RMJ Ramathibodi Medical Journal

Rama Med J | Case Report

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

Likhasit Sanglutong[1], Somchai Insiripong[2]

[1] Department of Medicine, Bangkok Hospital Muangraj, Ratchaburi, Thailand

[2] Department of Medicine, Maharat Nakhon Ratchasima Hospital, Nakhon Ratchasima, Thailand

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

Rama Med J: doi:10.33165/rmj.2022.45.2.253353

Received: September 2, 2021 **Revised:** March 14, 2022 **Accepted:** June 13, 2022

Corresponding Author:
Likhasit Sanglutong
Department of Medicine,
Bangkok Hospital Muangraj,
59/3 Phetchakasem Road,
Na Muang, Muang Ratchaburi,
Ratchaburi 70000, Thailand.
Telephone: +668 4911 5775
E-mail: lickhasit1986@gmail.com

Introduction

Granulocytic sarcoma (or myeloid 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.[1, 2] It is considered a very rare disease so far. Half of cases are asymptomatic[3] 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.[4] Others may include CD99, CD68/PG-M1, lysozyme, terminal deoxynucleotidyl transferase, CD56, CD61, CD30, glycophorin 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.[5] The locations where tumors have been reported to be include the orbital cavity, lymph node, tonsil,[6] small intestine,[7] bone,[8] skin, soft tissue, testis, lymph node, mediastinum,[9] salivary gland, paranasal sinuses, brain, lung, pelvic organs,[3] and breast.[10]

Herein we reported a case of granulocytic sarcoma originating from the stomach which has been hardly found so far.[3, 11-14]

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, panmyelosis 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 present 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 × 10^9/L; neutrophil 55%, lymphocyte 45%; platelet 228 × 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: A_2A, Hb A_2 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(1:15)[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%.[15] Its rate at 20 years is estimated at less than 10%,[16] but for granulocytic sarcoma transformation, it has been very unusual. So far it was found at the malleolus[17] and the retroperitoneum.[18] 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.[19]

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 × 10^9/L, no anemia, no thrombocytopenia, and no systemic symptom, hence secondary myelofibrosis after polycythemia vera was less likely, neither[20] although extramedullary hematopoiesis was pathologically shown in the resected spleen.[21]

Figure 1. The Esophagogastroduodenoscopy Showed Multiple Sessile Polyps at the Gastric Body

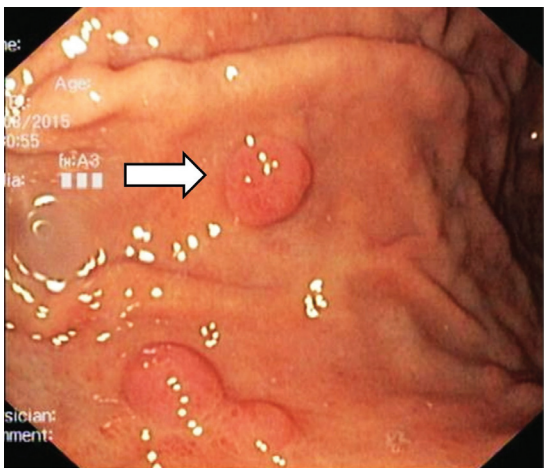


Figure 2. Stomach Was Diffused Infiltrated by Myeloblasts (x400)

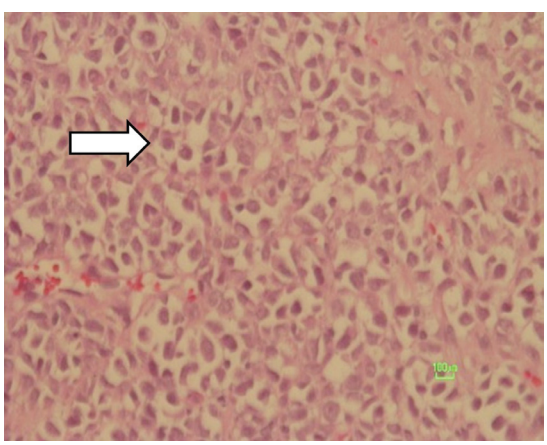
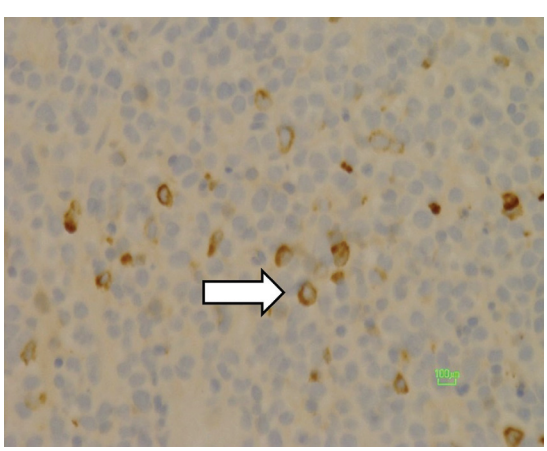


Figure 3. Small Number of Abnormal Cells Mark With MPO Immunostaining (x400)



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.[22]

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.[23] Eight from 30 patients with MPN have upper gastrointestinal bleeding as compared to 0 from 93 patients with dyspepsia without MPN[23] or 14 from 108 patients with MPN have overt gastrointestinal bleeding.[24] 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).[25] 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,[2] 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.[26]

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

1. Yilmaz AF, Saydam G, Sahin F, Baran Y. Granulocytic sarcoma: a systematic review. *Am J Blood Res*. 2013;3(4):265-270.
2. Paydas S, Zorludemir S, Ergin M. Granulocytic sarcoma: 32 cases and review of the literature. *Leuk Lymphoma*. 2006;47(12): 2527-2541. doi:10.1080/10428190600967196
3. Guermazi A, Feger C, Rousselot P, et al. Granulocytic sarcoma (chloroma): imaging findings in adults and children. *AJR Am J Roentgenol.* 2002; 178(2):319-325. doi:10.2214/ajr.178.2.1780319
4. Klco JM, Welch JS, Nguyen TT, et al. State of the art in myeloid sarcoma. *Int J Lab Hematol.* 2011; 33(6):555-565. doi:10.1111/j.1751-553X.2011.01361.x
5. Magdy M, Abdel Karim N, Eldessouki I, Gaber O, Rahouma M, Ghareeb M. Myeloid sarcoma. *Oncol Res Treat.* 2019;42(4): 224-229. doi:10.1159/000497210
6. Noh BW, Park SW, Chun JE, Kim JH, Kim HJ, Lim MK. Granulocytic sarcoma in the head and neck: CT and MR imaging findings. *Clin Exp Otorhinolaryngol.* 2009;2(2): 66-71. doi:10.3342/ceo.2009.2.2.66
7. He T, Guo Y, Wang C, et al. A primary myeloid sarcoma involving the small intestine and mesentery: case report and literature review. *Int J Clin Exp Pathol.* 2018;11(8):4158-4162.
8. Goh BS, Tang CL, Tan GC. Myeloid sarcoma of temporal bone: a rare manifestation of relapse acute myeloid leukemia. *Indian J Otolaryngol Head Neck Surg.* 2019;71(Suppl 2): 1023-1026. doi:10.1007/s12070-015-0930-8
9. Jelić-Puskarić B, Kardum-Skelin I, Sustercić D, et al. Izolirani mijeloidni sarkom medijastinuma [Isolated myeloid sarcoma involving the mediastinum]. *Acta Med Croatica.* 2011;65(Suppl 1):133-138.
10. Jelić-Puskarić B, Ostojić-Kolonić S, Planinc-Peraica A, Obad-Kovacević D, Kardum-

Skelin I, Jaksić B. Myeloid sarcoma involving the breast. *Coll Antropol.* 2010;34(2):641-644.

11. Koehler M. Granulocytic sarcoma of the stomach. *Gastrointest Endosc.* 1998;48(2):190. doi:10.1016/s0016-5107(98)70162-2
12. Sekaran A, Darisetty S, Lakhtakia S, Ramchandani M, Reddy DN. Granulocytic sarcoma of the stomach presenting as dysphagia during pregnancy. *Case Rep Gastrointest Med*. 2011;2011:627549. doi:10.1155/2011/627549
13. Huang XL, Tao J, Li JZ, et al. Gastric myeloid sarcoma without acute myeloblastic leukemia. *World J Gastroenterol.* 2015;21(7):2242-2248. doi:10.3748/wjg.v21.i7.2242
14. Gadage V, Zutshi G, Menon S, Shet T, Gupta S. Gastric myeloid sarcoma--a report of two cases addressing diagnostic issues. *Indian J Pathol Microbiol.* 2011;54(4):832-835. doi:10.4103/0377-4929.91544
15. Mesa RA, Verstovsek S, Cervantes F, et al. Primary myelofibrosis (PMF), post polycythemia vera myelofibrosis (post-PV MF), post essential thrombocythemia myelofibrosis (post-ET MF), blast phase PMF (PMF-BP): consensus on terminology by the international working group for myelofibrosis research and treatment (IWG-MRT). *Leuk Res.* 2007;31(6):737-740. doi:10.1016/j.leukres.2006.12.002
16. Tefferi A, Barbui T. Polycythemia vera and essential thrombocythemia: 2017 update on diagnosis, risk-stratification, and management. *Am J Hematol*. 2017;92(1):94-108. doi:10.1002/ajh.24607
17. Nafil H, Tazi I, Mahmal L. Myeloid sarcoma developing in prexisting hydroxyurea-induced leg ulcer in a polycythemia vera patient. *Case Rep Med.* 2013;2013:497593. doi:10.1155/2013/497593
18. MacCallum PK, Newbould MJ, Sambrook PS, Burton IE. Extramedullary haemopoietic tumours complicating polycythaemia vera. *J Clin Pathol.* 1988;41(6):609-614. doi:10.1136/jcp.41.6.609
19. Finazzi G, Caruso V, Marchioli R, et al. Acute leukemia in polycythemia vera: an analysis of 1638 patients enrolled in a prospective observational study. *Blood*. 2005;105(7):2664-2670. doi:10.1182/blood-2004-09-3426
20. Masarova L, Bose P, Daver N, et al. Patients with post-essential thrombocythemia and post-polycythemia vera differ from patients with primary myelofibrosis. *Leuk Res.* 2017;59:110-116. doi:10.1016/j.leukres.2017.06.001
21. Singh I, Mikita G, Green D, Risquez C, Sanders A. Pulmonary extra-medullary hematopoiesis and pulmonary hypertension from underlying polycythemia vera: a case series. *Pulm Circ*. 2017;7(1):261-267. doi:10.1177/2045893217702064
22. Cerquozzi S, Tefferi A. Blast transformation and fibrotic progression in polycythemia vera and essential thrombocythemia: a literature review of incidence and risk factors. *Blood Cancer J.* 2015;5(11):e366. doi:10.1038/bcj.2015.95
23. Karaoglu AO, Kadikoylu G, Yukselen V, Yasa MH, Bolaman Z. Gastrointestinal lesions and helicobacter pylori in patients with myeloproliferative disorders. *Saudi Med J.* 2004;25(12):1913-1916.
24. Soylu AR, Buyukasik Y, Cetiner D, et al. Overt gastrointestinal bleeding in haematologic neoplasms. *Dig Liver Dis.* 2005;37(12):917-922. doi:10.1016/j.dld.2005.07.017
25. Rebora P, Czene K, Antolini L, Gambacorti Passerini C, Reilly M, Valsecchi MG. Are chronic myeloid leukemia patients more at risk for second malignancies? a population-based study. *Am J Epidemiol*. 2010;172(9):1028-1033. doi:10.1093/aje/kwq262
26. Hu B, El Hajj N, Sittler S, Lammert N, Barnes R, Meloni-Ehrig A. Gastric cancer: classification, histology and application of molecular pathology. *J Gastrointest Oncol.* 2012;3(3):251-261. doi:10.3978/j.issn.2078-6891.2012.021

RMJ Ramathibodi Medical Journal

Rama Med J | Case Report

มะเร็ง Granulocytic Sarcoma ที่กระเพาะอาหารในฐานะที่เป็นการกลายร่างเป็นมะเร็งเม็ดเลือดขาวชนิดเฉียบพลันเฉพาะที่ในผู้ป่วยมะเร็งเม็ดเลือดแดงเรื้อรัง

ลิขสิทธิ์ แสงลู่ทอง[1], สมชาย อินทรศิริพงษ์[2]

[1] กลุ่มงานอายุรกรรม โรงพยาบาลกรุงเทพเมืองราช ราชบุรี ประเทศไทย

[2] กลุ่มงานอายุรกรรม โรงพยาบาลมหาราชนครราชสีมา นครราชสีมา ประเทศไทย

Granulocytic sarcoma เป็นเนื้องอกของเซลล์ชนิด Granulocytic เกิดที่อวัยวะใดก็ได้นอกไขกระดูก พบได้น้อยส่วนมากพบร่วมกับมะเร็งเม็ดเลือดขาว รายงานนี้นำเสนอโรค Granulocytic sarcoma พบที่กระเพาะอาหาร ในผู้ป่วยมะเร็งเม็ดเลือดแดงเรื้อรัง (Polycythemia vera) ซึ่งเป็นชายไทย อายุ 66 ปี มีอาการถ่ายดำเป็นเวลา 2 วัน โดยเมื่อ 2 ปีก่อนหน้านี้ได้รับการวินิจฉัยว่าเป็นมะเร็งเม็ดเลือดแดงเรื้อรัง และได้รับการรักษาด้วยการเจาะเลือดทิ้งเป็นครั้งคราว และรับประทานยา Hydroxyurea ผลส่องกล้องกระเพาะอาหารพบติ่งเนื้อขนาดเล็กที่กระเพาะอาหารจำนวนมาก ผลตรวจทางพยาธิวิทยาพบตัวอ่อนของเม็ดเลือดขาวแทรกกระจายในเนื้อเยื่อกระเพาะอาหาร ย้อมติดชัดเจนด้วย LCA, CD34, CD117, และติด MPO เล็กน้อย แทรกกระจายตัวอยู่ทั่วไป เข้าได้กับระยะ Blastic phase ของมะเร็งเม็ดเลือดเรื้อรัง การวินิจฉัยโดยสรุปคือ Granulocytic sarcoma ที่กระเพาะอาหาร หรือการกลายร่างเป็นมะเร็งเม็ดเลือดขาวชนิดเฉียบพลันที่กระเพาะอาหาร โดยมีเบื้องหลังเป็นมะเร็งเม็ดเลือดแดงเรื้อรัง Granulocytic sarcoma ที่กระเพาะอาหารมีโอกาสพบได้ยาก และยังไม่เคยมีการรายงานมาก่อนในผู้ป่วยมะเร็งเม็ดเลือดแดงเรื้อรัง

คำสำคัญ: มะเร็ง Granulocytic sarcoma ที่กระเพาะอาหาร มะเร็งเม็ดเลือดแดงเรื้อรัง เลือดออกทางเดินอาหารส่วนบน

Rama Med J: doi:10.33165/rmj.2022.45.2.253353

Received: September 2, 2021 **Revised:** March 14, 2022 **Accepted:** June 13, 2022

Corresponding Author:
ลิขสิทธิ์ แสงลู่ทอง
กลุ่มงานอายุรกรรม
โรงพยาบาลกรุงเทพเมืองราช
59/3 ถนนเพชรเกษม
ตำบลหน้าเมือง อำเภอเมือง
ราชบุรี 70000 ประเทศไทย
โทรศัพท์ +668 4911 5775
อีเมล lickhasit1986@gmail.com