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CASE REPORT

Gastric signet-ring cell carcinoma with paraneoplastic eosinophilia: A case report and literature review

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Abstract

We report the case of a 40-year-old female Chinese patient with gastric signet-ring cell carcinoma that was first diagnosed because of paraneoplastic eosinophilia. The patient's eosinophil count reduced markedly to normal levels within 24 h after radical gastrectomy and Billroth II anastomosis. The patient recovered well after the surgery and no abnormalities were found during the regular follow-ups. Paraneoplastic eosinophilia is an unusual manifestation that usually remains asymptomatic; moreover, cases of solid malignant tumors with eosinophilia are uncommon. To our knowledge, this is the first reported case of paraneoplastic eosinophilia in a patient with gastric carcinoma. We considered eosinophilia as a manifestation of a paraneoplastic syndrome, which can be the first clinical manifestation of a malignancy.

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A 40-year-old Chinese female patient with two week history of epigastric discomfort was admitted to our hospital on September 1, 2016. Physical examination findings were unimpressive, and there was no significant decrease in performance status according to the patient's history. She was a life-long non-smoker without a history of allergic or parasitic diseases. An abdominal computed tomography (CT) scan only revealed a lightly thickened gastric wall and a small amount of pelvic effusion. The peripheral blood leukocyte count was normal at 5,110/μL. However, 24.5% of the leukocytes were mature eosinophils (absolute eosinophil count, 1,250/μL); this eosinophil ratio is significantly higher than normal (reference range, 0–4.5%). Immunological tests showed no remarkable findings. Serum tumor markers were as follows: CEA: 0.541 ng/mL, CA 19-9: 3.90 U/mL, and CA72-4: 0.863 U/mL. The patient declined a bone marrow biopsy. Gastroscopy and biopsy findings were suggestive of a malignant gastric carcinoma, and a part of the pathological type demonstrated gastric signet-ring-cell carcinoma. Contrast-enhanced chest CT was performed, and no cancerous lesions were observed. Radical gastrectomy for gastric cancer and Billroth II anastomosis were performed on September 5, after excluding all contraindications. Histological and pathological examinations confirmed the diagnosis of a (stomach) signet-ring-cell adenocarcinoma, located in the lamina propria, and the cutting edge was negative for malignant cells. Immunohistochemical results revealed the following: CK8/18 (+); CEA (+); HER2 (0); positive rate of Ki-67, approximately 20%; TNM stage, T1N0M0; and AJCC stage, IA. Her white blood cell count was 6500/μL, of which 360/μL were eosinophils 1 day postoperatively. At 5 and 20 days postoperatively, the percentages of peripheral eosinophils were both less than 5%, and the absolute counts were 602/μL and 462/μL, respectively. According to the National Comprehensive Cancer Network guidelines, postoperative adjuvant chemotherapy is not recommended for stage IA gastric carcinoma. The patient recovered appropriately after surgery, and no abnormalities were found during her regular follow-ups.

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Discussion

Eosinophilia (absolute eosinophil counts in peripheral blood exceeding 450–550 cells/μL, depending on laboratory standards) is a hallmark of or a related finding in many allergic, infectious, autoimmune, idiopathic, malignant, and miscellaneous clinical scenarios [1, 2]. Eosinophils typically make up approximately 1–5% of all peripheral blood leukocytes[3, 4]. The patient in this case was a middle-aged woman who was admitted to our hospital with a complaint of only upper abdominal discomfort. There was no significant decrease in performance status according to the patient's history. Physical examination did not find any mass in the abdominal region. Routine blood examination revealed that her peripheral blood leukocyte count was 5110/μL (reference range: 4000–9500/μL), and 24.5% (reference range: 0–4.5%) of the leukocytes were mature eosinophils. No other abnormal laboratory findings were observed. The abdominal CT scan revealed only slight thickening in the gastric wall. The patient had no history of smoking, specific drug use, food allergies, parasitic infections, or exposure to tuberculosis. Parasites and their ova were not found in the patient's stool.

Eosinophilia is considered one of the manifestations of a paraneoplastic syndrome. Paraneoplastic eosinophilia is an unusual manifestation that usually remains asymptomatic [5, 7]. The clinical significance of paraneoplastic eosinophilia is undefined8. Paraneoplastic eosinophilia is uncommon in solid tumors, but it has been reported in several malignancies, including colorectal, lung, renal, cervical, head, and neck squamous cell carcinomas, Hodgkin's lymphoma, and prostate cancer [8–12]. In Table 1, we have listed important and relatively interesting clinical case reports of solid malignant tumors with paraneoplastic eosinophilia.

The pathogenesis of hypereosinophilia in solid malignant tumors is controversial and dubious. Scientists have postulated numerous explanations. Bone marrow stimulation via circulatory factors secreted by tumors is the most acknowledged and accepted theory [12, 13]. Interleukin-5, GM-CSF, and G-CSF are the most commonly implicated factors; however, the involvement of other factors remains possible. Moreover, the ectopic endocrine function of tumors which stimulates the proliferation of the bone marrow is another widely accepted theory [14, 15].

Whether an increase in eosinophils leads to a favorable or an unfavorable prognosis remains controversial [7, 16]. Most studies suggest that paraneoplastic eosinophilia reflects a more advanced disease and poor prognosis8. The patient in our report had hypereosinophilia on admission, but her eosinophil count dropped sharply to normal levels within 24 h of malignant tumor surgery. This indirectly supports the suggestion that eosinophilia in the context of a malignancy generally reflects the aggressiveness and poor prognosis of the malignancy. Our case has unique features that are worth reporting. Paraneoplastic eosinophilia in solid malignant tumors is very rare. To our knowledge, this is the first reported case of paraneoplastic eosinophilia occurring concurrently with gastric carcinoma. The patient was diagnosed with gastric signet-ring cell carcinoma, which is a pathological type with a relatively severe malignant degree. However, the tumor was still in a very early stage and could be completely surgically removed, because of early diagnosis prompted by her extremely elevated eosinophil count. Furthermore, as a paraneoplastic syndrome, eosinophilia may be considered as a predictor of early malignant tumors in the future. Do we consider the possibility of a tumor only after excluding all underlying diseases that could lead to eosinophilia, or is it possible to use eosinophil levels as a predictive factor or antitumor biomarker? We hope that our case report provides scientists with some

Table 1 Demographic and clinical characteristics of patients with malignant tumor and eosinophilia

Literature	Age (years)	Sex	Pathologic type	pTNM stage	Therapeutic strategy	Absolute eosinophil count (/μL)		Year
						Before the treatment	After the treatment	
Renu Pandit	72	Male	Non-small cell lung cancer	IIIA	Surgery	90,000	0	2006 [12]
Weiwei Zhou	75	Male	Clear cell renal cell carcinoma	pT3aN1M0, G4	Surgery	3,660–4,200	Normal level	2015 [8]
Axel Balian	60	Male	Hepatocellular carcinoma	No data	Surgery	1,500	Normal level	2008 [9]
El-Osta H	53	Male	Large cell lung carcinoma	IV stage	Palliative chemotherapy	14,560	53,760	2008 [10]
Walter R	66	Male	Head and neck squamous carcinoma	IV stage T4N2cM0	Radiotherapy and chemotherapy	9,700	Patient died	2002 [11]
Hiroki Kato	72	Female	Colon adenocarcinoma	IV stage	Prednisolone and hydroxyurea	141,580	Patient died	2010 [17]

insights on further explorations.

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Conflicts of interest

The authors declared that they have no conflicts of interest.

Author contributions

Shuguo Wang and Ping Sui collected data and wrote the original draft. Haixia Wang re-collected the data and revised the manuscript. Bo Han conceived the manuscript and revised it. All authors read and approved the final manuscript.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethical approval

Not applicable.

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