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Dates: Received: 10 July, 2017; Accepted: 28 July, 2017; Published: 31 July, 2017

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Keywords: Multiple myeloma; Scleroderma; Second malignancy

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Case Report

Multiple Myeloma with scleroderma and second malignancy: A case report

Abstract

Living long term with multiple myeloma recently seems to increase the long term sequel such as second primary malignancy. Several studies on second malignancy in multiple myeloma have been suggested that therapy related factors and predisposing host factor also are responsible. Scleroderma is reported with solid tumors in several studies, but association with multiple myeloma has seldom been reported. In this report we present a patient with multiple myeloma, scleroderma and second primary malignancy.

Introduction

The overall survival of multiple myeloma (MM) has increased in recent years; therefore, second malignant neoplasms may become an issue for longer term survivors with MM. The secondary malignancy may be related to the treatment for myeloma, and also due to underlying immunologic, genetic, or environmental factors [1]. Recently, an increased incidence of second malignancies has been observed with lenalidomide compared with controls in patients with newly diagnosed MM receiving lenalidomide in combination with melphalan or autologous stem cell transplantation [2]. Multiple myeloma is associated with an increased risk of hematologic malignancies such as; AML and non-Hodgkin lymphoma, MDS; and Also associated with solid tumors like lung cancer, stomach and renal cell carcinoma has also been reported [3]. The risk of second malignancy seems to be primarily confined to patients less than 70 years of age at diagnosis [4].

Scleroderma is a rare connective tissue disorder of unknown etiology characterized by thickening of skin of the skin. Scleroderma is reported to be associated with solid tumors such as lung, breast, stomach and rectum, but association with multiple myeloma has seldom been reported [5]. The coexistence of these conditions; MM with scleroderma and second malignancy; was not reported previously. We report here a 68 years old man with MM, and scleroderma and T cell lymphoma.

Case report

A 68-year-old man was admitted in the hospital because of fever and dyspnea in 2013/Aug/20. The dyspnea increased gradually during recent 3 month, and he was febrile from

one week ago. His vital sign blood pressure was normal, temperature: 38 o C, Pulse rate: 86/min, and respiratory rate: 22/min. On physical examinations, he had anemia, bone tenderness especially in sternum. Other signs or symptoms were normal.

Investigation

White Blood Cell count:2000/ μ l, Neut:46%, Lymph:34%, Mono:4%, Metamyelocytes:4%, Myelocytes:12%, RBC:1.8mil/ μ l, Hb:5.5gr/dl, MCV:103fl, MCH:30pg, MCHC:30.7gr/dl, PLT:59000/ μ l, ESR:121mm/h, LDH:664U/l, Urea:60mg/dl, Creatinine:1mg/dl, T.Bilirubin:2.2mgr/dl, D. Billirubin:0.5mgr/dl were noted. PT, INR, PTT, Calcium, Phosphor, AST, ALT, Alp, Uric Acid were normal. Blood and urine culture were negative. He had monoclonal gammopathy in protein electrophoresis. Total protein: 11.3g/dl, IgG: 2590mg/dl, IgA: 39mg/dl, IgM: 67mg/dl, and in urine protein electrophoresis: Alb: 30% and Low Molecular Wight protein: 70% were reported. Skeletal survey showed the generalized osteopenia, and in chest X ray he had consolidation in lower lobe of left lung.

He took 3 units packed red blood cells, and antibiotic was begun. Bone marrow aspiration and biopsy showed hypercellular marrow with decreasing normal hematopoietic cells and increasing neoplastic cells with plasmocytoid picture which some of them were immature (plasmablast) Figure 1, and also fibrosis increased in bone marrow biopsy.

Treatment

Treatment with thalidomide (100 mg/day) and dexamethasone (40 mg/day for 4 days) and Bortezomib (1.3 mg/m²) was started. After 4 month he achieves complete remission and thalidomide was continued as maintenance.

Follow up

During his follow up he visited with hypertension and edema in lower extremities about one year later, and we found that he had heart failure with ejection fraction of 40%. During this time he also complaint from Reynaud's phenomenon (Figure 2), and we found skin stiffness especially in his fingers. Rheumatoid factor, antinuclear antibodies, anti DNA, and anti-Scl-70 antibodies were absent. We consult with rheumatologist and his scleroderma was confirmed; therefore he treated with prednisone and chloroquine and his heart failure also was treated. His symptoms of scleroderma and heart failure became better gradually, but 8 month later he visited with multiple large subcutaneous nodules (Figure 3). Biopsy was done from nodules, and T cell lymphoma was diagnosed. Immunohistochemistry study showed LCA: strong membrane staining, CD3: positive in most of large atypical cells, CD20: Negative, S100: Negative, HMB45: Negative, which is compatible with Non-Hodgkin Lymphoma (NHL) in favor of peripheral T cell lymphoma. The abdominal and pelvic CT scan showed the Para-aortic lymphadenopathy. His treatment continued by thalidomide, cyclophosphamid, etoposide and prednisone. He had a good partial response to this treatment,

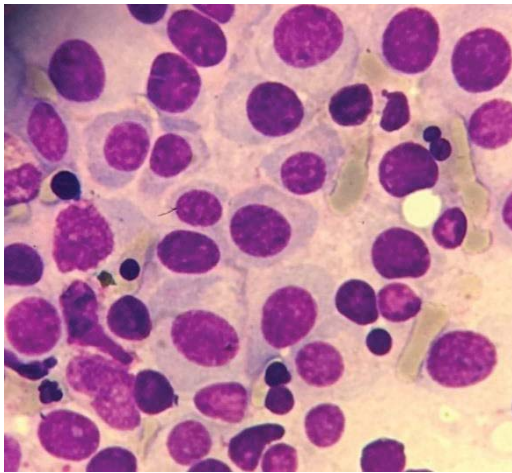


Figure 1: Plasma cell in bone marrow more than 50%.



Figure 2: Reynaud's phenomenon in our patient.



Figure 3: Subcutaneous nodule.

after 3 month treatment he did not came back and stop his treatment, unfortunately he visited after 4-5 month with progression of NHL, therefore previous treatment started again and he achieve complete remission, and in 5 years follow up he is alive and has a good condition.

Discussion

The extended survival in multiple myeloma patients may acquire second malignancies, the estimated incidence ranging between 1% and 10%. Therefore living longer with multiple myeloma seems to increase second malignancies of both solid tumor and hematologic malignancies. Therapy related factors have been suggested as a cause, such as long term exposure to melphalan and immunomodulatory drugs (IMiDs) such as thalidomide and lenalidomide. In several trial studies the risk of second primary malignancy in placebo group was 2% to 3% versus 7% to 8% in the thalidomide group which difference was significant. Based on some randomized trials reports have consistently demonstrated more second hematologic malignancies in patients treated with lenalidomide as maintenance versus placebo [6-7].

In addition, in other review study suggested that it seems reasonable to propose that second malignancies in multiple myeloma may not be attributable solely to prior treatment. The development of second malignancies may reflect combinations of influences, including treatment-related, multiple myeloma-related, host-related, environmental, and behavioral factors. Indeed, it has been estimated that genetic variations in drug disposition and effects, also polymorphisms in genes encoding drug-metabolizing enzymes, DNA repair pathways, drug transporters, and targets may also contribute for second malignancies as well [8-9].

Also some prior studies indicate that exposure to ionizing radiation, increases the risk of developing multiple myeloma and MGUS in addition to leukemia, MDS, and solid tumors [10], and also exposure to chlorinated solvents is associated with development of non-Hodgkin lymphoma, leukemia, and multiple myeloma [11]. Chronic antigen stimulation and immune dysregulation may play a role in pathogenesis of both multiple myeloma and AML/MDS [12].

Scleroderma is a generalized disorder of connective tissue disorder characterized by inflammatory, fibrotic and degenerative changes. Sclerodermatous processes coexisting with monoclonal gammopathy such as multiple myeloma have been reported in literature, but it is unusual association, and coexistence of both may have prognostic implications [13]. Some authors speculate that immunological abnormalities related to MM may cause scleroderma-like changes [14]. One study suggested that polychemotherapy, with vincristine, melphalan, cyclophosphamide and prednisolone, may have immunosuppressed profoundly the patient affecting the pathogenic mechanisms of scleroderma [15].

In management of patients who have coincidental several malignancies, treatment must be directed to the more life threatening condition [16], but our patient had secondary malignancy and we treated him based on the second malignancy and he took maintenance for multiple myeloma.

In conclusion it seems that abnormal immunological reactions related to multiple myeloma caused both second primary malignancy and scleroderma like lesion. This can related to several factors such as drug related and predisposing factors of the host. Therefore we should find the patients who are high risk for secondary malignancy and other condition, such as scleroderma, and treated them based on these factors.

Acknowledgement

The author thanks Dr M. Saghafi, and Mashhad Pathobiology laboratory for co-operating in diagnosis of patient.

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