Gastric Granulocytic Sarcoma as a Localized Blastic Crisis in a Patient With Polycythemia Vera

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Granulocytic sarcoma is a tumor of immature granulocytic cell that can be found at any organ outside the bone marrow. It has been rarely reported and most cases are associated with leukemia. This report presented a case of granulocytic sarcoma originating from the stomach of a polycythemia vera patient. He was a 66-year-old Thai patient who passed melena for many times in 2 days. Two years prior this presentation, he had been diagnosed as having polycythemia vera and treated with occasional phlebotomy and hydroxyurea. The gastroscopy showed multiple sessile polyps at gastric body of which the pathology showed diffuse infiltration by myeloblasts; the tumor cells diffusely marked with LCA, CD34, CD117, sparsely marked with MPO, compatible with blastic phase of myeloproliferative neoplasm. The diagnosis of gastric granulocytic sarcoma or localized blastic transformation at the stomach with underlying polycythemia vera was concluded.

Keywords: Gastric granulocytic sarcoma, Polycythemia vera, Upper gastrointestinal bleeding

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Introduction

Granulocytic sarcoma (or myloid sarcoma or chloroma) is a tumor of immature granulocytic cell outside the bone marrow. It can occur as an isolated entity or de novo if the bone marrow biopsy shows no hematologic malignancy and preceding, coinciding or following the myeloproliferative neoplasm especially chronic myeloid leukemia (CML), acute myeloid leukemia or myelodysplastic syndrome. It is considered a very rare disease so far. Half of cases are asymptomatic and half have the clinical presentations relating the tumor mass effect and/or dysfunction of the organs involved. The tumor mass may be single or multiple which cannot be distinguished from lymphoma, hence the immunohistochemistry is necessary and the myeloid sarcoma will express the markers that are specific for myeloid disease such as CD33, myeloperoxidase, CD34 and CD117. Others may include CD99, CD68/PG-M1, lysozyme, terminal deoxynucleotidyl transferase, CD56, CD61, CD30, glycoporin A, and CD4. Some may have chromosomal abnormalities including mixed lineage leukemia (MLL) rearrangement, t(8;21), monosomy 7, trisomy 8, trisomy 11, trisomy 4, inversion (16), monosomy 16, 16q deletion, 5q deletion, and 20q deletion. The locations where tumors have been reported to be include the orbital cavity, lymph node, tonsil, small intestine, bone, skin, soft tissue, testis, lymph node, mediastinum, salivary gland, paranasal sinuses, brain, lung, pelvic organs, and breast.

Herein we reported a case of granulocytic sarcoma originating from the stomach which has been hardly found so far.

Case Report

A 66-year-old Thai man was admitted because of passing melena without abdominal pain for many times in 2 days. Two years prior this admission, he had chronic abdominal discomfort, fullness and had been diagnosed as having polycythemia vera based on the combination of hemoglobin (Hb) concentration of 188 ± 4 g/L, serum erythropoietin of 1.4 IU/L, pancytopenia in the bone marrow and negative JAK-2V617F mutation and treated with oral omeprazole, hydroxyurea 500 mg a day and occasional phlebotomy since then. During regular follow-up, his Hb concentration was still high due to inadequate phlebotomy, and abdominal discomfort was not well responsive to medication. His current physical examination revealed no pallor, mild hepatomegaly, and huge splenomegaly just below the left iliac crest. His current diagnosis was upper gastrointestinal bleeding.

The current blood tests were performed: Hb 196 g/L; hematocrit (Hct) 0.64 proportion of 1.0; mean corpuscular volume (MCV) 104.1 fL; mean corpuscular hemoglobin (MCH) 31.9 pg/cell; mean corpuscular hemoglobin concentration (MCHC) 306 g/L; white blood cell (WBC) 15.4 x 10^9/L; neutrophil 55%, lymphocyte 45%; platelet 228 x 10^9/L; serum ferritin 537.3 μg/L; serum iron 9.49 μmol/L; total iron binding capacity (TIBC) 20.59 μmol/L; lactate dehydrogenase (LDH) 18.99 μkat/L; uric acid 547.22 μmol/L; creatinine 132.63 μmol/L; albumin 32 g/L; globulin 40 g/L; aspartate aminotransferase (AST) 31 U/L; alanine aminotransferase (ALT) 18 U/L; alkaline phosphatase (ALP) 84 U/L; and oxygen saturation 98%. Hb analysis using the high performance liquid chromatography (HPLC) method was determined: A2A, Hb A2 2.9%, and Hb F 0%. Hepatitis B surface antigen (HBsAg), hepatitis C antibody (anti-HCV), and HIV antigen/antibody were all negative.

The chromosome analysis from the peripheral blood showed: 46,XY, der(1)t(1;15)(q21;q15) ins(1;?)(q21;?) dup(1)(q21q23) del(4) (q21q25) der(15)(t:15)[38]/46,XY [1]=97.4% / 2.6%. JAK-2V617F mutation and BCR-ABL translocation were negative.

The computerized tomography (CT) of the abdomen showed huge splenomegaly 2 fingerbreadth below left iliac crest and mild hepatomegaly. The chest film was unremarkable study.

The esophagogastroduodenoscopy showed multiple sessile polyps at greater curvature of gastric body (Figure 1).

The pathology of the stomach lesion found: diffusely infiltrated by myeloblasts (Figure 2), clinically and histomorphologically compatible with blastic phase of myeloproliferative neoplasm, tumor cells diffusely marked
with LCA, CD34, CD117, sparsely marked with MPO, did not mark with CD3, CD20, TdT, and cyclin D1 immunostaining (Figure 3).

The splenectomy was performed because of chronic abdominal discomfort due to huge splenomegaly.

The spleen was 2200 g, with diffuse extramedullary hematopoiesis with marked myeloid hyperplasia, and some suspected dysplastic megakaryopoiesis favoring CML, MPO staining highlighted these leukemic cells, CD34 staining showed no CD34 + blasts, CD20 staining showed residual white pulp, glycophorin C staining showed red blood cell (RBC), and glycoprotein (GP) IIIa staining showed occasional scattered megakaryocyte.

He was diagnosed as having localized blastic transformation at the stomach with an underlying polycythemia vera. Few days after splenectomy under general anesthesia, he succumbed from ventilator-associated pneumonia.

Discussion

Polycythemia vera usually runs chronic course without symptom. One of its late complications is blastic or leukemic transformation (LT) which is defined as blasts in peripheral blood or in bone marrow more than 20%. Its rate at 20 years is estimated at less than 10%, but for granulocytic sarcoma transformation, it has been very unusual. So far it was found at the malleolus and the retroperitoneum. Older age was confirmed as the main independent risk factor (hazard ratio [HR], 4.30; 95% confidence interval [CI], 1.2 - 15.9; \( P = .02 \)) for progression to acute myeloid leukemia or myelodysplastic syndrome.

Our case had no peripheral blast therefore the systemic blastic transformation was less likely whereas he had no leukoerythroblastic blood picture, WBC less than \( 25 \times 10^9/L \), no anemia, no thrombocytopenia, and no systemic symptom, hence secondary myelofibrosis after polycythemia vera was less likely, neither although extramedullary hematopoiesis was pathologically shown in the resected spleen.
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Based on large multicenter polycythemia vera patient data, rates of LT in polycythemia vera are estimated at 2.3% at 10 years, 5.5% at 15 years, and remain less than 10% at 20 years. Theoretically, patients with myeloproliferative disorder (MPN) have propensity to develop acid dependent peptic ulcer because they have more basophil that has high histamine content in granules. Histamine stimulates acid secretion in the stomach. In fact, they are found to have more gastritis, Helicobacter pylori infection and gastrointestinal bleeding. Eight from 30 patients with MPN have upper gastrointestinal bleeding as compared to 0 from 93 patients with dyspepsia without MPN or 14 from 108 patients with MPN have overt gastrointestinal bleeding. Besides benign lesions, the incidence of gastric cancer is also increased in comparison with the population (standardized incidence ratios [SIR], 2.76; 95% CI, 1.33 - 5.08). Therefore, endoscopy is essential for differentiating the cause of upper gastrointestinal bleeding in cases of MPN.

Among 32 cases with granulocytic sarcoma of various organs, 27 had associated diseases that consisted of 13 with acute myeloid leukemia, 11 with chronic myeloid leukemia, 2 with myelodysplastic syndrome and 1 with acute lymphoblastic leukemia, no one had polycythemia vera like our patient. Focus on granulocytic sarcoma of the stomach it is not only the rare complication of polycythemia vera but also it has never been found before. Likewise, it is the very rare pathology of the gastric cancer.

Conclusions

A 66-year-old Thai man presented with gastrointestinal bleeding whereas his underlying disease was polycythemia vera. The pathology of the stomach was blastic infiltration. Without blast in the peripheral blood, he was diagnosed as having local blastic transformation at the stomach that had never been mentioned before.

References

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มะเร็ง Granulocytic Sarcoma ที่กระเพาะอาหารในฐานะที่เป็นการกลายร่างเป็นมะเร็งเม็ดเลือดขาวชนิดยับยั้งพื้นผิวที่ในผู้ป่วยมะเร็งเม็ดเลือดแดงเรื้อรัง

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Granulocytic sarcoma เป็นเนื้องอกของเซลล์ชนิด Granulocytic เกิดที่อวัยวะใดก็ได้นอกไขกระดูก พบได้โดยส่วนมากร่วมกับมะเร็งเม็ดเลือดขาว รายงานนี้นำเสนอ Granulocytic sarcoma พบที่กระเพาะอาหาร ในผู้ป่วยมะเร็งเม็ดเลือดแดงเรื้อรัง (Polycythemia vera) ซึ่งเป็นชายไทย อายุ 66 ปี มีอาการถ่ายด่าเป็นเวลา 2 วัน โดยมี 2 ปีก่อนหน้านี้ได้รับการวินิจฉัยว่าเป็นมะเร็งเม็ดเลือดแดงเรื้อรัง และได้รับการรักษาด้วยยาเจาะเลือดทิ้งเป็นประจำ และรับยา Hydroxyurea ตลอดจนมีอาการติดตามเนื้องอกดังกล่าวยุงที่กระเพาะอาหารจำนวนมาก ผลตรวจทางนวัตกรรมพบตัวอย่างของมีเลือดขาวพบกระจายกระจายในเนื้อเยื่อกระเพาะอาหาร ย้อมด้วย LCA, CD34, CD117, และติด MPO เทียบเท่ากับระยะ Blastic phase ของมะเร็งเม็ดเลือดแดงเรื้อรัง การวินิจฉัยโดยสรุปได้ Granulocytic sarcoma ที่กระเพาะอาหาร หรือการกลายร่างเป็นมะเร็งเม็ดเลือดขาวชนิดยับยั้งพื้นผิวที่ในผู้ป่วยมะเร็งเม็ดเลือดแดงเรื้อรัง แต่ยังไม่เคยมีการรายงานมาก่อนในผู้ป่วยมะเร็งเม็ดเลือดแดงเรื้อรัง

คำสำคัญ: มะเร็ง Granulocytic sarcoma ที่กระเพาะอาหาร มะเร็งเม็ดเลือดแดงเรื้อรัง เลือดออกทางเดินอาหารส่วนบน

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