Sarcoidosis following Chemotherapy of Essential Thrombocythemia with Hydroxyurea

Col MPS Sawhney*, Lt Col DK Mishra⁺

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Introduction

Sarcoidosis and sarcoidal reactions occur in various malignancies including myeloproliferative disorders. Primary or essential thrombocythemia is a chronic myeloproliferative disease characterized by sustained and unexplained proliferation of megakaryocytes leading to increased platelet count, usually in excess of 1,000,000 per cubic milliliter. Only one case of essential thrombocythemia in association with sarcoidosis has been described [1]. We describe yet another such case.

Case Report

A 70 year old male presented with purpuric lesions from March to May 2001, had thrombocytosis of more than 1,000,000/cmm, was diagnosed as a case of essential thrombocythemia and treated with hydroxyurea in May 2001. He developed thrombocytopenia (6000/cmm) with recurrence of purpura and bleeding gums, requiring platelet infusion. Purpura disappeared, however the patient developed intractable dry cough with dyspnea in September 2001, with intermittent moderate grade fever and weight loss of 6 kg over 6 months. He was treated with antibiotics and antimalarials with no relief. A few days later he developed itchy papular lesions over his back and chest. There was marked excoriation with symptoms not getting relieved with antihistaminics. He was prescribed oral corticosteroids with which his itching and respiratory symptoms got relieved but reappeared as soon as the same was tapered. Radiograph of the chest revealed bilateral hilar lymphadenopathy. He was diagnosed as pulmonary tuberculosis and was put on ATT in October 2001. Patient continued to have chronic cough despite ATT. There was aggravation of cutaneous symptoms, he developed ichthyosis over legs and possibility of sarcoidosis was entertained.

Skin biopsy was not contributory but bone marrow (Fig. 1) revealed non-caseating epithelioid cell granuloma without acid-fast bacilli, confirming sarcoidosis. The patient was put on long term oral prednisolone (30mg per day) tapered

Fig. 1 : Bone marrow biopsy showing non-caseating epithelioid cell granuloma (H&E, original magnification x 10)

gradually over the next 6 months with good response.

Thrombocytopenia occurring in sarcoidosis is known, but thrombocytosis could not be explained. Thus in retrospect this was a case of essential thrombocythemia, who after chemotherapy developed sarcoidosis.

Discussion

Sarcoidosis and sarcoidal reactions have been reported to occur in association with malignancies [2]. They have also been reported to occur in various lymphoproliferative and myeloproliferative disorders like large granular lymphocyte leukemia (T cell)[3], acute lymphoblastic leukemia[4], chronic lymphocytic leukemia [5], chronic myelogenous leukemia[6] and acute myeloid leukemia [7-9]. Sarcoidosis can precede the onset of myeloproliferative disorder by many years [7], may be found simultaneously [8] or develop subsequently [9]. Sarcoidosis may also develop following treatment of these disorders [7,10]. Interferons have been implicated as a cause of sarcoidosis, as they stimulate the pulmonary macrophage leading to formation

*Senior Advisor (Dermatology and Veneral Diseases), Base Hospital, Barrackpore, ⁺Classified Specialist(Pathology and Heamatology)Army Hospital (R&R),Delhi Cantt.

of non-caseating granulomas in various tissues [10]. The only other case of essential thrombocythemia reported with sarcoidosis was precipitated following treatment with interferon alpha [1]. However sarcoidosis became manifest in our case, few months after treatment with hydroxyurea. A case of chronic myelogenous leukemia treated by Kikawada et al [7] had also developed sarcoidosis following treatment with hydroxyurea in combination with interferon alpha. Hence, sarcoidosis developing in association with various myeloproliferative disorders, including essential thrombocythemia, is most likely due to increased T-cell response to the presence of tumor antigen. This process may be exaggerated in few of them due to killing of tumor cells following chemotherapy.

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