Anti-tumour Necrosis Factor-Alpha Treatment of Juvenile Idiopathic Arthritis in a Patient with Common Variable Immunodeficiency

Common variable immunodeficiency (CVID) refers to an immunogically heterogeneous group of disorders characterized by a generalized failure of antibody synthesis. Approximately 20 per cent of patients diagnosed with CVID will develop an autoimmune complication, which reflects an element of immune dysregulation in addition to symptomatic immunodeficiency.[1] Tumour necrosis factor-alpha (TNF-α) is considered a potent proinflammatory mediator in the inflammatory arthritis. Infliximab, a chimeric human-mouse monoclonal antibody to TNF-α, has demonstrated efficacy in the treatment of juvenile idiopathic arthritis (JIA).[2,3]

We describe an 8-year-old boy with CVID who developed JIA at the age of 5 years. He was diagnosed with CVID at 2 years of age and put on regular intravenous immunoglobulin infusions. His immunological findings are shown in Table 1.

At age 5 he began to experience oligoarthritis involving the right knee and left elbow. The patient had low grade fever and complained of pain in the right knee and walked with a limp. Physical examination revealed splenomegaly and markedly swollen right knee and left elbow. The joints were tender and warm, but there was no erythema. Uveitis was not detected. Laboratory investigations showed an increase of C reactive protein (CRP) and erythrocyte sedimentation rate (ESR). Tests for antibodies against smooth muscle mitochondria and antinuclear antibodies were negative. According to the revised International League of Associations for Rheumatology (ILAR) criteria,[4] the disease was classified as oligoarticular JIA.

TABLE 1
Immunological parameters of the patient

	Patient	Normal
Absolute lymphocyte count (mm^3)	2880	1700–6900
IgG (mg/dl)	280	605–1430
IgA (mg/dl)	<25	30–107
IgM (mg/dl)	27	66–228
Tetanus toxoid antibodies	Absent	
CD3, % (absolute counts/mm^3)	54 (1566)	43–76 (900–4500)
CD19, % (absolute counts/mm^3)	21 (609)	14–44 (200–2100)
CD4, % (absolute counts/mm^3)	31 (899)	23–48 (500–2400)
CD8, % (absolute counts/mm^3)	26 (754)	14–33 (300–1600)
Lymphocyte proliferation, phytohemagglutinin (counts/min)	80.750	125.650–360.735

No consistent benefit with any conventional anti-rheumatic therapy, including non-steroidal anti-inflammatory drugs, steroids or methotrexate, was observed for 2 years. Infliximab, 3 mg/kg, was given at weeks 0, 2, 6, 14, and 22 without any additional therapy. The JIA response criteria were applied to evaluate treatment response of the patient at weeks 0, 2, 6, 14, 22, and 24. The patient was evaluated as having 50 per cent improvement in at least three of the six response variables. A long-term effect on inflammatory articular symptoms and CRP values was observed over 24 weeks. Infliximab was well tolerated by the patient and no infusion reaction or delayed hypersentitivity reaction was noted.

TNF-α is a primary cytokine and is elevated in CVID, and specific inhibition of TNF-α in these patients may be effective in moderating autoimmune disorders, including joint disease. Therapeutic TNF blockade has been successfully used to treat various conditions in which TNF seems to be of importance in mediating inflammation.[5] It is now clear that TNF-α blockade results in decreased formation of new blood vessels in the synovium, in addition to reducing joint inflammation and leukocyte infiltration. Few major adverse effects have been reported in the clinical trials; however, serious adverse events, including malignancy, fatal fibrosing alveolitis, demyelination, and increased susceptibility to infections including tuberculosis have been observed at follow-up.[6–8]

To our knowledge, this is the first case of a patient who had CVID with JIA and was treated with infliximab for severe joint disease. In these patients, TNF blockade can be successfully used for treating inflammatory conditions in which TNF seems to be of importance in mediating inflammation.

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