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# Letters to the Editor

## Leukemoid reaction with metachronous tumors

*Key words: Leukemoid reaction. Hepatocellular carcinoma. Cecum carcinoma. Leukocytosis. Synchronous.*

*Dear Editor,*

Patients with malignant tumors may unusually have aberrant production of granulocyte colony-stimulating factor (G-CSF) or G-CSF like substances by tumor cells (1) causing leukocytosis. Here, we report a rare case of metachronous HCC and cecum carcinoma related leukemoid reaction and highlight leukocytosis could be an effective detector of early tumor recurrence.

### Case report

A 50-year-old female presented with a three-day history of watery diarrhea and frequently abdominal distension. She also complained the incomplete evacuation sensation following defecation. There were no changes in her appetite and body weight. In the medical history, she had diabetes mellitus but no gastrointestinal disease. Her vital signs revealed temperature of 36.8 °C, pulse of 84 /min and blood pressure of 127/76 mmHg. Physical examination showed one palpable mass over right lower quadrant abdominal region with mild tenderness. There is no remarkable finding on digital examination. The blood tests showed white blood count of 32 x $10^9$/L with 65% segmented neutrophils. Tumor markers, such as the α-fetoprotein (AFP) level, the carcinoembryonic antigen (CEA) level, and the carbohydrate antigen 19–9 (CA19-9) level, were within the normal range. Barium studies showed marked segmental luminal narrowing with mucosa destruction over the proximal ascending colon and cecum. Computed tomography (CT) of abdomen revealed one huge heterogeneous mass lesion over cecum. Colonoscopy disclosed a 5.5 cm submucosal mass in cecum with firm consistency, locating at 130cm from the anal verge and biopsy report showed hyperplastic polyp of the colon tissue. Therefore, the patient underwent right hemicolectomy and a huge submucosal tumor about 8 x 7 x 5.5-$cm^3$ in size over cecum with central necrosis was found at operation. The pathological findings revealed undifferentiated carcinoma located in the cecum from submucosal layer to pericolonic fat. The postoperative course was uneventfully and the WBC count gradually decreased to 20 × $10^9$/L postoperatively.

Two months after the surgery, Unfortunately, ultrasonography of abdomen showed hypoechoic target-like lesion about 6.9 x 5.3 cm at segment 7of liver with his leukocyte counts ranging from 15 to 52 x $10^9$/L. Computed tomography (CT) of abdomen revealed a well-defined tumor about 6.4 x 5.5 x 6 cm at segment 7 and 8 of liver with portal vein tumor thrombi. She underwent right lobectomy of liver. Pathology report showed poor differentiated hepatocellular carcinoma (HCC). The postoperative course was uneventfully and the WBC count gradually decreased to 12 x $10^9$/L postoperatively. At approximately three months after surgery, recurrences were detected in the segment 2 of liver with WBC count up to 24 x $10^9$/L. The patient underwent wedge resection of segment 2 of liver. The patient was discharged in a stable condition 5 days after surgery. Two months later, the WBC count gradually decreased to 5.4 x $10^9$/L. The diagnosis of leukemoid reaction was finally established after surgical resection of the tumor was followed by normalization of the leukocyte count (Fig. 1). However, the patient died of tumor recurrence and multiple metastases one year later.

### Discussion

Leukocytosis presents an inflammatory process and usually occurs in patients with current infection. Some tumors, however,

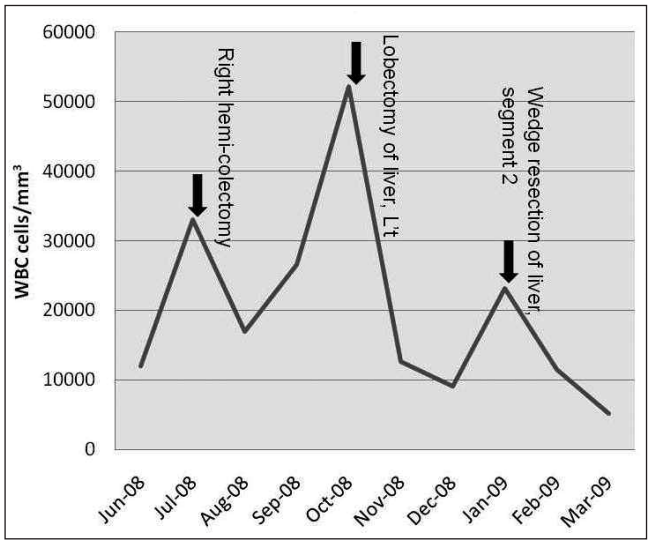


Fig. 1. Leukemoid reaction was established after surgical resection of the tumor was followed by normalization of the leukocyte count.

could unusually cause leukocytosis, as a paraneoplastic leukemoid reaction, which had been described in association with lung, gastrointestinal, genitourinary, gynecology and head and neck cancers in the literature (2). Paraneoplastic leukemoid reactions are attributed to the auto-production of granulocyte colony-stimulating factor (G-CSF), a hematopoietic growth factor that stimulates the proliferation and maturation of precursor cells in the bone marrow into fully differentiated neutrophils (3).

The mechanism by which certain HCCs produce G-CSF has not been clarified, but the differentiation state of HCC cells may play an important role in the expression of G-CSF. Some studies showed production of GM-CSF was demonstrated in poorly differentiated HCC at more immature stage (4). Moreover, paraneoplastic granulocytosis is often associated with rapid tumor growth and poor clinical prognosis and resolves with the treatment of underlying cancer (5).

To our knowledge, this is the first case of metachronous HCC and cecum carcinoma with leukemoid reaction reported in the literature. Paraneoplastic granulocytosis resolves each time after radical resection were performed. Therefore, as patients presented with unknown etiology of leukocytosis, we physician should be always keep in mind with the possibility of tumor origin especially when infection is not likely.

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## References

1. Nagata S, Tsuchiya M, Asano S, Kaziro Y, Yamazaki T, Yamamoto O, et al. Molecular cloning and expression of of cDNA for human granulocyte colony stimulating factor. Nature 1987;319:415-8.
2 Robinson WA. Granulocytosis neoplasia. Ann NY Acad Sci 1974; 230:212.
3. Lieschke GJ, Burgess AW. Granulocyte-colony stimulating factor and granulocyte-macrophage colony stimulating factor. N Engl J Med 1992;327:28-35, 99-106.
4. Wang SY, Chen LY, Tsai TF, Su TS, Choo KB, Ho CK. Constitutive production of colony-stimulating factors by human hepatoma cell lines: possible correlation with cell differentiation. Exp Hematol 1996;24:437-44.
5. Tachibana M, Miyakawa A, Tazaki H, Nakamura K, Kubo A, Hata J, et al. Autocrine growth of transitional cell carcinoma of the bladder induced by granulocyte-colony stimulating factor. Cancer Res 1995; 55:3438-43.