Peripheral Blood Eosinophilia: An Unusual Presentation of Bone Marrow Involvement in a Patient with Relapsed Thyroid Papillary Carcinoma

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Peripheral blood eosinophilia is a well-known paraneoplastic manifestation, but its underlying mechanism is still unclear. Bone marrow metastasis may be a cause of malignancy-associated eosinophilia. However, there is limited evidence of the relationship between bone marrow metastasis and eosinophilia. Herein, we present a unique case of peripheral blood eosinophilia associated with bone marrow invasion in a patient having a history of papillary thyroid carcinoma. A 68-year old woman showed peripheral blood eosinophilia (91,525/mm^3). Since the time she was initially diagnosed as having papillary thyroid carcinoma, eosinophilia had never been found and the other causes of eosinophilia were excluded. A bone marrow study revealed cancer cell infiltration; multiple lymphadenopathies and liver metastasis were also detected. We treated her with steroid; however, her eosinophilia did not respond to steroid and the patient died due to disease progression. Although peripheral blood eosinophilia and bone marrow metastasis are rare findings in patients with papillary thyroid carcinoma, we suggest that eosinophilia might be a sign of the bone marrow metastasis of papillary thyroid carcinoma. ***(Korean J Hematol 2005;40:274-277.)***

Key Words: Thyroid, Bone marrow metastasis, Eosinophilia

INTRODUCTION

Peripheral blood eosinophilia associated with malignancy (paraneoplastic eosinophilia) is a well-known paraneoplastic manifestation and the incidence is less than 0.5%. Most paraneoplastic eosinophilia is presented in hematologic malignancy, but rare in solid cancer.[1,2] So far, paraneoplastic eosinophilia associated with solid malignancy has been reported in head and neck, ovary, uterus, breast, pancreas, lung, liver, thyroid gland, and gastrointestinal tract cancer.[3-7] Thyroid carcinoma with paraneoplastic eosinophilia has been reported in giant cell carcinoma,[8] poorly differentiated thyroid carcinoma,[9] and medullary carcinoma.[7] In Korea, sclerosing mucoepidermoid thyroid carcinoma with eosinophilia (SMECE) has been reported,[10] but this is tissue eosinophilia, not peripheral eosinophilia. Our case is the first case of

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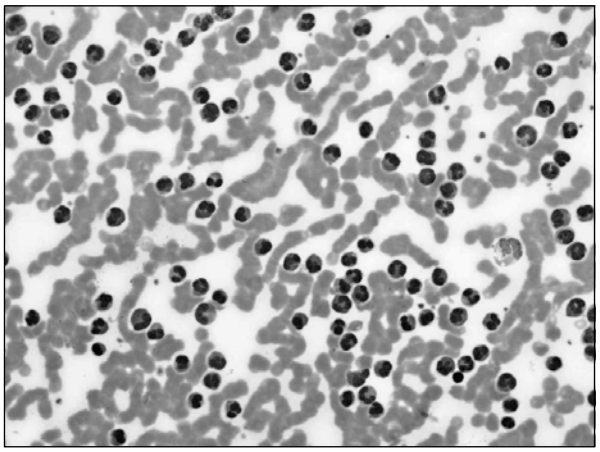

Fig. 1. This figure shows many eosinophils. They are mature form eosinophils, and no blast forms (×100, Giemsa stain, peripheral blood smear).

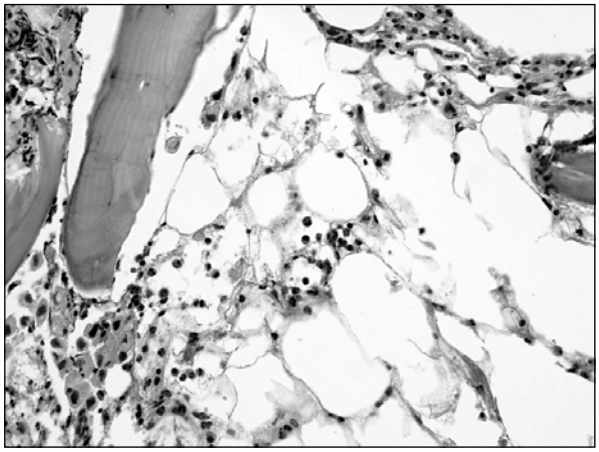

Fig. 2. This figure shows bone marrow with eosinophilic infiltration. Infiltrated eosinophils are mature form (X400, H & E stain).

paraneoplastic eosinophilia associated with papillary thyroid carcinoma (PTC), in MEDLINE search. So, we Reported our case with literature consideration.

CASE REPORT

This is a case of 68-year-old woman who presented with general weakness for two months. She had previous surgical history of total thyroidectomy for stage III papillary thyroid carcinoma (PTC) in 1992. She relapsed into regional lymph node in 1995 and 1997, was treated with radioactive iodine (using 200mCi) for recurrence and achieved complete remission. During follow-up, she began to complain general weakness, poor oral intake and dyspnea. Physical examination revealed cervical lymphadenopathy and abdominal wall mass. The hemoglobin level was 13.1 g/dL, leukocyte level markedly increased to rose at 120,700/mm^3 (10% polymorphs, 75% eosinophils), and the platelet count 153,000/mm^3. Blood biochemical tests were unremarkable. Peripheral blood smear showed eosinophilia with mature eosinophils (Fig. 1). We found disease relapse by fine needle aspiration smears from the cervical lymph node. A bone marrow aspirate and trephine biopsy showed hypercellular marrow (cellularity of 65~75%) with eosinophilic infiltration (mature eosinophil 63.2%), and increased M/E ratio (14.8 : 1) (Fig. 2). There were metastatic carcinoma cells (Fig. 3). Chest X-ray films and computed tomography (CT) scan showed multiple lung metastasis, multiple cervical lymphadenopathy, supraclavicular lymphadenopathy, multiple liver masses, left adrenal mass and abdominal wall mass (Fig. 4). Since there were no identifiable causes of eosinophilia, we diagnosed her as paraneoplastic eosinophilia. We started treatment with methylprednisolone 40mg/day and hydroxyurea 2g/day for eosinophilia. We maintained this treatment for 14 days, but eosinophilia did

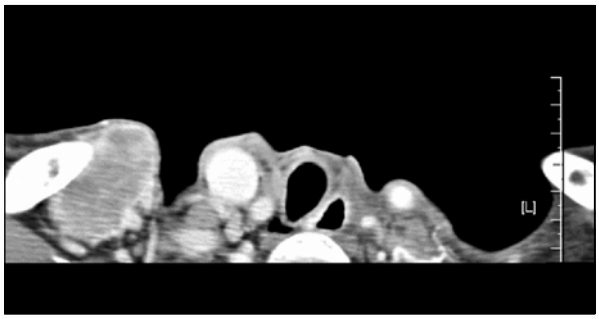

Fig. 3. This figure shows bone marrow with malignant carcinoma cell infiltration. Malignant cells are high N/C ratio and small irregular nucleus (X400, H & E stain).

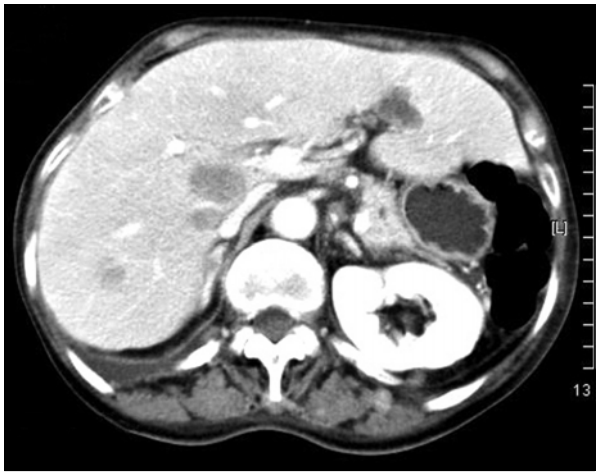

Fig. 4. Abdominal pelvic CT. This shows multiple liver metastasis and adrenal metastasis.

not respond. The patients general condition was aggravated and died on the treatment day 14.

DISCUSSION

Paraneoplastic eosinophilia has been found to be unrelated to the histological type of tumor, but most frequently occurs in hematologic malignancies, most commonly in Hodgkins lymphoma (7.5 to 20%).[1,2] It has been suggested that eosinophilia is associated with tumor necrosis. Cytokines associated with eosinophilia are primarily interleukin-5 (IL-5), but also granulocyte-macrophage colony-stimulating factor (GM-CSF) and interleukin-3 (IL-3). Eosinophilia is usually mild, but absolute counts may occasionally exceed 25,000/mm^3, and clinical complications of eosinophilia may occur.[1,2] Clinical meaning is not clear, but studies have shown that paraneoplastic eosinophilia was more frequently identified with extensive metastatic tumors and was generally a poor prognostic sign.[4,11-13]

PTC is a malignancy that has a good prognosis. Lymph node recurrence occurs in 10～14% of patients but PTC is considered to be associated with relatively good prognosis because of high response to radioactive iodine therapy. About 10% of patients with PTC develop distant metastasis, and lung is the most common site of metastasis, bone marrow metastasis is rare. The natural course of well- differentiated PTC is slow growing, and even if stage 3 cancer, 10 year survival rate is nearly 80%.[14] Our patient died due to rapid cancer progression with eosinophilia unlikely as usual PTC. PTC with bone marrow infiltration is very rare, and associated paraneoplastic eosinophilia has been not reported. Our case is compatible to previous reports in the aspect that paraneoplastic eosinophilia is associated with poor prognosis of cancer. The cause of rapid progression may be patients old age, but may be eosinophilia. Previous reports show that eosinophilia with malignancy is paraneoplastic syndrome, but Chung studied eosinophilia in 1988, and concluded that cause of idiopathic eosinophilia was malignancy in 7.5% later.[15] Thus, eosinophilia with malignancy may be aggravating cancer progression. In our case, eosinophilia was found incidentally, and during work-up, we found that peripheral eosinophilia was associated with disseminated PTC with bone marrow metastasis. To know whether eosinophilia can aggravate cancer, further study is needed. Generally in about half of the patients with solid tumors, a positive bone marrow biopsy specimen is associated with an abnormal peripheral blood smear or an abnormal bone scan. Only 50% of patients with a positive bone scan had a positive marrow biopsy. The hematologic manifestations of bone marrow invasion with cancer are as follows: anemia, leukocytosis, monocytosis, thrombocytosis, and leukoerythroblastosis.[16] Although eosinophilia may be possible in patients with bone marrow metastasis, it is known to be extremely rare. Our patients presented peripheral eosinophilia, but no identifiable causes of eosinophilia, thus we performed bone marrow aspiration and biopsy, and found bone marrow metastasis. The exact mechanism of eosinophilia in this patient is not clear, however,

eosinophilia may be associated with bone marrow metastasis. Thus, we suggested that peripheral eosinophilia with PTC could be the manifestation of bone marrow invasion by PTC. In conclusion, peripheral blood eosinophilia might be an indicator of bone marrow metastasis in papillary thyroid carcinoma; however, further study should be warranted to explain the underlying mechanism of this phenomenon.

요 약

저자들은 갑상선 유두암 치료 후 추적 중에 말초혈액 호산구증다증이 발견되면서 골수 침범을 동반한 광범위한 전이로 재발이 진단된 된 1예를 경험하였기에 문헌고찰과 함께 보고하는 바이다.

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