RHEUMATOID ARTHRITIS ASSOCIATED SCLERITIS

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Case Report

A 77-year-old white male presented with a history of painful, red right eye. The patient was diagnosed with mild iritis in the right eye four months prior to presentation by her local ophthalmologist. The uveitis resolved with topical steroids.

The patient's past medical history was significant for weight loss of 10 pounds over the past four months, recent onset of fever, chills, night sweats and fatigue. He also had arthritis involving both the knee joints, muscle aches and a maculopapular rash over arms and chest. His past medical history was also significant for adult onset diabetes mellitus, benign prostatic hypertrophy, atrial fibrillation, seasonal allergies and gastric ulcers.

On examination, visual acuities were 20/40 on the right and 20/200 on the left eye. Slit lamp examination of the right eye showed a sectoral nodular scleritis superotemporally and a normal left eye. There were trace cells in the anterior chambers of both the eyes, nuclear sclerotic cataracts 2+ in both the eyes. Dilated fundus examination of both the eyes showed clear vitreous, cup disc ratio of 0.3 bilaterally and no retinal lesions were noted.

Systemic work-up was positive for rheumatoid factor, a high ESR of 106 and raised C-reactive protein levels. Other work-up including ANA, RPR, complete blood analysis, liver and renal function tests and urine analysis were normal. Chest CT-scan was normal and a biopsy was performed of the skin lesions. The skin biopsy showed interface dermatitis with focal eccrine ductular involvement and a pallisading granulomatous reaction. Hence a differential diagnosis of scleritis associated with systemic rheumatoid disease was entertained.

TREATMENT:

The patient was started on Vioxx at a dosage of 25 mg twice daily and was to follow-up in three weeks.

A week later, the patient presented with worsening eye pain involving the left eye as well. He was hospitalized following upper gastrointestinal bleeding and Vioxx was discontinued. On examination the patient had acuties of 20/40 in both the eyes and a 2+ diffuse nodular sectoral injection in the left eye. Immunosuppressive therapy using cyclophosphamide was initiated.

The goal was to abolish the inflammation, prevent scleral destruction, and prevent progression of systemic vasculitis clinically manifesting as scleritis to other organs.

INTRODUCTION:

Rheumatoid arthritis (RA) is a chronic inflammatory disease of unknown etiology.

The synovial membrane of the joints is the main target of damage, but patients can also have involvement of extraarticular tissues such as eyes, skin, lungs, heart and peripheral nerves. It has a worldwide prevalence of 1% of the population (0.3 to 2.1%). The average age of onset is in the fourth to fifth decade of life, with a three times greater predilection in women than in men. It is by far the most common systemic condition associated with scleritis.

PATHOPHYSIOLOGY:

There is evidence to implicate autoimmune mechanisms in the pathogenesis of the disease: Rheumatoid factors (RF), are autoantibodies directed against the Fc region of immunoglobulin G. RF can be of the IgG, IgA, IgE, or IgM but most commonly are IgM. They are present in 90% of patients with RA. RF titers correlated positively with disease severity, and it is believed that RF initiates or contributes to the amplification of joint inflammation in RA by the formation of immune complexes and the activation of complement.

Genetic factors have also been implicated in the development and severity of the disease. The HLA-DR4 has a higher association with white RA patients, predominantly seropositive for rheumatoid factor. The HLA-Dw4 is the major HLA gene accounting for susceptibility to RA.

Subcutaneous nodules, a pathognomonic feature of the disease, occur in patients with rheumatoid factor, although without correlation with the titer. Vasculitis may also be present. The term inflammatory microangiopathy has been used to define the histopathological neutrophilic infiltrate in and around the vessel wall of capillary and postcapillary venules. It may also be defined as immunoreactant deposition in the vessel wall, as detected by immunoflourescence studies.

CLINICAL MANIFESTATION

In 55-70% of patients, RA begins with the insidious development of malaise, anorexia, fatigue, weakness, weight loss and diffuse musculoskeletal pain.

Although initially the joints may be asymmetrically involved, they eventually become symmetrical. It begins with an acute onset of symptoms. A rapid development of polyarthritis may appear, accompanied by fever, splenomegaly, and lymphadenopathy. The diagnosis of the disease is made on the basis of clinical criteria summarized in Table 1. Involvement of other organ systems is summarized in Table 2.

Keratoconjunctivitis sicca is the most common ocular manifestation; scleritis and peripheral keratitis are the most severe. Other ocular manifestations in RA include episcleritis, corneal involvement and ocular motility disturbances. Corneal involvement of the disease includes filamentary keratitis, sterile central ulceration, microbial keratitis, peripheral ulcerative keratitis, sclerosing keratitis, stromal keratitis and keratolysis. Episcleritis may be simple or nodular. Scleral manifestations of the disease include an anterior scleritis which may be diffuse, nodular, necrotizing or can present as scleromalacia perforans or posterior scleritis which is uncommon.

Rheumatoid scleritis is most common in the sixth decade of life, affects women more frequently than men, and is often bilateral. Although it maybe an initial sign of rheumatoid disease it typically presents many years after the onset of RA and often at the time when joint inflammation is in remission. Scleral inflammation in RA may extend to adjacent structures and may cause keratitis, anterior uveitis, glaucoma, cataract, retinal, choroidal and optic nerve changes and motility disturbances. Patients with rheumatoid scleritis have more advanced joint disease and more extraarticular manifestations than do rheumatoid patients without scleritis. The onset of scleritis may be a harbinger of occult systemic vasculitis. For this reason, immunosuppressive therapy using alkylating agent such as cyclophosphamide is indicated.

TREATMENT:

Patients with rheumatoid arthritis who develop simple diffuse scleritis are treated with oral nonsteroidal anti-inflammatory drugs (NSAIDs). If the scleritis does not respond to or recurs an immunosuppressive therapy needs to be introduced.

Methotrexate is typically the first choice in patients with diffuse scleritis. Azathioprine or mycophenolate mophetil is reserved for individuals with nodular scleritis or for those with diffuse scleritis who do not respond or respond partially to methotrexate.

Alkylating immunosuppressive agents, such as cyclophosphamide, are the treatment of choice in patients with necrotizing scleritis. Scleritis of autoimmune etiology responds very well to systemic corticosteroids, but their long-term use should be avoided because of high incidence of side effects.

PROGNOSIS:

Prognosis for life is poorer in patients with RA complicated with scleritis. The 3-year mortality rate of patients with scleritis associated with RA is 36 to 45% if not aggressively treated with immunosuppressive therapy. Extraarticular disease manifestations particularly systemic vasculitis is the most common cause of death in these patients.

The course of RA is intermittent, fluctuant, and progressive. The overall prognosis depends on the baseline disease activity interpreted by the radiographic synovial changes, high rheumatoid factor and C-reactive protein levels.

Table 1 Diagnostic criteria for Rheumatoid Arthritis

Morning stiffness in and around joints lasting at least 1 hour before maximal improvement
Soft-tissue swelling of three or more joint areas observed by a physician
Swelling of the proximal interphalangeal, metacarpophalangeal, or wrist joints
Symmetrical joint swelling
Subcutaneous nodules
Positive test for rheumatoid factor
Radiological erosion or periarticular osteopenia in hand and wrist joints

Table 2 Extraarticular involvements in Rheumatoid Arthritis

Cardiac: Pericarditis, myocarditis, endocarditis, coronary arteritis
Neurologic: Compression neuropathy, distal sensory neuropathy, distal sensorimotor neuropathy
Lymphadenopahthy
Pulmonary involvement
Laryngeal involvement
Amyloidosis
Miscellaneous: Gastrointestinal system, Renal system and Bone involvement etc

Rheumatoid arthritis associated scleritis

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1. The worldwide prevalence of rheumatoid arthritis is:

a) 2%

b) 3%

c) 7%

d) 13%

e) 23%

2. The most common systemic disease associated with scleritis is:

a) rheumatoid arthritis

b) Wegener°s granulomatosis

c) psoriasis

d) ankylosing spondylitis

e) sarcoidosis

f) systemic lupus erythematosus

3. The most common ocular manifestation in patients with rheumatoid arthritis is:

a) episcleritis

b) scleritis

c) dry eye syndrome

d) peripheral ulcerative keratitis

4. Genes accounting for susceptibility to rheumatoid arthritis are:

a) HLA-DR3 and HLA-DR4

b) HLA-Dw4 and HLA-DR3

c) HLA-DR3 and HLA-B27

d) HLA-Dw4 and HLA-DR4

5. All of the following corneal manifestations are likely to be seen in a patient with rheumatoid arthritis EXCEPT:

a) filamentary keratitis

b) sterile ulcers

c) peripheral ulcerative keratitis

d) sterile central ulceration

e) endothelitis

f) stromal keratitis

g) microbial keratitis

h) keratolysis

6. The onset of scleritis in a patient with rheumatoid arthritis is most likely a harbinger of:

a) occult systemic vasculitis

b) non-erosive arthritis

c) erosive arthritis

d) erosive oligoarthritis

7. An appropriate therapy for scleritis in a patient with rheumatoid arthritis would be all of the following except:

a) long-term use of non-steroidal anti-inflammatory drugs

b) long-term use of high dose corticosteroids

c) long-term use of methotrexate

d) long-term use of cyclophosphamide

8. The drug of choice for treatment of necrotizing scleritis in a patient with rheumatoid arthritis is:

a) methotrexate

b) cyclophosphamide

c) azathioprine

d) mycophenolate mophetil

Correct answers:

1-a, 2-a, 3-c, 4-d, 5-e, 6-a, 7-b, 8-b