INTRODUCTION

Association of secondary neoplasms and systemic connective tissue diseases has been debated for years; among them association of systemic sclerosis (SSc) with solid and haematological malignancies is emphasized.1 Upto 3 – 7% of SSc patients can be complicated by cancers. 2 The causal association between SSc and neoplasm is less clear and a challenging issue, and secretion of pro-inflammatory cytokines from tumoural cells or cross-reactivity of autoimmune reactions with extratumoural tissues are possible mechanisms for development of autoimmune diseases in case of pre-existing known or unknown malignant tumours.3 The most common malignant neoplasms associated with SSc are breast and lung carcinomas followed by leukemia and lymphoma.1 With better control of SSc, complications of SSc such as renal crisis have become less prevalent. Together with respiratory failure, more attention to screen cancers is the major concerns among SSc patients.

CASE REPORT

Visual Problem and Low Back Pain as Initial Manifestation of Multiple Myeloma Complicating Pre-existing Systemic Sclerosis

Mohammad Bagher Owlia1, Oliver Distler2, Mohammad Foratyazdi1 and Mojtaba Akhtari3

ABSTRACT

Some connective tissue diseases are associated with an increased risk of developing neoplastic disorders. Association of rheumatoid arthritis and systemic lupus erythematous with lymphoma, and of dermatomyositis with different malignancies including ovarian and lung cancer has been reported in the literature. Here, we describe a 58 years old man with systemic sclerosis (SSc) for 15 years who developed severe lumbar pain when he was admitted for intravenous infusion of prostaglandin E1 for his fingertip ulcers. He was found to have abnormal skeletal imaging. Laboratory tests including bone marrow aspiration and biopsy determined multiple myeloma causing extensive bony infiltration. The patient expired after two cycles of VAD and Bortezomide chemotherapy.


INTRODUCTION

A 58 years old man with a known history of systemic sclerosis (SSc) for 15 years was referred to our centre for the first time due to accentuation of finger pallor and skin stiffening and some cough. He was a smoker with a history of 30 pack-years. He had participated in the Iraq-Iran war for about 6 months. He received varying doses of weekly oral methotrexate, folic acid, aspirin, amlodipine, omeprazole and pentoxyfylline during those years. He had no family history of cancer. He had two hospitalizations 7 and 9 years ago due to exacerbation of skin, digital ulcers and esophageal symptoms receiving iloprost and other supportive managements. His esophageal biopsy was negative for malignancy or Barrett's esophagus in 2005.

Positive findings in physical examination included sclerotic changes in the skin of his face, upper and lower limbs with Modified Rodnan Total Skin Score (mRTSS) of 31. Hypoperfusion of fingers with pallor was evident; and finger tip atrophy and resorption, along with marked nailfold capillary changes and pitting scars were observed.

CASE REPORT

His initial laboratory investigations revealed: WBC count of 9300/mm³, haemoglobin level of 9.2 g/dl, MCV of 96/ fl, platelet count of 486000/mm³ and ESR at 120/mm after first hour, calcium, alkaline phosphatase, blood sugar, liver and kidney function tests values were within normal limits.

He was started on vasodilatory therapies including calcium channel blockers and prostaglandin E1 infusion for the first 3 days. On the second day of hospitalization, he complained of sudden diplopia and inward inclination of his left eye. An MRI of brain revealed a soft tissue mass in right posterior ethmoid bone with extension to right orbital fissure and multiple lytic bone lesions on the
skull. In addition, a severe low back pain appeared in the left groin interfering with his sleep. A lumbosacral MRI showed extensive infiltrative lesions and signal changes in all vertebrae. Considering his anaemia and high erythrocyte sedimentation rate, skull X-ray and bone marrow aspiration and biopsy was performed. There were sheets of abnormal looking plasma cells in his bone marrow aspiration. Bone marrow biopsy also showed hypercellularity with increased plasma cells infiltrating the entire marrow space (Figure 1). His skull X-ray films showed multiple punch-out lytic lesions compatible with multiple myeloma. His serum protein electrophoresis showed increased peak in beta-1 band with normal gamma band. Serum IgA was 2965 mg/dl, while IgG and IgM levels were within normal levels. Immunofixation was not available in our city at the time of presentation.

He was not a candidate for autologous haematopoietic stem cell transplantation to his poor performance status; and he was treated with two cycles of combination chemotherapy (VAD) with Vincristine 0.4 mg, Adriamycin 9 mg/m², and Dexamethasone 40 mg to which he had a fair response. Subsequently, he received two cycles of Bortezomide 1.3 mg/m². However, he died following an acute illness with sepsis-like feature, 2 months later.

**DISCUSSION**

Musculoskeletal symptoms are frequent in malignant tumours either primarily, metastatic or as paraneoplastic syndrome. Musculoskeletal manifestations of haematopoietic malignancies include symmetric or migratory polyarthritis, bone pain, and spinal pain mimicking a radiculopathy secondary to meningeal involvement. Dermatomyositis is a classical paraneoplastic disease, and upto 24% of patients with dermatomyositis (and far less common for polymyositis) have associated malignancy.

The chronic nature of connective tissue diseases with long-term activation of the immune system is, on the other hand, a potential risk factor for the development of malignant neoplasms. This may lead to understanding possible common pathogenesis of malignant and connective tissue diseases and better evidence to link rheumatology to medical oncology. It could be postulated that the degree and type of aberrancy in the immune system might underlie a clinical presentation spectrum from atopy, autoimmune disorders or frank malignant neoplasm. Valeriano believes that autoimmune disease could be "benign proliferative diseases" related to abnormal growth of specific cell lineage. Interestingly, chronic administration of anti-inflammatory and disease-modifying anti-rheumatic drugs interfering with immune system postulated to be responsible for this malignant transformation of potentially neoplastic cells. This is especially true for some definite carcinogenic drugs such as cyclophosphamide, but this causal association with commonly used medications in common rheumatic diseases and secondary neoplasm needs better designed controlled studies.

On the other hand, evolution of secondary neoplasm in a patient with pre-existing specific connective tissue disease could be matter of debate regarding possible common basic pathophysiology and needed careful follow-up for detecting smoldering neoplasm beneath the rheumatism. Albeit this could be a simple co-existence of scleroderma and MM, the certainty of causal relation needs to be more studied.

Alveolar cell carcinoma of the lung is one of the most associated lung cancer among SSc patients. Although cytotoxic agents could be culprit agent in the pathobiology of secondary neoplasms in these conditions, Szekanecz's work on more than 218 SSc cases showed that most patients with neoplasms on pre-existing SSc have not received cytotoxic agents, and that sustained inflammatory activity might be the primary risk factor for development of malignancy. Thus, it could be postulated that drug induced malignant transformation of connective tissue diseases has a minimal role in generating neoplasm in rheumatic disorders and is opposed to current concept, accentuation of treatment in existing connective tissue diseases could halt malignant transformation in rheumatic disorders. Smoking, a known risk factor for most malignancies believed not to be associated with incidence of SSc, but as in this case, it could increase the risk of secondary neoplasm.

Colovic et al. reported a 55 years old woman with long standing SSc who developed MM 20 years later presented with intense facial pruritus. A significant association between anti-RNA polymerase-III antibodies and secondary neoplasm was observed by Airo et al. in a cohort of Italian patients with systemic sclerosis. But these antibodies are associated with rapidly progressive diffuse cutaneous diseases and associated renal crises.

In conclusion, considering reported female cases with SSc and secondary neoplasm, this is the first reported case of a man with SSc with secondary MM so far. Further studies are needed to show casual versus coincidental association between these two conditions.
REFERENCES


