Metastatic adenocarcinoma presenting as microangiopathic hemolytic anemia (MAHA) and leukoe-rythroblastic blood picture is rare. We report three patients who presented with MAHA as the initial symptom of metastatic signet ring cell gastric adenocarcinoma. One patient had past history of gastric ulcer. In all these patients the initial diagnosis was based on peripheral blood smear followed by bone marrow biopsy; upper GI endoscopy showed presence of gastric ulcers with focally scattered neoplastic signet ring cells on histopathology. All patients died within a week of diagnosis. [Indian J Gastroenterol 2007;26:185-186]

Diffuse infiltration of bone marrow from gastric cancer metastasis is uncommon, often presents late and has a rapid clinical course. The outcome is grave due to hematological disorders such as microangiopathic hemolytic anemia (MAHA) and disseminated intravascular coagulation (DIC).^1^

Case 1: A 52-year-old woman presented with shortness of breath and progressive pallor since one and a half months. Endoscopy performed for abdominal pain one and a half years ago showed a gastric ulcer, which on biopsy showed focal intestinal metaplasia and Helicobacter pylori infection. Pallor was the only positive finding on examination.

**Investigations:** hemoglobin 7.2 g/dL, hematocrit 23.7%, white cell count 12,200/mm³, platelets 62,000/mm³. Peripheral film was leukoeorthythroblastic with the presence of spheroocytes. Coombs test was negative. All three samples of stool for occult blood were positive. Bone marrow biopsy showed non-hemopoetic clumps (Fig 1); trephine biopsy showed extensive replacement of marrow by sheets of tumor cells with hyperchromatic and pleomorphic nuclei with abundant cytoplasm (Fig 2a). Immuno-histochemistry showed positivity for pan-cytokeratin AE1/AE3 and cytokeratin 7, consistent with metastatic adenocarcinoma, most likely from the stomach (Fig 2b). Upper GI endoscopy showed a large, irregular ulcer with heaped up margins which on bi-
 biopsy revealed scattered neoplastic cells with signet ring appearance, consistent with poorly-differentiated infiltrating adenocarcinoma.

Case 2: A 28-year-old man presented with fever and shortness of breath since one month. His past history was insignificant. On examination, the only positive finding was pallor.

**Investigations:** Hemoglobin: 7.5 g/dL, hematocrit 20.5%, corrected white blood cell count 17,200/mm³, (neutrophils 80%), platelets 77,000/mm³. Peripheral film showed anisocytosis, dimorphic blood picture, polychromasia, nucleolated red blood cells, fragmented red blood cells, spherocytes and leukoerythroblastic blood picture along with neutrophilia, consistent with MAHA. INR was 1.52, liver function tests were deranged (total bilirubin 2.0 mg/dL, direct 0.8 mg/dL), LDH 7019 IU/L (normal 100-190), D-dimer 3.69 FEU (normal 0.5) and direct Coombs test negative. Chest X-ray showed bilateral infiltrates with lytic lesions in the iliac spine. Bone marrow biopsy showed metastatic adenocarcinoma, with gastrointestinal tract as the most likely primary site. Endoscopy showed multiple small areas of erythematous gastric mucosa along with one to two foci of non-healing ulcers which were biopsied and the diagnosis was consistent with signet cell gastric carcinoma.

Case 3: A 21-year-old man presented with weakness, weight loss and bone pains since one and a half months. Bone pains were accompanied by severe backache, which led to difficulty in walking. His past history was insignificant. On examination he was pale.

**Investigations:** Hemoglobin: 6.1 g/dL, hematocrit 19%, white blood cell count 9,800/mm³, (neutrophils 6400), platelets 342,000/mm³. Peripheral blood film showed anisocytosis, polychromasia, Rouleaux formation and nucleolated red blood cells along with leukoerythroblastic blood picture. Bone marrow biopsy showed diffuse infiltration by sheets and clusters of large neoplastic cells with abundant clear to pale eosinophilic cytoplasm. The cells also showed positivity for acid mucin on special stain. These findings were consistent with metastatic adenocarcinoma. Endoscopy showed presence of focal erosions with small hemorrhagic areas. Gastric mucosal biopsy revealed signet ring cell carcinoma.

All the patients died within one week after diagnosis.

**Discussion**

Microangiopathic hemolytic anemia can be the first manifestation of metastatic carcinoma. In this series, all metastases were of gastric origin with morphology of signet ring type adenocarcinoma. All our patients presented with Coombs-negative hemolytic anemia and fragmented red blood cells on peripheral smear. This pattern of initial presentation correlates with MAHA as a rare paraneoplastic syndrome in patients with metastasized signet cell carcinoma. Among the hematological complications associated with carcinoma, a leukoerythroblastic blood picture along with MAHA is rarely reported together.

Two of the three patients were very young while the third was a middle-aged woman, all with poorly differentiated (signet ring type) adenocarcinoma of stomach. This type of gastric cancer, which is more aggressive than the usual intestinal type, is highly prevalent in this part of the world. Unfortunately all our patients quickly succumbed to the disease.

**References**


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