TNF-α-mediated disease; i.e.: (i) T-cell clones reactive to type II collagen have been identified in RP, suggesting a Th 1-type autoimmune disease producing TNF-α; and (ii) TNF-α has been found in vitro to induce increased synthesis of matrix-degrading proteinases from chondrocytes, resulting in damage in RP [7]. Few reports have, in fact, described previously improvement of auricular, nasal, ocular and joint complications in patients, who were unresponsive to cytoxic drugs, after the initiation of infliximab [8, 9]. Moreover, Mpofu et al. [7] and Subrahmanyam et al. [10] have also reported a patient with recalcitrant respiratory tract localizations, in whom infliximab led to resolution of active disease. Our case is also original in that our patient with refractory RP-related aortic involvement (aneurysm of the abdominal aorta and active abdominal aortitis) was successfully given infliximab. We therefore suggest that infliximab may be an effective therapy for RP-related aortic involvement that is unresponsive to conventional therapy. In fact, at 3-year follow-up, our patient was symptom free and CT scan revealed no deterioration of aortic impairment. Moreover, our patient did not develop adverse effect (e.g. infectious complications) related to infliximab.

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Disseminated tuberculosis in a patient with idiopathic CD4+ lymphocytopenia

Sir, We report on a 34-year-old woman presenting with back pain, fever and weight loss due to spondylodiscitis with myelitis. Biopsies revealed disseminated granulomatous lesions in spine, lungs, liver and bone marrow (Fig. 1). Infection with Mycobacterium tuberculosis was confirmed by polymerase chain reaction (PCR) and culture. After the exclusion of HIV infection idiopathic CD4+ lymphocytopenia (ICL) was diagnosed.

Cytokine production by T cells was initially reduced after stimulation with phytohemagglutinine (PHA) and anti-CD3/anti-CD28. After the initiation of anti-tuberculous treatment, the patient recovered clinically and the CD4+ T-cell counts improved without reaching the normal range.

ICL is a rare immunodeficiency syndrome affecting 0.0002% of the adults. It is defined by a CD4+ T-cell count <300/μl or a percentage of <20% CD4+ T cells of total T cells on at least two occasions. For diagnosis, HIV infection as well as any other defined immunodeficiency or cytoxic drug therapy associated T-cell lymphocytopenia has to be excluded [1].

The differential diagnosis of CD4+ lymphocytopenia in adults includes infections, malignancies, autoimmune diseases, drugs and primary immunodeficiency syndromes. Often, ICL becomes apparent through manifestation of opportunistic infections (OIs)—mainly, cryptococcosis, followed by mycobacteriosis, human papilloma virus and herpes zoster [2, 3].

The manifestation of OIs calls for evaluation of the cellular immune system and especially for CD4+ lymphocytopenia. The most important differential diagnosis is HIV infection. Since 1992, the US Center of Disease Control and Prevention (CDC) has identified a group of HIV-negative patients with ICL. CD4+ lymphocytopenia has previously been associated with extra-pulmonary tuberculosis. A retrospective study in West Africa [4] and a prospective study in Dakar observed CD4+ T-cell counts <300 cells/μl in 9.6 and 14.4% of the 115 and 430 HIV seronegative patients with tuberculosis, respectively [5].

In general, ICL is associated with more severe mycobacterial infections, but patients with disseminated mycobacterial infection demonstrated significant improvement of CD4+ T-cell counts after 4–8 weeks of anti-tuberculous therapy [6].

In the present case, no complete normalization of CD4+ T-cell count was observed after successful anti-tuberculous therapy within 5 years, suggesting that CD4+ lymphocytopenia was rather a pre-existing condition than the result of mycobacterial infection. In most patients with ICL, immunologic phenotyping reveals a concomitant, less pronounced decrease of CD8+ T cells, a slightly decreased CD4:CD8 ratio and normal B-cell numbers. Naive CD45RA+ T cells are more severely diminished than the CD45RO+ cells [3, 7, 8].

This case presented initially with panlymphopenia of 139 cells/μl (23.7%) CD4+ T cells and 219/μl (37.5%) CD8+ T cells resulting in a decreased CD4:CD8 ratio of 0.63. Among CD4+ T cells, naive CD45RA+ T cells were severely reduced to 29 cells/μl (21%). Also the B-cell count was diminished to 87 cells/μl (14.9%). Thus, the patient fulfilled the CDC criteria for ICL, presenting with a characteristic immunologic phenotype.

Functional T-cell evaluation revealed lymphoproliferation to mitogens and antigens in the lower normal range (data not shown). Cytokine production (IL-2, -10, IFN-γ) and TNF-α) was virtually normal after stimulation with Staphylococcal enterotoxin B (SEB) and soluble anti-CD3, but deficient after stimulation with PHA or anti-CD3/anti-CD28 coupled to beads (Table 1). This was not only due to the reduced total count of CD4+ T cells, since T-cell activation via anti-CD3/anti-CD28 also caused a reduced up-regulation of CD69 and CD25 (data not shown). Pre-activated CD4+ T cells of ICL patients express higher levels of Fas and Fas ligand that is associated with an increased apoptosis of these cells in vitro, particularly when stimulated with PHA or anti-CD3 [9, 10]. This increased apoptosis after stimulation causes reduced proliferation and possibly the alteration of cytokine production after certain stimulating mitogens. IFN-γ receptor expression and function and IL-12 production were normal (data not shown) excluding other...
primary immunodeficiency disorders associated with mycobacterial infections.

The treatment of ICL primarily consists of the treatment and prophylaxis of secondary complications, especially OI, and experimental approaches to enhance CD4+ T-cell counts. Prophylaxis complies with the guidelines for HIV-infected patients. IL-2 therapy for ICL was suggested to decrease the susceptibility to infection [9]. The clinical course cannot be predicted on the basis of laboratory markers. In ICL with mycobacterial infections, several reports describe the improvement of CD4+ T-cell counts with anti-mycobacterial treatment [8].

While CD8+ T-cell count and CD19+ B-cell count normalized after TB treatment, CD4+ T cells, especially naïve CD45RA+ cells (88μl), remained severely decreased even after 5 years (281μl; 31.8%). Despite the persistently low-CD4+ T cells, there was no recurrence of mycobacterial infection or any other OI. Interestingly, cytokine production improved (Table 1), possibly due to a reduced pre-activation of CD4 cells.

In conclusion, primary immunodeficiency needs to be considered as a differential diagnosis in patients with unusual presentation of spondylodiscitis. Patients with disseminated tuberculosis must be evaluated especially for cellular immunodeficiency.

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Tuberculosis of the greater trochanter

Sir, A 31-year-old female patient, with no medical history of tuberculosis, presented with complaints of mechanical trochanteric pain in the right trochanteric area. The patient was in good condition and willing to undergo operation.