| Direct Bili| 0.8 mg/dL  |
| AST        | 152 U/L    |
| ALT        | 44 U/L     |
| Alb        | 3.2 g/dL   |
| Alk Phos   | 644 U/L    |
| Total Pro  | 7.3 g/dL   |
| Lactate    | 8.1 mmol/L |
| Haptoglobin| 8.0 mg/dL  |
| WBC        | 9.3 K/cmm  |
| Hb         | 2.3 g/dL   |
| Hct        | 8.0%       |
| Plt        | 15 K/cmm   |
| MCV        | 80 fl      |
| MCH        | 25 pg      |
| MCHC       | 31.6 g/dL  |
| RDW        | 29.3%      |
| Auto neutro| 54.8%      |
| Auto lymph | 35.3%      |
| Auto mono  | 9.2%       |
| Auto baso  | 0.5%       |
The patient was started on daily plasmapheresis and steroids for a presumed diagnosis of TTP. However, after ADAMTS13 result came back negative, plasmapheresis was stopped and the steroid was tapered. On further evaluation, computed tomography (CT) scan of the head revealed mixed sclerotic and lytic lesions in the calvarium (Figure 2A), diffuse osteoblastic pelvic lesions (Figure 2B), and a 1.2-cm ovoid soft tissue nodular opacity in the 6 o'clock position of the right breast (Figure 2C). Subsequent tests including bone marrow aspiration yielded a dry tap further solidifying the concern for bone marrow infiltrative disease. Bone marrow biopsy from the ischial bone showed many atypical cells (Figure 3), which were highly suggestive of carcinoma and the immunohistochemistry report was consistent with metastatic lobular breast carcinoma with the tumor cells staining positive for both estrogen receptor (ER) and progesterone receptor (PR), and negative for HER2. She was started on combination therapy with letrozole (aromatase inhibitor) and palbociclib (cyclin-dependent kinase
inhibitor). The patient had significant clinical and hematological improvement within few days after starting the combination therapy. Her repeat laboratory test results are reported in Table 2. Two months later, the patient presented to the emergency room with deteriorated clinical status and severe pancytopenia. Despite aggressive measurements, she succumbed to her illness.

![Image](https://example.com/image1.png)

**FIGURE 2:** A) White arrows point to mixed lytic and sclerotic lesions of the calvarium found on computed tomography (CT) scan of the head without contrast. B) White arrows point to osteoblastic lesions of the pelvis found on CT scan of the abdominopelvic region without contrast. C) Yellow marker shows 1.2 cm ovoid soft tissue nodular opacity at the 6 o’clock position of the right breast.

![Image](https://example.com/image2.png)

**FIGURE 3:** Atypical tumor cells, as shown by the arrow.

| Laboratory | Value  |
|------------|--------|
| Na         | 145 mmol/L |
| Test        | Value  |
|------------|--------|
| K          | 3.6 mmol/L |
| Cl         | 111 mmol/L  |
| CO₂        | 25 mmol/L   |
| BUN        | 15 mg/dL    |
| Cr         | 0.8 mg/dL   |
| Total Bili | 1.0 mg/dL   |
| Direct Bili| 0.8 mg/dL   |
| AST        | 87 U/L      |
| ALT        | 16 U/L      |
| Alb        | 2.7 g/dL    |
| Alk Phos   | 181 U/L     |
| Total Pro  | 7.7 g/dL    |
| Lactate    | 1.6 mmol/L  |
| Haptoglobin| 12.0 mg/dL  |
| WBC        | 11.4 K/cmm  |
| Hb         | 7.7 g/dL    |
| Hct        | 25.0%       |
| Plt        | 140 K/cmm   |
| MCV        | 91 fL       |
| MCH        | 27 pg       |
| MCHC       | 29.9 g/dL   |
| RDW        | 21.7%       |
| Auto neutro| 58.6%       |
| Auto lymph | 24.5%       |
| Auto mono  | 16.4%       |
| Auto baso  | 0.5%        |
| Auto eos   | 0.0%        |
| Retic count| 3.8%        |
| LDH        | 764 U/L     |

**TABLE 2: Labs after combination therapy.**
Discussion

Myelophthisic anemia, also known as myelophthisis, is a type of bone marrow failure that results from displacement of bone marrow precursor cells from a multitude of etiologies such as storage diseases, fungal infections, or metastatic neoplasms. Myelophthisic anemia is a rare occurrence as it is found in less than 10% of patients with metastatic malignancies such as lung cancer, breast cancer, prostate cancer, or sarcomas [4]. These malignancies spread and invade the bone marrow with space-occupying lesions, replacing the hematopoietic stem cells in the marrow and ultimately resulting in pancytopenia and extramedullary hematopoiesis. These lesions can be identified by a peripheral blood smear demonstrating a leukoerythroblastic picture with immature and abnormal RBCs in the form of schistocytes with myeloid precursors [2, 4].

Due to discovery in the advanced stages of the malignancy, myelophthisic anemia is thought to be resistant to treatment and considered as a poor prognostic sign [3-4]. Previously held beliefs that some cases of metastatic breast cancer had undergone remission with manipulation of hormones led to androgen administration, adrenalectomy, hypophysectomy, and even castration. Unfortunately, these radical procedures were only found to provide temporary relief [5]. With the advancement of medical therapy, current treatment for myelophthisic anemia is by directly treating the primary cancer. Treating this patient’s ER-positive Stage IV lobular breast carcinoma with letrozole and palbociclib was found to initially improve the patient’s symptoms but there was no mortality benefit and the patient passed away after two months of chemotherapy. No prior studies have suggested chemotherapy regimen amelioration in both morbidity and mortality and the recommended duration and prognosis of the treatment is yet to be determined [5].

This patient’s distinct presentation was highly indicative of TTP on initial evaluation. Unable to obtain history from the patient and relying solely on papers received from the patient’s nursing home resulted in reflexive decision-making leading to the patient undergo superfluous sessions of plasmapheresis. A more careful approach is required to rule out all other possible etiologies of this patient’s symptoms and laboratory findings and, thereafter, consider TTP as a diagnosis of exclusion.

Conclusions

Myelophthisic anemia is not an obvious diagnosis and it is affirmed through laboratory findings, peripheral blood smear, and bone marrow biopsy. Treatment and prognosis of myelophthisic anemia is variable as it is based upon secondary management of the malignancy.

Additional Information

Disclosures

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