

Paraneoplastic Eosinophilia in Clear Cell Renal Cell Carcinoma

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To the Editor: Eosinophilia commonly occurs secondary to parasitic infections, allergy, collagen-vascular disease, hypersensitivity conditions, or underlying hematologic or solid malignancies. However, eosinophilia associated with clear cell renal cell carcinoma (CCRCC) is rare. Herein, we report a case of paraneoplastic eosinophilia associated with CCRCC.

A 75-year-old man with no remarkable previous history was admitted to Peking University First Hospital on May 23, 2014, because of a renal tumor found by abdomen ultrasound during a routine check-up. On admission, contrast-enhanced computed tomography (CT) of the abdomen revealed a renal tumor measuring 2.5 cm × 1.7 cm × 1.3 cm with neither venous tumor thrombus nor distant metastasis. Chest CT demonstrated no pulmonary metastasis. Physical examination showed no remarkable finding. Radical nephrectomy was performed without any complication. Histological and pathological examinations diagnosed CCRCC with sarcomatoid components (tumor stage: pT3a, pN1, M0, G4). On admission, laboratory tests showed eosinophilia, with leukocyte count as 13,000–14,000/mm³ (reference range: 3500–9500/mm³) with absolute eosinophil count (AEC) as 3660–4200/mm³ (reference range: 20–500/mm³) on microscopic examination. Eosinophil count decreased to normal level after radical nephrectomy. No other abnormal laboratory index showed up.

On the 45th day after the operation, he came back to hospital complaining of fever, abdominal pain, and 3 kg weight loss after nephrectomy. Physical examination did not find any mass in the abdominal region or any palpable superficial lymph node. Laboratory tests demonstrated leukocytosis with leukocyte count as 80,000–124,000/mm³, 50–70% of which were eosinophils (AEC 48,000–78,000/mm³). He denied any history of smoking, specific drug use, food allergies, parasitic infections, or exposure to tuberculosis. Stools were negative for ova and parasites. Autoimmune disease associated factor was not found such as C-reactive protein, antinuclear antibody, or anti-neutrophil cytoplasmic antibody. The IgE levels were normal. Chest CT demonstrated multiple poorly-circumscribed nodules and lymphangitic involvement

in both lungs indicating pulmonary metastasis. The abdomen ultrasound revealed multiple solid nodules in the liver, ascites in the peritoneal cavity, and enlarged retroperitoneal lymphatic nodes. The patient was treated with intravenous antibiotics (cefoperazone-sulbactam) and nutrition support. However, leukocyte and eosinophil counts continued increasing after antibiotic therapy.

The patient then received an ultrasound-guided biopsy of liver lesions, and histological and pathological examinations revealed hepatic metastasis of sarcomatoid renal cell carcinoma and hepatic mature eosinophils infiltration. Bone marrow biopsy demonstrated no evidence of leukemia, but moderate hypercellularity with a marked eosinophilia (up to 44.5%). Moreover, the bone marrow biopsy revealed poorly differentiated carcinoma metastases, for the shape of tumor cells was consistent with CCRCC. He was diagnosed as severe paraneoplastic eosinophilia with organ infiltration and put on a treatment of sorafenib and oral prednisolone. Unfortunately, he had no response to the treatment and his condition deteriorated rapidly. The patient eventually died from multiple organ failure at 60 days after surgery.

Eosinophilia refers to an increased AEC ($\geq 500/\text{mm}^3$) in the peripheral blood. The severity of eosinophilia has been arbitrarily divided into mild (AEC from the upper limit of normal to 1,500/mm³), moderate (AEC 1,500–5,000/mm³), and severe (AEC >5,000/mm³).^[1] Since a number of medical conditions are associated with eosinophilia, paraneoplastic eosinophilia can only be diagnosed till excluding all other causes. Paraneoplastic eosinophilia is an unusual manifestation that usually remains asymptomatic. The clinical significance of paraneoplastic eosinophilia is undefined. Most studies come to an agreement that paraneoplastic eosinophilia reflects a more advanced disease and poor prognosis.^[2] In this reported case, eosinophilia disappeared following primary tumor removal and reappeared with tumor dissemination. It suggested that the recurrence of eosinophilia might be an indicator of tumor remission or distant metastasis. Eosinophilia is usually successfully treated with corticosteroid.^[1] Hydroxyurea is another reported first-line agent, and combined medication of hydroxyurea and corticosteroid increases the response rate.^[1] Nevertheless, the treatment for secondary eosinophilia still mainly relies on the therapy used for the underlying primary disease. As

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Matsumoto *et al.*^[3] reported a return to normal hematologic status with chemotherapy and Pandit *et al.*^[4] demonstrated that resolution of leukocytosis and eosinophilia following tumor removal.

The presence of sarcomatoid change indicates poor prognosis. Sarcomatoid component can occur in all histologic subtypes of renal cell carcinoma and indicates an aggressive tumor. Cheville *et al.*^[5] reported the incidence of sarcomatoid transformation was approximately 5.2% in CCRCC. The presence of a sarcomatoid component was significantly associated with mortality both univariately and after adjusting for tumor-node-metastasis stage, tumor size, and histologic tumor necrosis.^[5]

In conclusion, paraneoplastic eosinophilia in CCRCC with sarcomatoid components is a very rare occurrence, which may indicate a poor prognosis. The recurrence of eosinophilia after tumor removal might be an indicator of tumor relapse. The treatment for paraneoplastic eosinophilia may include corticosteroid, hydroxyurea, and anticancer therapies.

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