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A Case of Posterior Scleritis with Negative Rheumatoid Factor and Positive Anti-Cyclic Citrullinated Peptide Antibody Status: Case Report

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Type of article: Case report.

Abstract

Background: Posterior scleritis is a potentially vision threatening condition which is often underdiagnosed due to varied clinical presentation, several non-infectious inflammatory diseases can cause this disorder, although infectious diseases should be ruled out.

Case presentation: A 56 years-old-female with acute unilateral decreased vision in right eye and positive history for rheumatoid arthritis (RA) was referred, based on ophthalmic examination the diagnosis of posterior scleritis was considered. The only positive inflammatory marker was found is high serum titer of Anti-Cyclic Citrullinated Peptide (Anti-CCP).

Conclusion: This is the first case of posterior scleritis with only positive Anti-CCP. Elevated serum Anti-CCP titer may be considered as risk factor for inflammatory scleritis in patient with RA.

Keywords: Scleritis, Rheumatoid Arthritis, Anti-CCP, Case report

1. Introduction

Scleritis is an inflammation of the sclera, the outer layer of the globe. Although the majority of scleritis cases are due to an autoimmune etiology, approximately 5 to 10% of cases are infectious. (1, 2) Scleritis can be induced by multiple immune-mediated systemic inflammatory diseases (IMIDs) including rheumatoid arthritis (RA), sarcoidosis and inflammatory bowel diseases. Also systemic vasculitis such as: wegener's granulomatosis, polyarteritisnodosa as well as infectious diseases like syphilis and tuberculosis may play a role in its development(1). The incidence of RA in patients who present with scleritis is 33% (2). Over a recent encounter at our clinic, we reported a patient with posterior scleritis and positive history for RA, but the only positive inflammatory marker was anti-Cyclic Citrullinated Peptide (Anti-CCP), indeed rheumatoid factor (RF) was negative.

2. Case presentation

A 56 years-old-female referred to poostchi ophthalmology clinic (Shiraz-Iran) complaining of unilateral decreased vision in right eye since seven days prior to presentation. Patient had positive history of RA from 15 years ago and she used oral prednisolone 5mg/day irregularly. No other significant past medical history was found. The visual loss was profound associated with minimal pain. Her best corrected visual acuity was20/200 and 20/25 in the right (affected) and left (unaffected) eyes, respectively. On examination, the relative afferent pupillary defect (RAPD) was +2 in the right eye. No cellular reaction was seen in the anterior chamber or vitreous cavity. In addition, retinal examination revealed optic disc blurring, patchy white discoloration over retinal nerve fiber bundles, diffused horizontal choroidal folding and macular edema with incomplete stellate shape. [Fig-1] Meanwhile, no significant finding was documented in the left eye. Optical Coherence Tomography (OCT) was requested showing sub-retinal

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and intra-retinal fluid collection plus retinal pigment epithelium wrinkling. [Fig-2] B-scan ocular ultrasonography from right eye showed optic nerve swelling with scleral thickening and posterior echolucent halo as characteristic "T" sign due to tenon fluid collection. [Fig-3 A)

An initial laboratory panel with the primary focus on bacterial and rheumatologic evaluation was requested. Results of the laboratory panel showed lymphocytosis with increased absolute lymphocyte count (4200 lymphocytes/µL), CRP and ESR were low. Meanwhile rheumatologic markers including Perinuclear Anti-Neutrophil Cytoplasmic Antibodies (P-ANCA), Cytoplasmic Antineutrophil Cytoplasmic Antibody(C-ANCA), Rheumatoid Factor (RF), Anti Nuclear Antibody (ANA), C3, C4, Anti-double stranded DNA (Anti-dsDNA) were within normal range.

The Angiotensin Converting Enzyme (ACE) serum level was within normal limits and serum viral PCR and blood bacterial culture were negative. Patient tuberculin skin test, serum venereal disease research laboratory (VDRL) and anti-toxoplasmosis antibodies were negative. Nevertheless, laboratory tests revealed an enhanced level of anti-CCP (512 U/ml-normal range is less than 20 U/ml).

Based on the above, oral prednisolone (1mg/kg/day) plus azathioprine (100mg/day) were administered. In 20 days, patient reported significant visual improvement, although choroidal folds were still existed but they were decreased from baseline examination. [Fig-1B] Notable resolution of sub-retinal fluid and intra-retinal edema was seen in her OCT study. [Fig-2] Likewise, sonography revealed an improvement in scleral thickening. [Fig-3B] After 3 months, oral prednisolone reduced to 5 mg/kg/day and azathioprine reduced to 50 mg/day, and her vision improved to 20/40 and patient is being followed by an ophthalmology and rheumatology service.

Fig.1- Wide field optos fundus photograph of the right eye, (A) Shows mild optic disc blurring (arrow head) and diffuse horizontal choroidal folds (arrows). (B) Twenty days after treatment, optic disc border is sharper and choroidal folds are decreased from baseline image.

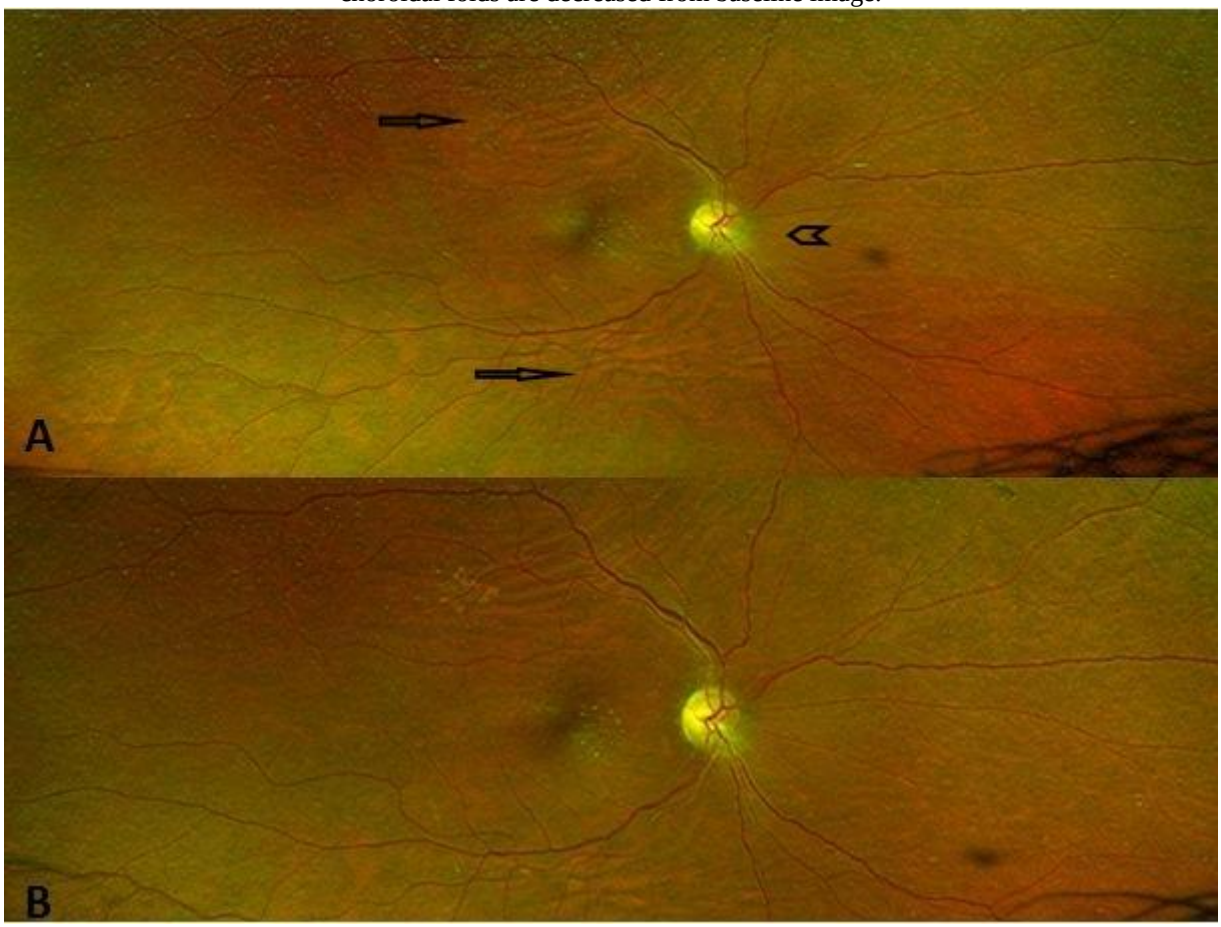


Fig.2-Optical coherence tomography of right eye, (A) Shows increased retinal thickness due to sub-retinal and intra-retinal fluid collection (arrow). (B) Twenty days after treatment, sub- retinal and intra-retinal fluid disappear.

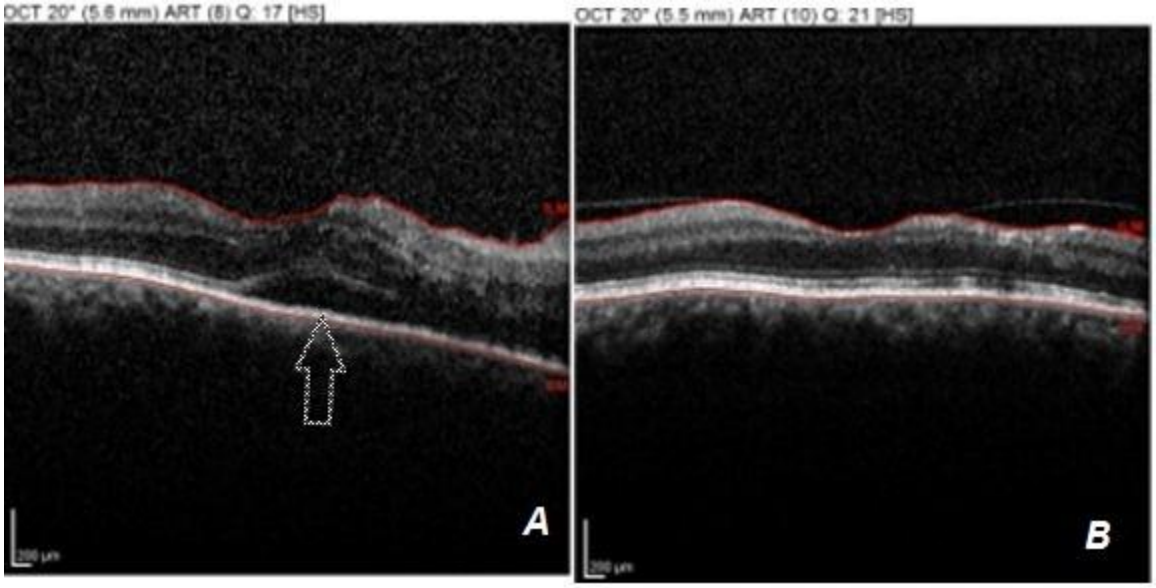
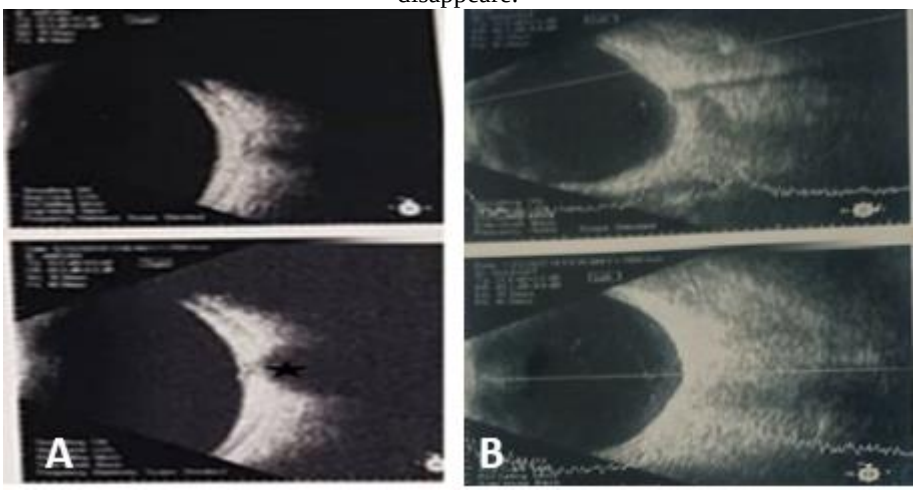


Fig.3- B-scan ocular ultrasonography from right eye before (A) and after (B) treatment show increase posterior scleral thickening and characteristic "T" sign(asterisk), after treatment scleral thickening decrease and "T" sign disappeare.



3. Discussion

Posterior scleritis is a rare type of scleral inflammation that affecting the sclera and tenon's capsule behind the pars plana that result in different symptoms in adjacent structures in the posterior globe such as choroid, retina and optic disc(1). In many cases the etiology is unknown, in nearly 45% of cases, associated with variety of Immune-Mediated Systemic Inflammatory Diseases (IMIDs) including but not restricted to RA, Wegener's granulomatosis, polyarteritisnodosa, sarcoidosis, and inflammatory bowel diseases(2). RA with the incidence of 33% is a most common underling disease in patients presenting with scleritis (3). Infectious causes such as syphilis and tuberculosis are account for less than 10% of scleritis. Middle-aged women especially in cases of connective tissue disorders are more frequently affected than men (2).

Pain behind eye or during eye movement and loss of vision are the main symptoms, conjunctival chemosis and injection, anterior chamber or vitreous reaction, macular edema and exudative sub-retinal fluid may be observed (2). Ultrasonography B-scan is the main modality to diagnose posterior scleritis, it can show scleral thickening and fluid collection in posterior tenon space. Multimodal imaging such as fluorescein and indocyanine green angiography,

Optical coherence tomography can also be used for diagnosis. Sometimes treatment of posterior scleritis is challenging, topical steroids and nonsteroidal anti-inflammatory drugs (NSAIDs) are not effective alone, so systemic treatment should be started initially, oral NSAIDs, corticosteroids and immunosuppressive drugs are used (4).

As it mentioned, posterior scleritis is a pathology commonly associated with rheumatologic diseases namely RA. Traditionally, Rheumatoid Factor (RF) is used for the diagnosis of RA. RF is the autoantibody against the Fc portion of Immunoglobulin G, first detected in patients with RA (3, 5).

Besides, anti-CCP is autoantibodies with the affinity directed against citrullinated peptides and proteins. Such peptide markers are found in abundance in cases with RA (6, 7). What's more, anti-CCPs are considered as more sensitive and specific indicators of systemic involvement in RA than RF. Now, anti-CCP antibody is applied as the accurate diagnostic marker especially in patients with early-onset RA. Such antibody also retains the potential to predict the future occurrence of the disease in a form of undifferentiated arthritis. American College of Rheumatology reported the sensitivity and specificity of anti-CCP reactivity for RA patients as 73% and 100%, respectively (8).

Based on a report by Itty et al, patients who had concomitant anti-CCP and RF antibodies experienced more severe ocular involvement in compare to ones who were negative for these factors (9). Indeed, the ophthalmic complications are mostly faced in the later phases of RA when both classes of such antibodies turn to be positive (10).

Despite anterior scleritis, ocular manifestations and etiologies of posterior scleritis are more diverse. Maggioni et al, reported a case of posterior scleritis presenting with hemi-facial pain, all immunological exams were normal in their patients, they emphasized the importance of ultrasound in diagnosis (11). Some studies reported cases of posterior scleritis due to tuberculosis (12, 13). Che et al, recently reported a Human Immunodeficiency Virus (HIV) affected patient who was diagnosed as presumed immune recovery posterior scleritis that was unassociated with infectious causes or rheumatologic disorders (14). In our patient case, the only positive systemic work up was enhanced level of anti-CCP that was associated to her past systemic rheumatologic disease.

Nonetheless, the above scenario would possibly pose no diagnostic challenge while yielding a prognostic value. As such, in rare instances where we face severe ophthalmic complications in the presence of negative RF, evaluating the anti-CCP status is deemed to be of prognostic significance.

Arguably, in the above clinical vignette, the patient could have portraited idiopathic choroidal folds with superimposed scleritis. On the other hand, neuro-retinitis would need to be considered in such a situation. Despite the above possibilities, very high titers of such specific marker are strongly suggestive of rheumatoid arthritis and therefore posterior scleritis rested on the top of our list of differential diagnoses.

4. Conclusion

In conclusion, Elevated serum Anti-CCP titer may be considered as risk factor for inflammatory scleritis in patient with rheumatoid arthritis.

The most important limitation of this study is the small number of samples, case-report studies do not identify a cause-and-effect relationship, but they are a starting point for larger investigations.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Shiraz University of Medical Sciences. Informed consent was obtained from patient and necessary explanations were given to her regarding the study objectives. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Consent for publication

Written consent to publish this information was obtained from study participant.

Availability of data and materials

Data is available upon request from author.

Competing interests

None of the authors has conflict of financial and non-financial interest with the submission.

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Authors' contributions

MF: conception and design, acquisition. MKJ: conception, design, contributed in drafting, writing and responsible for critical revision. AA and ZF: design, acquisition and interpretation of data and writing.

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