RETINAL VASCULITIS IN TWO PATIENTS WITH RHEUMATOID DISEASE

Saoussen Miladi[1], ons boudriga[1], ALIA FAZAA[1], Hiba Boussaa[1], Kawther Ben Abdelghani[1], and ahmad laatar[1]

[1]University Hospital Center Mongi Slim

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Abstract

Rheumatoid arthritis(RA) is a systemic autoimmune disease characterized by inflammation of the synovial membrane of joints. However, RA can be associated with extra-articular manifestations including vasculitis that occurs exceptionally in the retina. We report two retinal vasculitis (RV) cases was a direct consequence of rheumatoid disease in active RA patients.

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Saoussen Miladi MD*, Ons Boudrigua MD*, Alia Fazaa MD*,

Hiba Boussaâ MD*, Kawther Ben Abdelghani MD*, Ahmed Laatar MD*

From the * Mongi Slim Hospital, Rheumatology Department, La Marsa, Tunisia.

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Reprint requests : Saoussen Miladi MD, Ons Boudrigua MD, Mongi Slim Hospital, Rheumatology Department, La Marsa, Tunisia ; e-mail:*saoussenmiladi@gmail.com*, *onsoussa1995@gmail.com* .

Summary: Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by inflammation of the synovial membrane of joints. However, RA can be associated with extra-articular manifestations including vasculitis that occurs exceptionally in the retina. We report two retinal vasculitis (RV) cases was a direct consequence of rheumatoid disease in active RA patients.

Key words: Retinal vasculitis, Rheumatoid Arthritis

Abstract:

Background: Rheumatoid arthritis(RA) is a systemic autoimmune disease characterized by inflammation of the synovial membrane of joints. However, RA can be associated with extra-articular manifestations including vasculitis that occurs exceptionally in the retina.

Objectives: We aimed to show two retinal vasculitis(RV) cases as a direct consequence in active RA patients.

Results: Case1:A 45-year-old man, followed for an immunopositive and erosive RA, developed bilateral occlusive venous RV. It occurred concomitantly with a flare-up of his RA and was treated with high doses of prednisolone. Recently, the patient had a recurrence of RV, and his RA was reactivated. Etiological

workup of RV, including infectious markers, antinuclear antibodies and autoantibodies to ANCA, was negative. The rheumatoid origin was retained in the presence of severe disease activity with strongly positive rheumatoid-factor(RF). The patient was started on intravenous corticosteroid therapy and was transitioned oral corticosteroid with favorable evolution. Since the visual prognosis is involved an immunomodulatory therapy treatment was considered.

Case2:A 33-year-old woman with a history of bilateral retinal detachment treated surgically, followed for immunonegative and erosive RA, presented with left RV complicated by a preretinal hemorrhage. Etiological workup, including anti-nuclear antibodies and other common infectious and autoimmune markers, was negative. An MRI of the hands was performed showing bilateral active synovitis. Rheumatoid origin of RV was retained. Systemic steroid therapy was initiated with articular and visual improvement.

Conclusion: The retina should be examined for evidence of vasculitis in rheumatoid disease and RV should be kept in mind as an ocular complication of RA.

Introduction: Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease that is characterized by significant inflammation of the synovial membrane of joints. However, RA can be associated with many extra-articular manifestations including vasculitis that occurs exceptionally in the retina.

We report here two cases of retinal vasculitis as a direct consequence of rheumatoid disease in patients with active RA.

Case1: A 44-year-old man has been followed since 2012 for an immunopositive and erosive RA treated by methotrexate at a dosage of 15mg/week and on oral corticosteroid therapy at a dosage of 10 mg/day of prednisone equivalent with a good initial response. Since 2018 the patient has stopped his treatment on his own initiative. In March 2021, he presented with a sudden bilateral blurred vision and myiodesopsias of the right eye. These symptoms were induced by bilateral venous occlusive retinal vasculitis and intravitreal haemorrhage of the right eye. The patient was given a pulse of solumedrol 1g/day for three consecutive days without incident and was putted back on his background treatment of methotrexate 15mg/week. The evolution was marked by a clear improvement of his retinal vasculitis especially since the patient benefited from a laser photocoagulation with his ophthalmologist. Currently, since August 16, 2021, the patient has presented a recurrence of his retinal vasculitis with a right vitreous hemorrhage, hence his re-hospitalization for solumedrol pulses. This ocular involvement was concomitant with a relapse of his RA, which was due to poor compliance with the treatment. The patient had no other extra-articular manifestations (pulmonary, cutaneous, digestive, and neurological).

The blood count showed a hyperleukocytosis of 13300/µL (PNN 11270, lymphocytes 1360/µL) with a hemoglobin of 13.3 g/dL and platelets of 254000/µL. C-reactive protein (CRP) was 10mg/L. Erythrocyte Sedimentation Rate (ESR) was mildly elevated (29 mm).

As part of the etiological work-up for bilateral venous occlusive vasculitis, a comprehensive evaluation was initiated. Firstly, we agreed to eliminate an infectious origin by carrying out serologies (EBV, CMV, toxoplasmosis, syphilis, Lyme disease and cat scratch disease) as well as the search for Koch's Bacillus in the sputum and QuantiFERON for tuberculosis. The results of serologies for EBV and toxoplasmosis have shown a long-standing immunity. Other infectious markers were all negative. Secondly, a systemic origin (sarcoidosis, Behçet disease, ANCA vasculitis, connectivitis) was suggested. A conversion enzyme assay was unremarkable at 7IU/L. Antinuclear antibodies and autoantibodies to SS-A, SS-B, pANCA and cANCA were all negative. Therefore, rheumatoid origin of retinal vasculitis was retained in the presence of a flare-up of rheumatoid disease (DAS28-ESR=4.4) with strongly positive rheumatoid factor (RF) (200 UI/ml) and anti-citrullinated protein antibody (ACPA) (181,51 RU/mL).

Accordingly, the patient was started on pulses of intravenous Solumedrol at a dose of 1g/day for 3 days. The evolution was marked by a clear improvement of the visual blur and persistence of the myiodesopsias. A relay with oral corticosteroid therapy at 1mg/kg per day of prednisone equivalent was started with methotrexate at a dosage of 20mg/week.

case 2 : a 33-year-old woman with a history of bilateral retinal detachment treated surgically in 2014, has been followed since 2016 for immunonegative and non erosive RA treated with methotrexate up to 20 mg/week with good progression. In July 2020, the patient had noticed blurred vision with floating spots in the left eye. Ophtalmologic examination revealed left retinal vasculitis complicated by a preretinal hemorrhage. Simultaneously, the patient had progressive joint stiffness of the wrists and hands for two weeks; these symptoms were most prominent in the morning and seemed to improve as the day progressed. At examination, she manifested tender and swelling of metacarpophalangeal joints.

The blood count showed a hemoglobin of 11,3 g/dL and platelets of 304000/µL. CRP was 20 mg/L. ESR was mildly elevated (22 mm).

The diagnosis of RA was challenged, since there was nor erosion neither immunological markers.

An exhaustive etiological workup was undertaken. Infectious origin was eliminated by carrying out serologies (EBV, CMV, toxoplasmosis, syphilis, Lyme disease and cat scratch disease) as well as the search for Koch's Bacillus in the sputum and QuantiFERON for tuberculosis. The results were all unremarkable. Antinuclear antibody and antineutrophil cytoplasmic antibody, lupus anticoagulant, and anticardiolipin antibody were all negative. Rheumatoid factor (RF) and anti-citrullinated protein antibody (ACPA) were also negative.

A magnetic resonance imaging (MRI) of the hands and wrists was performed showing bony erosions at the metacarpophalangeal joints with bilateral active synovitis which were typical for RA. Thus, the rheumatoid origin of the retinal vasculitis was retained in the presence of active rheumatoid disease concomitantly to ocular symptoms.

The patient was put on pulses of intravenous methylprednisolone sodium succinate therapy for 3 consecutive days then relayed with oral corticosteroid at 1mg/kg per day of prednisone equivalent with a marked clinical improvement and disappearance of joint signs and attenuation of eye signs.

Discussion:

We report here two cases of retinal vasculitis (RV) occurring on young adult satisfying the 2010 ACR/EULAR Criteria for RA diagnosis.[1]

The two patients were younger comparing to the reported cases in literature noticing that RV occurred between the fifth and the sixth decade of life [2 34 5] . Disease duration was 8 years for the first case and 4 years for the second one otherwise, disease duration was more then 10 years in the most reported cases in literature except for one case in which RA was revealed few months before RV development [3 4 5]. Our patients did not have extra-articular manifestations including diffuse pulmonary interstitial fibrosis, pleuritis, pericarditis, muscular atrophy, leg edema and rheumatoid nodules. Also they did not show any feature of rheumatoid vasculitis manifested as petechiae, purpura, digital infarcts, gangrene, livedo reticularis, and lower extremity ulceration. The common ocular complications of RA including episcleritis, scleritis and peripheral ulcerative keratitis were not noted in our patients' clinical course. Retinal vasculitis associated with RA is rarely reported [6] . Since then, other potential etiologies of retinal vasculitis were suspected. Intensive investigation revealed no evidence of infection (Tuberculosis, EBV, CMV, toxoplasmosis, syphilis, Lyme disease and cat scratch disease), inflammatory or autoimmune diseases (Systemic vasculitis, SLE or antiphospholipid antibody syndrome) [7] . In the two cases, retinal vasculitis occurred concomitantly with a flare of RA as shown by a positive test for CRP and elevated ESR with high DAS28. Therefore, we cautiously hypothesize that RA led to RV development. RA is a systemic inflammatory rheumatic disease with extra-articular manifestations and rheumatoid vasculitis can accompany long-standing disease (in less than 1% of RA patients) [2] .The signs of rheumatoid vasculitis vary and may include peripheral neuropath, visceral ischemia and various skin lesions as purpura, skin ulceration and digital gangrenes. Rheumatoid vasculitis may also affect the retinal vessels. Because epidemiologic data and retinal vasculitis case reports in patients with RA are lacking, the pathogenetic association between RV and RA could not be fluently assessed [2] . It's reported that retinal vasculitis related to RA, usually occurs in nodular disease, with high titres of classical IgM rheumatoid factor and are often associated to Infarcts in nailfold capillaries, weight loss and general malaise

[8] [9]. Our patients did not have all these features except a high titer of rheumatoid factor noted in the first case. In contrast to what is previously reported, it is enough noticeable that our two patients with active RA developed diffuse inflammation of the retinal capillaries in the absence of systemic vasculitis. Our literature review identified that an association between RA disease activity and retinal vasculitis was presented in a report suggesting that suppressing RA-related inflammation improves vascular health [10]. Another report showed that orbital blood flow velocity in RA patients is lower than in healthy controls suggesting that systemic inflammation may also affect the ocular vessels [11]. In our current cases, we conjecture that retinal vasculitis development may reflect long-standing subclinical systemic inflammation. Timing of the retinal vasculitis and the observed clinical improvement after adequate inflammation control using corticosteroids or immunomodulatory therapy, suggest that the retinal changes were a direct consequence of their active rheumatoid disease. However, further research is needed to investigate pathophysiologic processes of retinal vasculitis in RA patients.

Conclusion : From these two observations, we concluded that the RV remain rare in the course of RA. However, retina should be examined for evidence of vasculitis in rheumatoid disease, and that collaborative efforts between the ophthalmologists and rheumatologists involved in the evaluation and treatment of patients with RA are essential to effectively manage any ocular complications that may arise.

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