A case of sarcoidosis with hematologic manifestation

Primer sarkoidoze s hematološkimi spremembami

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Abstract

A 30 year-old male with a history of pulmonary sarcoidosis presented with relapse and hematologic manifestations after successful treatment with corticosteroids and antimycotic itraconasole for pulmonary sarcoidosis (included in our previous study) is presented herein to discuss possible environmental fungal trigger since high exposure to fungi was found when the activity of mould enzyme β-glucan was measured in his home.

Izvleček

Pri 30-letnem moškem s preteklo pljučno sarkoidozo (vključen je bil v našo prejšnjo raziskavo) je po uspešnem zdravljenju plučne sarkoidoze s kortikosteroidi in antimikotikom itrakonazolom prišlo do ponovitve bolezni in hematoloških sprememb; predstavljeni primer odpira razpravo o možnih sprožilnih glivičnih dejavnikih iz okolja, saj je bila ob meritvah aktivnosti encima plesni beta glukana v njegovem bivališču ugotovljena visoka izpostavljenost glivam.

Introduction

Sarcoidosis is a systemic granulomatous disorder of unknown cause. Haematologic manifestations are rare and may include haemolytic anaemia, leukopenia, eosinophilia and thrombocytopenia.[1] Although thrombocytopenia associated with sarcoidosis was first described in 1938 by Jersilf, the actual frequency is still unknown.[2] There is just one report from Maycock et al., who reported an incidence of 1,9 % in his review of 324 cases.[3] In 1972, Dickerman et al. studied pathophysiological mechanisms of thrombocytopenia in sarcoidosis and therapeutic possibilities.[4] They suggested two pathophysiological mechanisms: increased platelet destruction by hypersplenism and a peripheral destruction led by auto-immune processes. Mahevas et al. conducted a case study and a thorough review of the literature, and concluded that different mechanisms were responsible. Among them are granulomas in the bone marrow, hypersplenism and immune thrombocytopenic purpura. However, other possible mechanisms including viral and Aspergillus infections were also mentioned.[5]

Case report

A 30-year-old male was diagnosed with sarcoidosis in 2005. From January 2006 to January 2007 he was treated with corticosteroids for the first time due to exacerbation of pulmonary sarcoidosis stage II ; the treatment being gradually discontinued by March 2007. The patient was enrolled in the interventional study of itraconazole in patients with sarcoidosis[6] and received itra-

conazole. An excellent response to therapy was observed with complete regression of pulmonary changes and normalisation of serum angiotensin converting enzyme (ACE) levels during treatment. However, already at tapering of the therapy with corticosteroids, ACE levels started to increase and were again increased above normal levels after discontinuation of the therapy (ACE on start, during and after discontinuation of therapy: 0.56 μKat/L, 0.19 μKat/L, and 0.63 μKat/L; reference value 0.13–0.47 μKat/L). In May 2008 he was admitted to the haematology department with severe thrombocytopenia (platelet count 4×10^9/L) and multiple petechiae on both legs and in the oral cavity. The complete blood count and blood smear were normal (leukocyte count was 5.9×10^9/L, haemoglobin level was 144 g/L). Coagulation screening tests and infectious parameters were negative. There was no fever, coughing, dyspnoea or pain; urine and stool were without changes. At that time he was receiving no medication. Chest X-ray showed nodules in lung parenchyma without enlarged mediastinal lymph nodes. Ultrasound of the abdomen showed an enlarged spleen and enlarged retroperitoneal lymph nodes. A bone marrow aspirate and a biopsy specimen showed sarcoid nodules in the bone marrow. Treatment with high doses of corticosteroids was started and was successful. Laboratory investigations showed increased ACE (0.50 μKat/L) and chitotriosidase (825 nmol/h/mL) and normalization during treatment: ACE (0.17 μKat/L) and chitotriosidase (17.8 nmol/h/mL). In addition β-glucan activity was measured at his working place, where he was working with old cars' climate equipment. The activity was high: 9.2 ng/m^3 as compared to 0–2.5 U/m^3 usually found inside buildings.

Discussion and conclusion

Different pathophysiologic mechanisms are responsible for haematologic changes in patients with sarcoidosis and thrombocytopenia. Besides auto-immune thrombocytopenic purpura, bone marrow involvement with granulomatous infiltration and spleen enlargement with hypersplenism may be causative. A combination of all three mechanisms was probably the cause of thrombocytopenia in our patient. An excellent response to immunosupresive and antimycotic therapy was observed in our patient and a relapse after discontinuation of therapy was preceded by a slow increase of ACE levels, a marker of granuloma burden. We suggested that there must be a continuous disturbance in the immune system and/or some yet unidentified environmental agent, which continuously triggers immune reactions with granuloma formation. According to our previous experience with antimycotic treatment and relapse of sarcoidosis with systemic and hematologic manifestations in this patient after discontinuation of both antimycotic and corticosteroid treatment, prolonged environmental exposure to fungi has been suggested as a possible triggering factor of the disease.[6,7] The hypothesis was supported by increased levels of chitotriosidase, an enzyme produced by activated macrophages involved in the defense against chitin containing organisms including fungi, which was recently found to correlate with the activity and progression of sarcoidosis.[8,9] Prolonged environmental exposure to fungi has been suggested as a risk factor for sarcoidosis also in previous case-control studies.[10] Thus exposure to fungi was measured at his workplace, where a possible source of fungi was old cars' climate equipment, and was found to be increased. Besides the treatment with corticosteroid and antifungal medications, strict antifungal measures in the home environment were advised to prevent further relapses of sarcoidosis in this patient.

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