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A Case of Relapsing Polychondritis Associated with Myelodysplastic Syndrome with Erythroid Hypoplasia/Aplasia

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Relapsing polychondritis (RP) is a rare multisystem disorder. Myelodysplastic syndrome (MDS) with erythroid hypoplasia/aplasia is a rare form of myelodysplasia. Several cases of RP associated with MDS have recently been described. However, RP associated with MDS with erythroid hypoplasia/aplasia has never been reported. There was only one case report of polymyalgia rheumatica associated with MDS with erythroid hypoplasia/aplasia. In this study, we report a 79-year-old patient with RP, who developed MDS subtype refractory anemia (RA) with erythroid hypoplasia/aplasia, a very characteristic subtype of MDS.

Key Words : Relapsing polychondritis (RP), Myelodysplastic syndrome (MDS)

INTRODUCTION

Relapsing polychondritis (RP) is a rare autoimmune disease of unknown etiology characterized by recurrent inflammatory episodes primarily affecting the auricular, nasal or laryngotracheal cartilage, as well as the ocular, audiovestibular and cardiovascular systems[1, 2]. The myelodysplastic syndromes (MDS) are clonal disorders of hematopoiesis characterized by peripheral cytopenias and a dysplastic bone marrow that are usually hypercellular. MDSs characteristically exhibit a high number (between 5% and 50%) of erythroid precursors in the marrow[3]. However, a minority have merely a small amount (less than 5%) of recognizable erythroid cells in the bone marrow. Within this group, most of the patients with erythroid hypoplasia have the so-called MDS with erythroid hypoplasia/aplasia whose pathogenic mechanism remains unclear.

A review of the literature reveals only 16 well-documented cases of MDS with erythroid hypoplasia/aplasia[4]. There are several reports of a simultaneous or temporally close occurrence of RP and myelodysplastic/myeloproliferative conditions[5-9]. Here, we report a 79-year-old patient with RP who developed MDS subtype refractory anemia (RA) with erythroid hypoplasia/aplasia. To our knowledge, this is the first case of RP associated with MDS with erythroid hypoplasia/aplasia.

CASE REPORT

A 79-year-old male was admitted to our hospital in October 2002 because of a five-day history of fever, chills, and productive cough. He was diagnosed with RP in 1997 due to recurrent swelling and redness of both ears (Figure 1), conjunctivitis, general ache and myalgia, which was confirmed by an ear biopsy (Figure 2). Since then, he has been treated with low-dose glucocorticoid, NSAID and colchicine. Manifestations of RP were cleared under treatment with low-dose glucocorticoid over 5 years. On admission, he complained of fever, chills, and cough.

On physical examination, his blood pressure was 130/80 mmHg, pulse rate 108/min and body temperature 38.1℃. He

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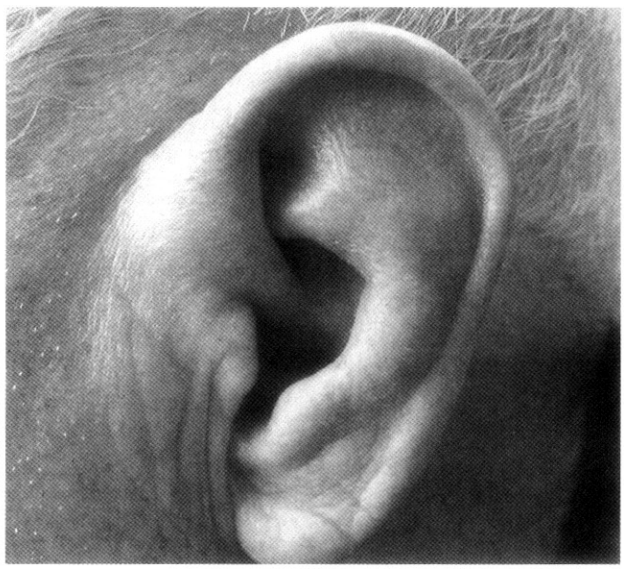

Figure 1. Left ear shows erythema and painful swelling without ear lobe involvement.

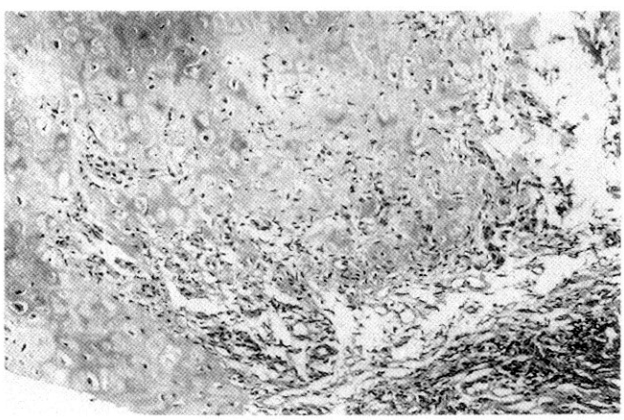

Figure 2. Biopsy of auricular chondritis. Biopsy of the ear shows perichondritis with presence of mononuclear cells and occasional polymorphonuclear leukocytes at the fibrochondral junction (H&E, ×100).

had a cushingoid appearance and pale conjunctivae. Auscultation revealed rales on the right lung.

The blood count showed macrocytic anemia: hemoglobin 6.8 g/dL, hematocrit 20.6%, MCV 107 fL, and MCH 35.2 pg. Slight leukocytosis (WBC count=10,400/μL) and moderate thrombocytopenia (platelet count=99,000/μL) were noted. ESR was 43 mm/h and CRP was positive (36.9 mg/dL). The peripheral blood smear showed anisocytosis, polychromasia, and poikilocytosis. Biochemical tests were all within normal ranges except for slightly elevated LDH (499 IU/L) and decreased protein/albumin levels (6.0/2.7 g/dL). Serum iron level and saturation of transferrin were increased (164 μg/dL and 91%, respectively). Serum ferritin levels were (923 ng/mL). There was no vitamin B12 deficiency (serum level: 963 pg/mL; normal 200-950 pg/mL) or folic acid deficiency (serum level: 14.5 ng/mL; normal 2.5-20 ng/mL). The Direct Coombs test was positive, while the indirect Coombs test was negative. Serological tests for HIV and hepatitis B were negative. Tests for serum anti-nuclear antibodies, anti-neutrophil cytoplasmic antibodies and rheumatoid factor were all negative.

Chest radiographs showed air-space consolidations in the upper and lower right lobes with a small amount of right pleural effusion. Broad-spectrum antibiotics were started. Four weeks later, there was marked improvement in his chest radiographs. He no longer had a fever, and his productive cough had also improved. However, transfusion-dependent anemia (hemoglobin=7.8 g/dL) and thrombocytopenia (platelet count=24,000/μL) remained.

Bone marrow aspiration and biopsy were performed (Figure 3). This revealed a hypercellular marrow for his age with decreased megakaryocytes. A myeloid to erythroid ratio was markedly increased (21:1) due to the markedly decreased erythroid series. Dysplastic changes were seen in the myeloid series and megakaryocytes. Approximately 4.5% of blasts were present. Cytogenetic analysis showed a normal karyotype (46 XY). Serological tests for human parvovirus B19 were positive for IgG and negative for IgM.

A diagnosis of MDS subtype RA with erythroid hypoplasia/aplasia was made. He was treated with prednisolone 5 mg daily until discharge, and received packed red cell transfusion once a week. With low dose prednisolone therapy and intermittent transfusion, the patient has remained in a stable

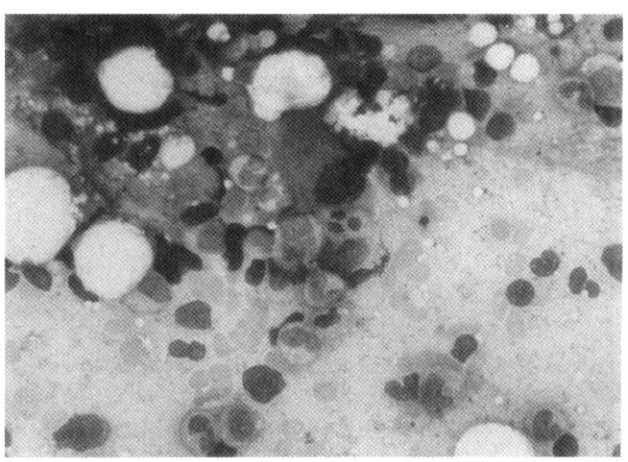

Figure 3. Bone marrow smear at the time of diagnosis shows markedly decreased erythroid series. Some of the myeloid cells show dysplastic changes such as hypogranulation. Megakaryocytes show dysplastic changes such as single lobed nuclei (Wright stain, ×1000).

clinical and hematologic condition. At a follow up three months after diagnosis, his blood count showed WBC count 2,800/μL, hemoglobin 6.4 g/dL and platelets 119,000/μL.

DISCUSSION

RP is a rare, episodic inflammatory condition affecting cartilaginous tissues, especially the ear, nose and tracheobronchial cartilage[1, 2]. Diagnosis is based on the characteristic clinical features. The diagnostic criteria were described by McAdam et al[1]. Our patient fulfilled these criteria, having both recurrent auricular chondritis and ocular inflammation. Furthermore, the diagnosis was confirmed by a biopsy of the left ear cartilage.

RP is thought to be an autoimmune disorder. Autoantibodies to type 2 collagen, association with other autoimmune disorders and response to steroids by reduction of the inflammatory response all support this view. In our patient, the manifestations of RP were cleared under treatment with low-dose glucocorticoid over 5 years.

MDSs are a group of acquired neoplastic disorders of bone marrow, characterized by quantitative and functional abnormalities of all three hematopoietic lineages caused by a defect at the stem cell stage[3]. MDSs characteristically exhibit a high number of erythroid precursors in the marrow. However, a minority have merely a small amount (less than 5%) of recognizable erythroid cells in the bone marrow. Within this group, most of the patients with erythroid hypoplasia have the so-called MDS with erythroid hypoplasia/aplasia[4]. Our patient showed 4% of erythroid precursors and markedly increased myeloid to erythroid ratio (21:1) in the marrow.

The association of RP and MDS has only occasionally been described. Michet et al. reviewed 112 cases of RP, amongst whom six patients developed hematological clonal disorders[10]. Van Besien et al. reported a case of RP associated with MDS subtype refractory anemia with excess blasts in transformation (RAEB-t)[5]. Mongin et al. reported 12 cases of RP associated with MDS, in which MDS preceded RP, occurred simultaneously, or developed subsequently[11]. In 1997, our patient was diagnosed with relapsing polychondritis. Initial investigations showed an anemia of hemoglobin 9.4 g/dL and normocellular marrow. Five years later, a diagnosis of MDS was made by a bone marrow aspiration. The association between MDS and RP certainly does not appear fortuitous, but the mechanism of this association continues to remain obscure[7, 8]. However, the fact that there was anemia when he was diagnosed with RP and that RP preceded the bone marrow changes by five years add currency to the notion that RP may represent a paraneoplastic phenomenon of an underlying MDS, or alternatively, that MDS and RP may be caused by a single immunological abnormality leading to an autoimmune condition[6].

Interestingly, the MDS in our case had further characteristic features. It showed a dearth of erythroid series', and he was diagnosed with MDS with erythroid hypoplasia/aplasia, a very rare subtype of MDS. Our patient is the first case reported in the literature with RP associated with MDS with erythroid hypoplasia/aplasia. Cook reported a case of polymyalgia rheumatica concurrent with erythroid hypoplasia/aplasia associated with myeloproliferative and myelodysplastic syndrome[12]. In his case, the patient initially responded well to prednisolone, but relapsed after tapering off the steroid.

Although MDS with erythroid hypoplasia/aplasia is usually highly resistant to therapy, the efficacy of steroids for erythroid hypoplasia/aplasia occuring in patients with MDS is also reported in several cases[4, 13]. Williamson et al. reported six cases of erythroid hypoplasia/aplasia occuring in patients with MDS[13]. They showed a diversity of clinical courses and prognoses. Three patients died within a short time of developing erythroid hypoplasia/aplasia associated with an increased blast percentage in the marrow. The other three patients showed at least a partial recovery of erythropoiesis after being treated with prednisolone. Their marrow initially showed MDS subtype RA with 1% or fewer erythroblasts. Williamson et al. suggested that the response to steroid supports an autoimmune etiology superimposed on MDS rather than an intrinsic stem cell defect[13]. This supports the view that those patients who have erythroid hypoplasia/aplasia and no excess of blasts may have a relatively good prognosis and should be considered for immunosuppressive treatment[13].

MDS with erythroid hypoplasia/aplasia is a rare form of myelodysplasia, with only 16 well-documented cases reported in the literature. Patients with this disorder were predominantly elderly males at presentation, all requiring regular blood transfusions, and with an unfavorable prognosis because of a high risk of blastic transformation[4].

The pathogenic mechanism of MDS with erythroid hypoplasia/aplasia in RP patients remains uncertain. Although, a number of autoimmune diseases including Crohn's disease, ulcerative colitis, Behcet's disease, pernicious anemia, hypothyroidism, polymyalgia rheumatica, inflammatory arthritis and RP-have been suggested to occur rather frequently in MDS, Garcia-Suarez et al. reported that most patients (15/16) with MDS with hypoplasia/aplasia did not have immunologic disorders known to be associated with autoimmune erythroid hypoplasia/aplasia[4, 7, 14]. There was only one case of polymyalgia rheumatica.

In this report, we add another immunologic disorder associated with the very rare MDS with erythroid hypoplasia/

aplasia. We believe that MDS with erythroid hypoplasia/aplasia may also be related to autoimmune diseases, a feature not different from other MDS subtypes.

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