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CASE REPORT

Neuroretinitis following typhoid fever in a 55-year-old female: case report

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ABSTRACT

Neuroretinitis (NR) is an inflammation of the optic nerve and the neural retina. NR is diagnosed clinically, and it is characterized by blurring of vision (BOV), optic disc swelling, and macular star exudates. Spontaneous resolution of NR is possible, but corticosteroids help in hastening recovery. Rarely, Salmonella typhi infection may produce an immune-mediated reaction that can cause NR. Immune-mediated retinitis occurs 3 to 6 weeks after the febrile period of a typhoid infection. We present the case of a 55-year-old female with a two-week history of painless, unilateral BOV occurring five weeks after the initial febrile episode of a typhoid infection. A diagnosis of NR was made after fundus examination on the affected eye showed optic disc edema and macular star exudates. An eight-week course of corticosteroid treatment afforded partial resolution of the disc edema and significant reduction in the macular exudates, and improved the patient's vision after six months.

Keywords. immune-mediated retinitis, *Salmonella typhi*, oral corticosteroids, optical coherence tomography

INTRODUCTION

Typhoid fever is caused by Salmonella typhi (S. typhi) or paratyphi, an infectious bacteria known to affect the blood and intestinal tract, causing gastroenteritis, enteric fever, and septicemia.[1] An immune-mediated reaction, which rarely follows S. typhi infection, can occur as a condition that affects the retina. Immune-mediated retinitis may occur following a recent history of typhoid fever, ranging from 3 to 6 weeks after a febrile episode.[2-4] Despite the fact that typhoid-related ocular manifestations has been reported as early as 1893, there is a paucity of literature pertaining to its occurrence.[1 4]

Neuroretinitis (NR), an inflammation of the optic nerve and the neural retina, is characterized by a triad of blurring of vision (BOV), optic disc swelling, and macular star exudates.[5-7] The diagnosis of NR is clinical—based on a comprehensive history taking and eye examination—however, the specific etiology of NR may warrant further laboratory tests and/or diagnostic imaging.[8]

The usual imaging findings that support NR are: macular sensory detachment on optical coherence tomography (OCT),[1 9] macular thickening, neurosensory detachment, and abnormal choroidal blood flow on optical coherence tomography angiography (OCTA), and increased choroidal thickness and dilated choroidal vasculature on deep range imaging (DRI).[10] The management of NR commonly includes oral corticosteroids.[10 11]

The rarity of NR following typhoid fever often causes delay in its diagnosis and treatment and requires a high index of suspicion.[12] We report the case of a 55-year-old female who presented with a sudden onset of painless BOV thirty-six days after the start of a febrile episode and was successfully treated with oral steroids.

CLINICAL FEATURES

A 55-year-old female consulted at our outpatient clinic with a two-week history of sudden-onset, painless BOV of the left eye. Thirty-six days prior to the initial onset of BOV, the patient complained of intermittent fever and occasional diarrhea. A private physician diagnosed her to have a urinary tract infection and prescribed oral co-amoxiclav. The patient's symptoms did not improve, so she was admitted at a local

IN ESSENCE

A clinician needs a high index of suspicion to diagnose neuroretinitis, owing to the rarity of the condition. Diagnosis entails a comprehensive history-taking and detailed eye examination.

In this case report, we describe the case of a 55-year-old female who presented with a sudden onset of painless blurring of vision of the left eye after a recent typhoid infection.

The patient's vision improved after an eight-week course of oral corticosteroid treatment.

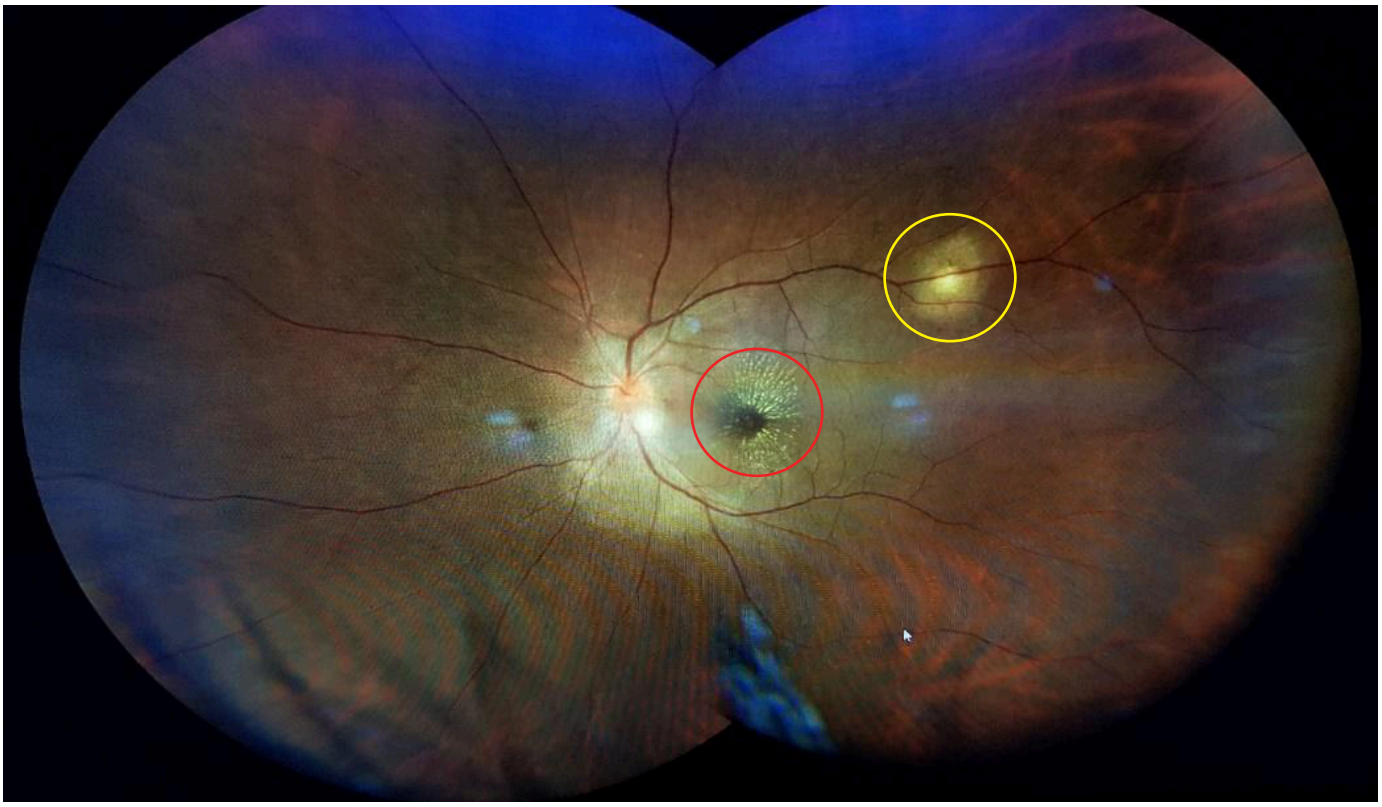

Figure 1 Intraoperative findings of the hepatic mass (A) and its adjacent structures. Lateral view with liver and gallbladder (B: yellow circle). Inferior attachment of the mass showing segments V and VI of the right lobe of the liver (C: green circle) and the porta hepatis (C: blue circle).

hospital where she was diagnosed and managed as having typhoid fever. Her diagnosis was confirmed by a positive Widal test, which showed significant titers for S. typhi 'O' and 'H' antigens. She was given intravenous ceftriaxone and subsequently discharged three days after admission, with oral ciprofloxacin as home medication. Two days postdischarge, the patient started to have BOV. The patient denied any recent history of eye trauma. She also denied the presence of diabetes mellitus or hypertension, or previous episodes of BOV. The patient did not experience any other symptoms—such as fever, abdominal pain, or diarrhea—along with the BOV. She has no known family history of glaucoma or hereditary dyschromatopsia. On initial ocular examination, visual acuity was logMAR 0.0 OD and logMAR 2 OS. Anterior segment findings were unremarkable and intraocular pressure for both eyes was within normal range. We noted a grade 1 relative afferent pupillary defect (RAPD) with dyschromatopsia and metamorphopsia on the left eye. Fundus examination of the left eye revealed a clear media with disc edema and macular star exudates. There were also areas of retinitis noted at the peripapillary area and the distal third of the supero-temporal arcade. (Figure 1). Fundus examination of the right eye was unremarkable. The rest of the physical examination findings were also unremarkable.

DIAGNOSTIC APPROACHES

The patient underwent blood workup, which was found to be negative for human immunodeficiency virus (HIV) and syphilis. Erythrocyte sedimentation rate was elevated at 57 mm/hr. The patient's complete blood count revealed a normal WBC count with mild neutropenia (44%; normal range: 55% to 75%). Liver function tests, chest x-ray, and peripheral blood smear were all unremarkable.

OCT of the left eye revealed a thickened perifoveal area and an accumulation of subretinal fluid with multiple hyperreflective foci in the outer plexiform layer (OPL), which signifies the presence of exudates. Hyporeflective areas, which suggest edema, are also seen in the outer neurosensory retina (Figure 2).

THERAPEUTIC APPROACHES

We started the patient on oral prednisone,

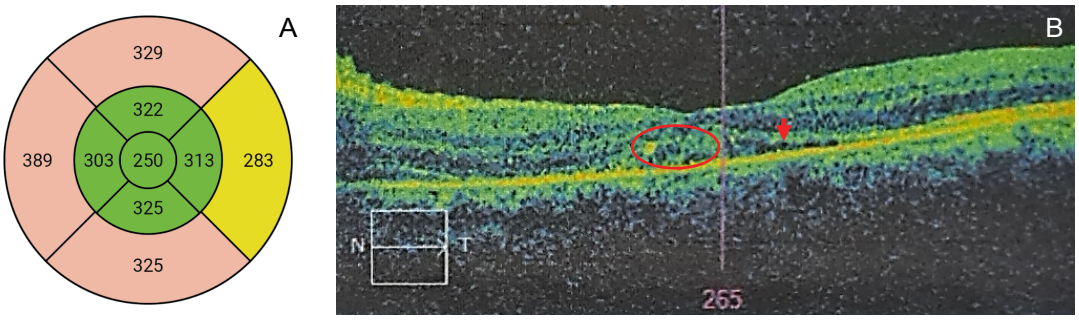

Figure 2 Optical coherence tomography (OCT) scan (Cirrus 6000®) of the left eye at presentation. Perifoveal area is thickened (A). There is accumulation of subretinal fluid with multiple hyperreflective foci in the outer plexiform layer, representing exudates (B: red circle). Hyporeflective areas are seen in the outer neurosensory retina suggestive of edema (B: red arrow).

initially at a dose of 50 mg per day, then gradually tapered weekly for eight weeks. We monitored the patient's visual acuity and color vision weekly. Signs of scotoma and metamorphopsia gradually resolved during follow-up. At eight weeks after initiation of corticosteroid treatment, the patient's visual acuity (logMAR 1) on the left eye improved. At six months post-initiation of treatment, the patient's visual acuity (logMAR 0.3) demonstrated great improvement. Signs of RAPD, dyschromatopsia, and metamorphopsia were absent in the sixth month. A fundus examination done at six months post-treatment revealed partial resolution of disc edema and residual macular exudates at the distal third of the supero-temporal arcade (Figure 3). OCT revealed partial resolution of the edema and residual exudates in the OPL. By this time, the patient noted an improvement in vision (Figure 4).

Figure 3 Image of the retina using the mydriatic/non-mydriatic retinal camera (Kowa VX 20®). Fundus photo of the left eye at six months post-treatment. There is partial resolution of disc edema with residual macular exudates at the distal third of the supero-temporal arcade.

DISCUSSION

Our patient presented with painless BOV 36 days after the initial febrile episode due to typhoid fever. A diagnosis of NR was established clinically based on the history of BOV and the findings of optic disc edema and macular star exudates on fundus examination. After an eight-week course of oral corticosteroids, the patient's vision significantly improved.

Typhoid fever is a potentially fatal multisystemic illness that is characterized by fever and other constitutional symptoms such as headache and abdominal pain.[13,14] S. typhi rarely affects any part of the eye either through direct infection or by an immune-mediated process.[1] Ocular manifestations may be observed during the acute stage or post-fever stage of typhoid fever. In the acute stage, ocular signs and symptoms may manifest as catarrhal conjunctivitis, iridocyclitis, vitritis, or optic neuritis.[11] Post-fever ocular signs may present as focal or multifocal retinitis with macular star, optic nerve edema, NR, or macular neurosensory detachment.[11]

The pathophysiology of NR following typhoid fever is based on the assumption that the microbial pathogen's retinal infil-

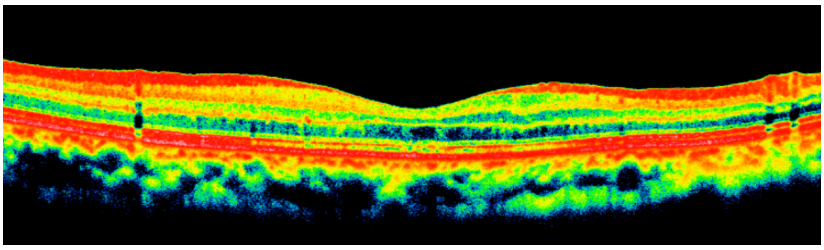

Figure 4 Optical coherence tomography (OCT) scan (Iptovue®) of the left eye six months after treatment, revealing partial resolution of the edema and residual exudates in the outer plexiform layer.

tration causes a cascade of immune-mediated responses that produce disturbances in the blood-retinal barrier. Another possible explanation for the NR after an infection is the presence of immune complexes, which can elicit an immune response that causes further tissue and/or vascular damage to the retina. Molecular mimicry, or homology between retinal and microbial peptides, leading to autoimmunity, is responsible for this damage.[1 10]

NR following typhoid fever is a clinical diagnosis based on a history of a recent typhoid infection,[9] acute BOV, optic disc swelling, and macular star exudates.[5-7] BOV is usually unilateral but can also be simultaneously or sequentially bilateral in 5% to 30% of cases.[15] Ocular findings may include a decrease in visual acuity, visual field defects, and oftentimes an ipsilateral RAPD.[7] The onset of ocular manifestations of post-fever retinitis may occur within days to weeks following a febrile episode.[11] NR that follows a typhoid infection, however, may manifest from 3 to 6 weeks after the onset of fever.[2-4]

The rarity of reports of NR following typhoid fever in literature and the unique ocular manifestations of the condition may delay the diagnosis and medical intervention. Hence, a clinician's high index of suspicion is of great importance to the approach of presenting symptoms.

The criterion standard for diagnosis of typhoid fever is culture and isolation, which has a specificity of 100%. Although not a very reliable method for detection of S. typhi due to its low sensitivity and specificity, Widal test, a serological test that measures agglutinating antibodies against lipopolysaccharide O and flagellar H antigens of S.typhi, can also be of value when culture is not readily available.[11 16-18] The patient's Widal test was positive, which confirms the diagnosis of typhoid fever prior to the appearance of symptoms of NR. At the time we saw the patient—five weeks following the initial febrile episode of a typhoid fever—her WBC count and liver transaminase levels indicated that the typhoid fever was not active.

Although spontaneous resolution of NR is possible, corticosteroids help in hastening recovery.[4 19] Various forms of corticosteroids —including topical, subconjunctival, subtenon, intravenous and oral corticosteroids—have been used.[1 11 20 21] Our patient was given an eight-week course of oral corticosteroids, which resulted in the resolution of the BOV after six months. OCT was used to monitor the status of the patient's macula and her response to corticosteroid treatment. Repeat OCT of the left eye showed resolution of the disc edema, and the improvement in the vision after six months was highly noticeable.

NR is generally a self-limiting disease that has a good prognosis in mild cases—showing spontaneous resolution of ocular symptoms in most patients.[1 10] However, some cases of NR may still have foveal thinning in instances of severe macular involvement, despite adequate corticosteroid treatment.[4] Patients with optic atrophy and retinal detachment may also have poor visual outcomes.[11]

We were presented with a middle-aged female who started to experience painless BOV five weeks after the initial febrile episode of typhoid fever. The patient was admitted for three days, treated with antibiotics, and prescribed an eight-week course of corticosteroid treatment. Serial OCT scans, which were used to monitor response to corticosteroid treatment, demonstrated a significant improvement in the patient's vision over a six-month period.

Contributors

CGM and RCG contributed to the diagnostic and therapeutic care of the patient in this report. Both of them acquired relevant patient data, and searched for and reviewed relevant medical literature used in this report. Both wrote the original draft, performed the subsequent revisions, approved the final version, and agreed to be accountable for all aspects of this report.

Patient consent

Obtained

Reporting guideline used

CARE Checklist
(http://www.care-statement.org/downloads/CAREchecklist-English.pdf)

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