Neurosarcoidosis in a patient with rheumatoid arthritis during treatment with infliximab.

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*The Journal of Rheumatology* is a monthly international serial edited by Earl D. Silverman featuring research articles on clinical subjects from scientists working in rheumatology and related fields.
Neuросаркоидоз в пациенте с ревматоидным артритом во время лечения инфликсимабом

Доклад.

Мы описываем 41-летнюю женщину с ерозивным ревматоидным артритом (RA) у которой была положительная динамика при использовании инфликсимаба (RE) и анти-цитратил пептида; она была подана на успешное лечение с инфликсимабом в сочетании с метотрексатом (MTX), без отрицательных эффектов. В течение нескольких лет после начала лечения наблюдался саркоидоз, включающийся в глаза и центральную нервную систему (CNS). Случай.

Пациентка, родившаяся в 1965 году, родилась в результате аденома сателлитов в возрасте 16 лет. К моменту ее 23 лет диагностирован RA на основе распространенного полиартрита, ревматоидных узлов, усыханий и двигательных нарушений. В течение следующих нескольких лет ужесточение суставного дегенеративного лечения было включено, включающее инъекции, сульфасалазин, MTX, и циклоспорина А. Из-за увеличения активности в медиастинуме прибилики и в парных железах наблюдается саркоидоз с обеих сторон, а также гранулематозная иридоциклит и периферическая периваскулярная, типичная для саркоидоза, были отмечены. Саркоидоз диагностировался по увеличению активности в медиастинуме и в парных железах.

Саркоидоз развивается из саркоидоза, включающегося в глаза и центральную нервную систему (CNS). Она была угнетена и в течение первых дней декабря она почувствовала слабость. При осмотре головы и сетчатки глаза были отмечены обратные изменения и терапия началась с 5 недель. В дальнейшем у нее не наблюдалось нейрологических симптомов, кроме головной боли.

Протозоа: Acanthamoeba, Toxoplasma, gnathostomiasis, angiostrongyliasis

Поперечная миелиновая дегенерация (PML), Cytomegalovirus (CMV), Herpesvirus (HSV), Epstein-Barr virus (EBV), Human Immunodeficiency Virus (HIV), Hepatitis B and C, BKV, JCV, Parvovirus, Lues.

Bacteria: Culture, 16SrDNA [polymerase chain reaction(PCR)], Lues (WR, TTPA), Mycobacterium tuberculosis (culture, acid-fast staining, PCR), Borrelia, Ehrlichia, Brucella, Bartonella, Leptospiira.

Virus: Culture, HSV, VZV, CMV, EBV, HHV-6, enterovirus, polyoma virus (BKV, JCV), parvovirus, HIV-1, HTLV-1 and 2, hepatitis B and C, TBE, Dengue virus, Japanese encephalitis B

Fungi: Culture, Cryptococcus, Histoplasma capsulatum, Blastomyces dermatoïdis, Coccioides immitis

Protozoa: Acanthamoeba, Toxoplasma, gnathostomiasis, angiostrongyliasis
In our experience coexistence of RA and sarcoidosis occasionally occurs and has been reported. Prior to the institution of infliximab therapy in our patient there were no clinical or radiological (repeated chest radiographs) signs of sarcoidosis. However, it cannot be entirely excluded that sarcoidosis occurred concomitantly with RA and it is possible that infliximab, not crossing the blood-brain barrier, in fact contributed to some control of sarcoidosis outside the CNS. Another possibility is that immunomodulation caused by anti-TNF treatment facilitated, or at least contributed to some control of sarcoidosis outside the CNS. Furthermore, it cannot be entirely excluded that immunomodulating therapy such as TNF antagonists may trigger a disease related to a dormant microorganism. Several microorganisms have been implicated as potential causes of sarcoidosis, i.e., mycobacteria, *Borrelia burgdorferi*, *Propionibacterium acnes*, and *Rickettsia helvetica*. However, their role in the pathogenesis of sarcoidosis remains obscure, although it cannot be excluded that immunomodulating therapy such as TNF antagonists may trigger a disease related to a dormant microorganism.

Our case, together with previous reports on sarcoidosis manifestations developing during treatment with TNF antagonists for RA and spondyloarthropathies, stress the importance of careful vigilance in monitoring patients treated with these drugs. These observations may contribute to understanding of the pathogenesis of autoimmune inflammatory diseases, especially sarcoidosis.

**REFERENCES**


**Idiopathic Osteonecrosis of Femur in Adult Morquio Type B Disease**

To the Editor:

Morquio syndrome is one of the mucopolysaccharidoses (type IV). Glysosaminoglycans accumulate within the cells, leading to many systemic alterations and skeletal abnormalities. There is shortening of the trunk and limbs, spinal curvature, odontoid hypoplasia with cervical instability, and lower-limb alignment problems. We describe a young man originally diagnosed with idiopathic osteonecrosis of femur.

A male patient born in 1975 had dystonia since he was 11 years of age. It was first localized to the upper limbs, but progressively generalized, with an axial predominance, when he reached age 20 years. The dystonia caused walking difficulties, but he had no mental problems and he worked normally in a computer business. No dysmorphic features (height 1.69 m, weight 57 kg) or visceral or other neurological abnormalities were found, cerebral magnetic resonance imaging examination was normal, and the dystonia was considered idiopathic.

At age 23 years, he suddenly complained of a pain in the right hip, when walking. On the pelvic radiograph there was a typical aspect of osteonecrosis of the right femoral head with a normal left hip and absence of dysplasia on both sides (Figure 1A, 1B). Radiographs of other joints (knees, shoulders, hands, wrists, ankles, feet) were normal, and the necrosis was thought to be probably idiopathic. Comorbidities known to be associated with osteonecrosis were ruled out. Surgery was not considered, as the hip lesion did not affect his quality of life.

After 4 years of regular followup, he mentioned that a recently born niece presented a progressive psychomotor retardation, and the possibility of a genetic disorder of mucopolysaccharide metabolism was suspected. His ophthalmologic examination was normal, but spine radiographs revealed vertebral dysplasia at the cervical, dorsal, and lumbar level. There was moderate dorsal scoliosis, and at the dorsal and lumbar level platyspondyly, mild anterior tonguing, concavity of the vertebral bodies, and irregular endplates. The craniovertebral junction was normal, but C5 was pear-shaped, centering a cervical kyphosis, with platyspondyly of the adjacent vertebrae (Figure 2).
Blood samples and a skin biopsy for fibroblast culture were sent to the Laboratoire de Génétique et pathologie métabolique at Hopital Cochin, Paris (Prof. L. Poenaru, Dr. C. Caillaud), and the Laboratoire de Génétique, Hopital Necker-Enfants malades (Dr. D. Geneviève), Paris. Screening for enzyme deficiency showed a very low level of leukocyte β-galactosidase (15 nmol/h/mg proteins) representing 7.5% of the low normal range (200–700). The skin fibroblast culture confirmed the deficient β-galactosidase activity (4 nmol/h/mg protein instead of 617 nmol/h/mg).

At age 30 years, the pain at walking had increased but was still acceptable, and the appearance of the right hip remained stable. The clinical problem was then dominated by the dystonia, which was resistant to treatment. The dystonia involved the entire body but was predominantly axial. In September 2006 a pallidal deep-brain stimulation was carried out (Prof. A.L. Benabid, Prof. P. Pollak) and after this, his walking improved significantly. A diagnosis of Morquio B was determined.

The usual form of Morquio disease is known as Morquio A. There is stunted growth, spondyloepiphyseal dysplasia, and frequently a cranio-cervical junction malformation requiring a surgical fixation. The β-galactosidase is normal, but α-galactose 6-sulfatase is undetectable. Morquio B disease is much rarer, and tends to be less severe. Lysosomal storage disorder is caused by β-galactosidase deficiency due to mutations in the GLB1 gene. Three major forms have been established on the basis of age of onset and severity of symptoms: infantile, juvenile, and adult. The adult form is characterized, as in our patient, by a progressive and generalized dystonia with speech and gait disturbance and slowly progressing dementia.

The physiopathology of femoral head osteonecrosis is still controversial. In most cases there is a conjunction of local blood flow reduction and increased fragility of bone. Femoral head collapse is often seen — in Gaucher disease — due to an accumulation of Gaucher cells in bone marrow. In most of the other inherited metabolic diseases there is a joint dysplasia with more or less destruction of bone extremities, but isolated femoral head osteonecrosis is quite rare. A few cases have been reported in Fabry’s disease. A case of Morquio disease was diagnosed as Perthes dis-

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Figure 1. A. Full pelvis view showing absence of dysplasia and necrosis of the right femoral head (arrows). B. Detail of the necrosis (arrows).
The association of Morquio B disease with femoral head necrosis may be coincidental, although no other risk factors were found in our patient. The accumulation of undegraded substrate in lysosomes of the affected tissues, such as bone marrow, chondrocytes, and osteocytes, may induce bone fragility, with microfractures responsible for the osteonecrosis.

REFERENCES


Book Review

Crystal–Induced Arthropathies, Gout, Pseudogout and Apatite-Associated Syndromes


Crystal-associated syndromes are common events in the emergency room and at rheumatology and orthopedic clinics. Often satisfying to treat because of the rapidity of clinical response, they are more often a challenge because of chronicity and progressive destruction, deformity, and disability. The editors of this volume, all respected clinician-scientists, along with 35 other experts in their fields, present historical reviews, prevalence, natural history, associated clinical conditions, epidemiology, clinical aspects, pathophysiology, diagnostic tools, biochemistry, pathology, and approaches to older established and newer therapies for gout (urate), pseudogout (calcium pyrophosphate dehydrate, CPPD), and basic calcium phosphate (BCP, calcium apatite) deposition diseases.

The identification and association of urate crystals with acute arthritis is a recent (1960) event. The editors write that “much of the present understanding of these diseases is the result of observations that have occurred during the span of our careers.” Population-based investigations suggest that the prevalence of gout is rising and that hyperuricemia is a strong, independent marker of mortality in coronary heart disease. Asymptomatic hyperuricemia and the concept of urate as a biomarker of endothelial dysfunction and vascular disease is intriguing although controversial. Prevalence data for CPPD and BCP deposition are derived from autopsy and radiographic reviews. The descriptions of the clinical aspects and genetics of the familial forms of crystal-associated arthropathies are interesting reading.

The management of crystal-associated arthropathies includes chapters on colchicine, nonsteroidal antiinflammatory drugs, corticosteroids, uricosuric agents, xanthine oxidase inhibitors, uricase, and therapeutic strategies.

The editors are to be congratulated on the presentation of this concise, in-depth, and current review. It is recommended reading for trainees and their mentors in rheumatology, orthopedic surgery, and physiatry, and others who have a particular interest in these common crystal-associated arthropathies.

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Figure 2. Cervical spine radiograph shows pear-shaped dysplasia of C5, platyspondyly, and kyphosis.