Pancytopenia and Isolated Bone Marrow Recurrence in a Case of Previously Resected Gastric Carcinoma: A Rare Finding

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Abstract Recurrences in resected cases of gastric carcinomas are well known. However isolated involvement of bone marrow is a rare presentation. We present a previously treated case of gastric carcinoma-signet-ring cell type who had a progressive shortness of breath since 1 month. A hemogram done at this occasion showed pancytopenia and leucoerythroblastic picture. Bone marrow examination revealed infiltration by signet-ring cells. All such patients who presents with unexplained pancytopenia should prompt us to suspect a bone marrow recurrence.

Keywords Bone marrow · Gastric carcinoma · Pancytopenia · Recurrence · Signet-ring cells

Introduction

The incidence of gastric cancer in India is low compared to developed countries, though there are certain geographical areas (Southern part and Northeastern states of country) where the incidence is comparable to high-incidence areas of world [1]. For patients with gastric carcinoma, the most frequent site of recurrence is the abdominal cavity and recurrence usually occurs within 5 years of surgery [2]. Recurrence limited only to bone marrow is rare and only few reported case are available in the literature [3–5]. The

prognosis of gastric cancer with bone marrow metastases is poor because of a rapidly deteriorating clinical course that is often refractory to conventional treatment [6]. Here we present a case of post resected gastric carcinoma who presents with shortness of breath and pancytopenia. The marrow examination subsequently showed diffuse carcinomatosis. The case is reported due to its unusual way of presentation and recurrence.

Case Report

A 62 year-old-male patient was on a routine follow up in radiotherapy department, presented with a progressive shortness of breath and easy fatigability since 1 month duration. Approximately 2 years and 3 months earlier, the patient was diagnosed as carcinoma stomach, in a private hospital for which a distal gastrectomy and gastro-jejunostomy was done. The histopathological evaluation of the resected specimen showed signet-ring carcinoma with metastatic deposits in the mesenteric lymph nodes. After this the patient had received six cycles of chemotherapy using daunorubicin, cisplatin, 5-fluorouracil (DCF) regimen followed by 8 Gy radiotherapy.

Now the routine hemogram revealed pancytopenia and comprises of Hemoglobin (Hb)-6.3 gm/dl, total leucocyte count (TLC)- $3.59 \times 10^9/l$ and Platelet count- $36 \times 10^9/l$. The reticulocyte count was 0.15 %. The differential count showed shift to left (myelocytes-8 %; metamyelocytes 2 % and 4 % nucleated red blood cells). The peripheral blood film showed mild anisopoikilocytosis along with few tear drop cells. Coagulogram was within normal limits. The biochemical parameters were also abnormal, serum lactate dehydrogenase (LDH) levels was increased to 456.0U/l (Normal: <248 U/l) and serum alkaline phosphatase was

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Fig. 1 Bone marrow aspirate smear shows clusters of atypical cells with eccentrically pushed hyperchromatic nuclei and abundant basophilic cytoplasm (MGG-Giemsa stain $\times 1,000$). (Color figure online)

raised to 187 U/l (Normal: 40–129 U/l). CA 19.9 levels were also raised to 186.87 U/ml (Normal: <37 U/ml). Due to presence of pancytopenia in the hemogram a bone marrow examination was planned to rule out any secondary myelodysplastic syndrome related to chemo-radiation.

The bone marrow aspirate was normocellular for age. A few scattered as well as clusters of atypical cells showing eccentrically pushed hyperchromatic nuclei with abundant basophilic cytoplasm were identified on bone marrow aspirate smears (Fig. 1). Bilateral trephine biopsies showed complete replacement of marrow spaces by tumor cells with signet ring morphology “floating” in pools of mucin (Fig. 2a). Alcian blue stain to demonstrate intracellular and extracellular mucin was positive (Fig. 2b). The reticulin stain was performed and grade 1–2+ fibrosis (European myelofibrosis network grading system [EUMNET]) was noted. There was no significant dysplasia in any of the hematopoietic lineage to suggest the possibility of myelodysplastic syndrome. No radiotherapy/chemotherapy induced changes were appreciated in any of the

hematopoietic lineages. Hence the diagnosis of carcinoma-tosis of bone marrow was given.

Following this the patient was started on chemotherapy regimen in the form of oxaliplatin, capecitabine and eltrombopag (TPO-receptor agonist) and is doing well.

Discussion

Gastric carcinomas recurrences are encountered usually within 5 years of surgery [6]. Commonly involved sites are liver, lung, peritoneum, adrenals, ovaries and skin. Bone metastases are rare in patients with gastric cancer, being observed in fewer than 2 % of patients after surgical resection [7]. Isolated recurrence in bone marrow is a very rare finding and not commonly reported [3–5].

Gastric cancer cases with bone marrow involvement have very poor prognosis with a survival period ranging from 1.5 to 4 months [8, 9]. Prognostic factors for poor survival are low performance status, multiple bone metastases, and elevated tumor markers. Patients with fewer than two of those adverse prognostic factors benefited from palliative chemotherapy [8]. The present case have isolated bone marrow metastasis and raised CA 19-9. The patient is on cytotoxic chemotherapy and is under follow up.

In patient with bone marrow recurrence, the common laboratory findings at the time of presentation are anemia, thrombocytopenia, elevated alkaline phosphatase and lactate dehydrogenase. Some of the patient might present with autoimmune hemolytic anemia or disseminated intravascular coagulation [10–12]. In this case the investigations showed pancytopenia with normal coagulogram and raised alkaline phosphatase level. Pancytopenia can be explained by the replacement of normal hematopoietic elements in the bone marrow by tumor cells.

Most of the cases with marrow recurrences show the histopathology of signet ring cell carcinoma or poorly differentiated adenocarcinoma [13]. To diagnose signet

Fig. 2 Trephine biopsy shows complete replacement of marrow spaces by signet-ring cells “floating” in pools of mucin (H&E $\times 400$, a). Alcian blue stain demonstrates the presence of intracellular and extracellular mucin which is blue in color (Alcian blue stain $\times 400$, b). (Color figure online)

ring cell carcinoma the morphological findings in the form of mucin pool, mucin filled cells with the appearance of signet ring are sufficient. Cytochemical stains like Alcian blue may be needed to characterize the nature of mucin. For undifferentiated carcinoma immunohistochemical stains might need. In the present case the morphology of signet ring cell carcinoma was observed which was further confirmed by cytochemical stain. It is important to note that Signet ring cells can also be seen in other gastrointestinal carcinomas; in breast, lung, prostate, and bladder cancers and hence these possibilities needs to be excluded if there is any miscorrelation with the prior diagnosis.

In conclusion, we present a case of isolated bone marrow recurrence in a case of post resected gastric carcinoma. The patient had pancytopenia along with raised alkaline phosphatase levels. As bone marrow recurrence is a rare finding and complete hemogram along with serum alkaline phosphatase can provide a clue to this process. If these are deranged than bone marrow examination is necessary. These investigations might help the oncologist to modify the treatment protocol of the patient for a better survival and outcome.

Conflict of interest The authors have no conflicts of interest to declare.

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