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Case Report

Refractory anemia in systemic sclerosis: myelodisplastic syndrome

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Abstract

Systemic sclerosis (SSc) is an autoimmune connective tissue disease characterized by small vessel vasculopathy, autoantibodies, and skin or visceral organ fibrosis (lung, oesophagus, kidney etc.) as a result of extracellular collagen deposition. The cancer risk is higher in many rheumatic diseases, including SSc. Various defined malignancies may develop in 3%-11% of patients with SSc. These solid tumors are generally observed in the lung, oesophagus, or breast. In addition, an increased risk for hematological cancers were reported in literature. Herein, we describe an interesting case of SSc complicated by myelodisplastic syndrome (MDS). Our aim is to draw attention to developing cancers and the rare occurence of MDS in patients with SSc.

Keywords: Systemic sclerosis, malignancy, myelodisplastic syndrome

Introduction

An increased cancer risk is known in many rheumatic diseases. Although lymphoproliferative disorders (particularly B-cell lymphomas) are associated with rheumatoid arthritis, Sjögren's syndrome, and systemic lupus erythematosus, hematological solid tumors may develop in the follow-up of systemic sclerosis (SSc) (1). An ıncreased risk for hematological cancers in patients with SSc was reported in many studies. In addition, the risk for hematological cancers has a lower frequency than solid tumors in SSc. (2-4). The occurence of myelodisplastic syndrome (MDS) secondary to SSc is rarely reported in literature (5, 6). Our aim is to report a 54-year-old male patient diagnosed with SSc since nearly 28 years who developed MDS in our follow-up.

Case Presentation

A 54-year-old male diagnosed with SSc was followed up at our rheumatology clinic. His general condition was moderate with exertional dyspnea. On physical examination, there was a pale appearance, bilateral inspiratory crackles, sclerodactyly, telangiectasia on face, and calcinosis around his fingers and in the gluteal region. He had a history of receiving 12 cycles of cyclophosphamide, and six cycles of rituximab was subsequently administered because of interstitial lung disease. He currently takes metoclopramide, acetylsalicylic acid, methylprednisolone, bosentan, nipedipine, and azathioprine as part of the medical treatment. Red blood cell transfusion was required since the last 1.5 years because of refractory anemia.

The hematological parameters were as follows: hemoglobin 8.5 g/dL, mean corpuscular volume (MCV) 83.9 fL, leukocyte count 8.250/mkrL, neutrophil 6.850/mkrL, lymphocyte count 780/mkrL, platelet count 172.000/mkrL, reticulocyte count 0.097/mkrL, and direct-indirect coombs tests were negative. Antinuclear antibody was positive at 1:320 nucleolar pattern (Scl-70). The level of serum iron was 14 µg/dL (n: 31-144), transferrin saturation was 8%, ferritin was 296 ng/dL (n: 21-274), and erythropoietin was 49.9 mIU/mL (n: 2.6-18.5). Although the iron replacement therapy was administered perorally and intravenously, refractory anemia still persisted. Sliding hiatal hernia was detected by endoscopy, and the colonoscopy was normal. The bone marrow aspiration/biopsy was performed for the etiology of refractory anemia. The cytoplasmic hypogranulation, hypo-lobulation in myeloid precursors, and internuclear bridging between two normoblast were observed during bone marrow aspiration (Figure 1). There were no blastic cells, and the iron level was normal during bone marrow aspiration. The patient was diagnosed with MDS with refractory anemia. Erythropoietin was added to the treatment regime and continued in our follow-up.

Discussion

Many reviews suggest an increased cancer risk, particularly lung cancer, and other dieases, including non-melanoma skin cancer, non-Hodgkin's lymphoma, esophageal cancer, and liver cancer in patients

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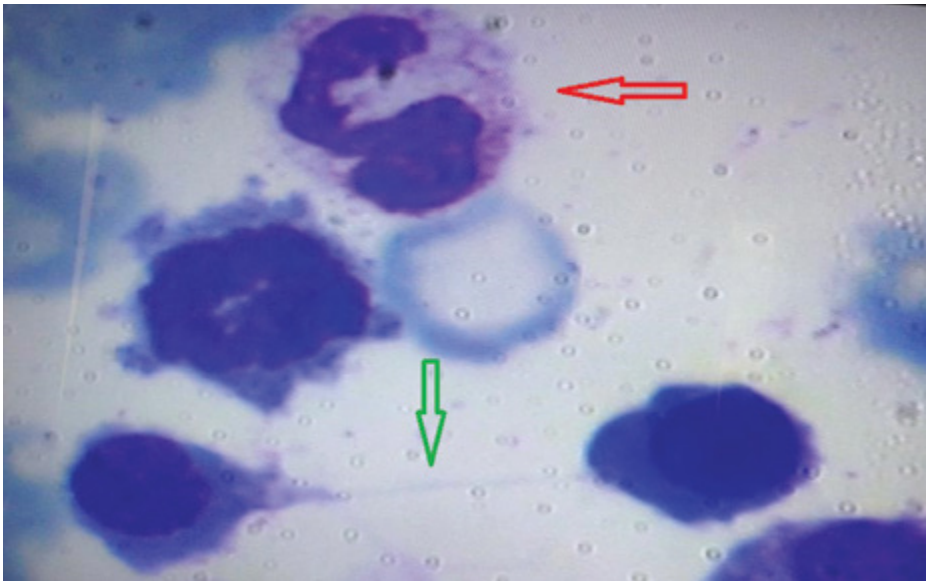

Figure 1. Bone marrow aspiration showing cytoplasmic hypogranulation, hypo-lobulation in myeloid precursors (green arrow), and internuclear bridging between two normoblast (red arrow)

with SSc (1-4). Very few studies have indicated no increased risk for cancers (7). The cancer risk is higher in the first year after SSc diagnosis (4). Szekanecz et al. (3) observed that malignancy occured 6.6 years after the diagnosis of SSc. Diffuse cutaneous SSc compared with localised cutaneous SSc and male patients compared with female patients have a higher cancer risk (8). However, it has been reported that cancer incidence based on gender is controversial (2). Our patient was a 54-year-old male, diagnosed with SSc, and developed MDS in the 28th year of follow-up.

Myelodisplastic syndrome is a hematological disorder characterised by dysplastic and ineffective hematopoiesis and has a risk for transformation to acute leukemia. In many cohort, prospective, retrospective, and case control studies, hematological cancers such as non-Hodgkin lymphoma, leukaemia, multiple myeloma, and myeloproliferative neoplasms were reported in patients with SSc (3-6). A 2.5-fold increased risk for hematological cancers in a nationwide population-based cohort study was reported by Olesen et al. (8) Paraneoplastic scleroderma may accompany hematologic malignancies (3, 4). An increased risk for non-Hodgkin lymphoma was reported in female patients with SSc (1). Conversely, hematological cancer occurs more frequently in male than female patients (8). MDS secondary to rheumatoid arthritis, systemic lupus erythematosus, Sjögren's syndrome, and SSc is very rare. However, a few case reports and series described patients with SSc and MDS (5, 6). Takashima et al. (5) reported a 63-year-old female patient with SSc for 16 years who had MDS with refractory anemia with excess of blasts. Hamamoto et al. reported MDS with refractory anemia in patients with an incomplete type of the CREST syndrome (6).

Genetic and environmental factors, including drugs and smoking, are involved in the multifactorial pathogenic mechanism for both SSc and MDS (8). The association between anti-centromere, anti-Scl 70 antibodies and cancer risk is not clearly known, except anti-RNA polymerase III for paraneoplastic scleroderma (7). Cigarette smoking is an independent risk factor for both lung and hematological cancers. The patient had no history of smoking and drinking alcohol. Immunosuppression, chronic B-cell stimulation, antirheumatic agents such as cyclophosphamide, azathioprine, methotreaxate etc., and chromosomal abnormalities are suspected risk factors and may increase the risk for hematologic malignancies in patients with SSc (2, 8). It is suggested that fragile genome, damaged DNA, or reactive oxygen radicals are observed in the association between SSc and malignancies (9). According to Pan et al. (10) chromosomal abnormalities are observed among patients with SSc than healthy controls. Our patient had a medical history of receiving cyclophosphamide for interstitial lung disease and had no chromosomal abnormalities.

Thus, patients with SSc have risk factors for hematological cancers and rarely for MDS. More studies are required to understand the relation between SSc and cancer risk. Therefore, continuous monitoring of patients with SSc is essential because of the risk of developing malignancies.

Ethics Committee Approval: N/A.

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

Peer-review: Externally peer-reviewed.

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