

OPTIC NEURITIS OCCURRING IN PULMONARY TUBERCULOSIS ON TREATMENT AN IMMUNOLOGICAL REACTIONS?

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ABSTRACT

Background: Tuberculosis Immune Reconstitution Inflammatory Syndrome (TB-IRIS) is not an uncommon condition occur after initiation of anti-tuberculous drugs commencement. However, optic neuritis occurring in a pulmonary tuberculosis patient as an immunological phenomenon is not common. We report such a case that possessed a diagnostic challenge in a tuberculosis patient.

Materials and Methods: Case report

Result: A 63-year-old lady who was diagnosed as pulmonary tuberculosis (sputum AFB positive) was 4 months into treatment when she presented with painless blurring of vision on both eye of 4 days duration. The visual acuity reduced more markedly on her left eye. She also had scotoma involving upper part of her left visual field. On admission, patient had positive relative afferent pupillary defect over her left eye and fundus examination showed bilateral optic nerve swelling which was worse on the left. Both anterior segments were normal. An urgent CT scan showed no evidence of space occupying lesion and MRI examination was normal. She was started on intravenous methylprednesolon 250mg QID for 5 days and anti-tuberculosis (TB) treatment was continued. She was discharge with oral prednesolone of 1 mg per kilogram body weight daily on tapering dose over 8 weeks. Her optic nerve functions improved markedly since the third day of intravenous methylprednesolon and bilateral optic disc swelling reduced. Her anti TB treatment were continued for a year.

Conclusion: Optic neuritis in tuberculosis can occur in isolation, drug induced, resistant cases, or an immune reconstitution reaction.

Keywords: Optic neuritis, ocular tuberculosis, TB-IRIS.

1.0 Introduction

Optic neuritis in tuberculosis can occur as primary ocular tuberculosis, direct dissemination from intra-cranial tuberculosis or from adjacent ocular structures and drug toxicity (Ethambutol and Isoniazid). Rarely, it can happen as paradoxical response in Tuberculosis Immune Reconstitution Syndrome (TB-IRIS) in reported cases of tuberculous meningitis. However, case of pulmonary tuberculosis presented with optic neuritis as a paradoxical response has never been reported before.

2.0 Materials and Methods

Case Report.

3.0 Case Report

A 63-year-old lady who was a known diabetic had been diagnosed as pulmonary tuberculosis (sputum AFB positive). She was 4 months into treatment when she presented with painless generalised blurring of vision on both eye of 4 days duration. The visual acuity reduced more markedly on her left eye. She also had scotoma involving upper part of her left visual field.

Examination revealed visual acuity of 6/60 on her right eye and 4/60 on the left. There was impaired colour vision, light brightness and red desaturation on both eyes. Confrontation test revealed scotoma involving the left upper part of her visual field. Proper Humphrey Visual Field examination was unable to be done due to poor vision.

Patient had positive relative afferent pupillary defect over her left eye and fundus examination showed bilateral optic disc swelling which was worse on the left. There were present of moderate non proliferative diabetic retinopathy without macular oedema on both fundus. The vitreous was clear and no evidence of retinitis or choroiditis.

She had bilateral immature cataract but the rest of the anterior segment findings were unremarkable. An urgent CT scan showed no evidence of space occupying lesion and MRI examination was normal. Blood Investigations taken showed normal full blood count with erythrocytes sediment rate of only 20ml/h. Renal and liver function test were normal. Result for other infectious screening were normal.

She had completed daily regime of intensive phase of Ethambutol, Isoniazide, rifampicin and Pyrazinamide (EHRZ). The daily regime was still continue till the 3rd month due to persistent positive sputum smear of AFB. The regime was then reduce to biweekly dosage of Isoniazide and Rifampicin (continuation phase) on the 4th month after the smear become negative accompanied by improvement in the chest x-ray. Her anti-tuberculous treatment was started at a different health centre and was being follow up in a family medicine specialist clinic. She noted improvement of her chest symptoms whereby she had less cough, no more fever with night sweating and improvement of appetite and weight.

Patient was started on intravenous methylprednesolon 250mg QID for 5 days and subsequently started on oral prednesolon 1mg/kg daily. The scotoma over her left visual field

markedly reduced on the 3rd day of intravenous methylprednesolon and she completed total of 5 days regime. Both optic disc swelling reduced slightly after the completion of her intravenous methylprednesolon.

The bilateral optic disc swelling markedly reduce after 6 weeks with her visual acuity improved to 6/30 on the right and 6/45 on the left on follow up review. Oral prednesolone was given over a slow tapering dose for 6 weeks. Her anti-tuberculosis regime was continue to complete one year. She was referred to physician for co-management of her blood sugar upon starting steroid

Figure 1: Bilateral Optic Neuritis On Presentation

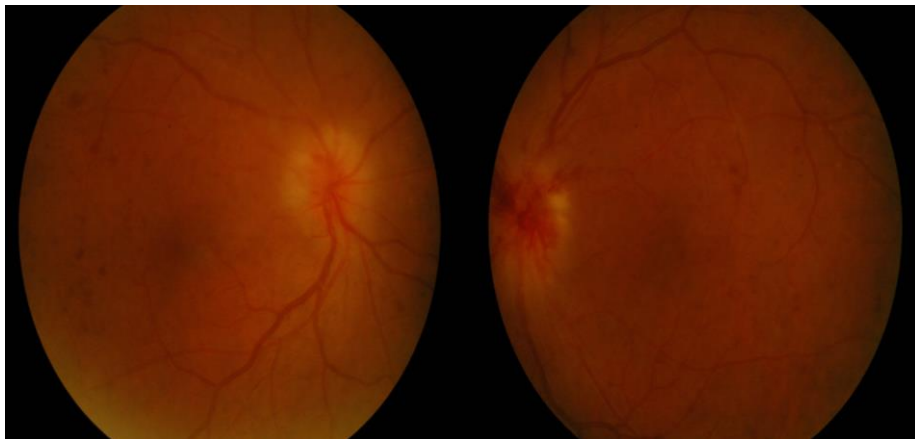
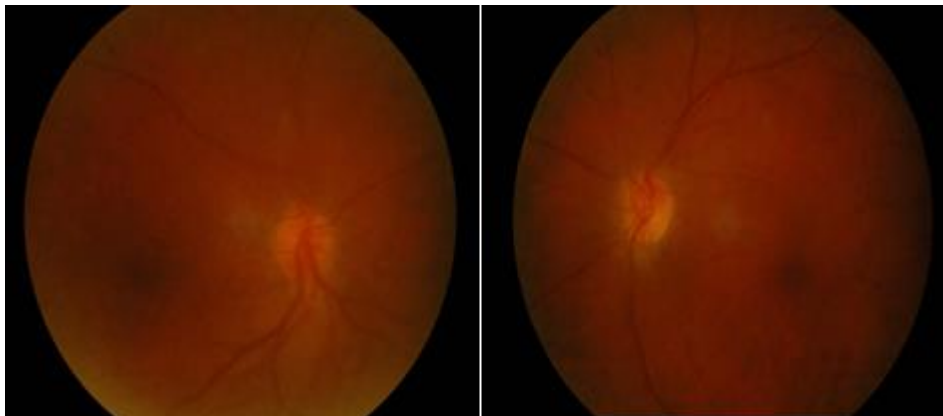


Figure 2: Optic disc on 1 month follow-up showing marked improvement.



4.0 Discussion

This case possessed a diagnostic challenge to us as there are few possibilities to consider regarding optic neuritis in this patient. The patient was a confirm case of pulmonary tuberculosis and had completed active phase of her treatment of Ethambuthol, Isonizide, Rifampicin and Pyrazinamide (EHRZ) for 3 months. Her review at 2 months upon starting the anti-tuberculosis treatment showed persistent AFB smear positive, hence unlike the usual two

months of intensive phase, this regime was continue for another 1 month. She was converted to continuation phase of anti-tuberculous drug after her sputum smear was negative and the chest x-ray improved. The blurring of vision only started until about 4 weeks after stopping Ethambutol. In an old study, toxicity of Ethambutol developed after 2 months of taking the drug (Brobowitz, 1966) and it was also dose dependent (Leibold, 1966). In previous report, the reversibility of the toxicity varies (Tsai, 1997; Kumar, 1993). Although Ethambutol is known for its side effect on the optic nerve, our patient had no symptoms when she was on the drug even after one month stopping the drug. Even in toxicity case, the treatment involved was to promptly stop the drug in order to stop the progression of optic neuropathy and allow for the recovery of the toxicity.

The patient was also on isoniazid, which although is rare, had also been associated with optic neuropathy (Karmon, 1979; Kass, 1957). The toxicity maybe enhanced in patients with co-morbidities like end stage renal failure requiring dialysis (Kocabay, 2006) and malnutrition (Kass, 1957). However, optic neuritis had also been reported in a case of tuberculous meningitis following the use of isoniazid (Keeping, 1955; Kulkarni, 2006). Apart from her diabetes, our patient did not have other co-morbidity and the renal function was normal.

We are also considering the possibilities of development of multidrug resistant to anti-tuberculosis drug. In other words, we are possibly dealing with pulmonary tuberculosis which already disseminated into the central nervous system and involve the optic nerve. There are lack of other signs of ocular involvement pertaining to intra-ocular tuberculosis. Apart from the swollen optic disc on both eyes, other changes were more of non-proliferative diabetic retinopathy without macula oedema. There was no choroiditis or retinitis to suggest that this is an intra-ocular tuberculosis. The most common findings of confirmed intraocular tuberculosis were presence of choroidal lesion or more specifically granuloma (Sheu, 2001). If choroidal findings were present, it may be the early sign of disseminated diseases, which was lacking in our patient.

Tuberculous optic neuritis dissemination from distant primary site had been reported in a case report (Cheng, 2007), which improved with commencement of antituberculous drugs. However, we think that this is not likely the case due to the improvement of the chest symptoms evidence by radiology investigation as well as sputum smear before the commencement of the continuation phase of anti-tuberculosis treatment.

Hence, we come to a conclusion that we may actually dealing with immunological- mediated response, more specifically tuberculosis- immune reconstitution inflammatory syndrome (TB-IRIS). This condition is define as paradoxical worsening or recurring of a pre-existing tuberculous lesions, or development of new lesions in a patients who is getting an effective anti-tuberculous treatment regime, during or even after completing treatment. (Cheng, 2002; Cheng, 2007) Strict criteria should be used in order to diagnosed these syndrome (Geri, 2013).

1. initial improvement of TB-related symptoms and/or radiographic findings after adequate anti-TB treatment for a certain time;
2. paradoxical deterioration of TB-related symptoms and/or radiologic findings at the primary or at new locations during or after anti-TB treatment;
3. absence of conditions that reduce the efficacy of anti-TB drugs (e.g., poor compliance, drug malabsorption, drugs side effects);

4. exclusion of other possible causes of clinical deterioration.

Our patient was possibly having paradoxical reactions on the treatment itself. The exact pathogenesis is still not fully understood, however the reactions is thought to occur due to massive release of mycobacterial antigen from the dead mycobacterium following commencement of anti-tuberculosis, strengthening of host immune response as well as decreased in immunosuppression (Meintjes, 2012). The reactions occur due to complex interactions of the host's immune system as well as the maycobacterial antigens itself.

Since this condition was related to immune reconstitution reaction, we started the patient on intravenous methylprednesolon following the optic neuritis treatment trial (ONTT) regiment of 250mg QID but the treatment was continued to five days due to its atypical presentation of optic neuritis. Patient responded well and we decided to continue with slowly tapering dose of oral prednesolon with careful monitoring of her condition for improvement as well as side effect of steroid or possible deterioration. The symptoms improved after starting on steroid. Although there is still some residual decrease visual acuity, we think that it was contributed by the present of immature cataract rather than the optic nerve function itself.

There is no consensus yet available for treating TB-IRIS. In a study, approximately half cases of tuberculous lymphadenitis with TB-IRIS resolved spontaneously (Cho, 2009). In some patients with lymph node, air- ways or soft tissue TB-IRIS, prolonged antituberculosis treatment may be required but the optimal treatment duration is unclear. Most patients show clinical improvement in the two months following antituberculosis treatment (Cheng,2007).

Systemic corticosteroid of 4-6 weeks improved the outcome in certain form of TB-IRIS (Meintjes, 2012; Vidal, 2005). A double blind, randomized, placebo-controlled clinical trial was performed in patients with paradoxical TB-IRIS showed that prednisone significantly reduced days of hospitalization and outpatient therapeutic procedures, more rapid improvement of symptoms, better quality of life score and improvement in chest radiography (Meintjes, 2010).

5.0 Conclusion and recommendation

Optic neuritis in tuberculosis can occur in isolation, drug related, resistant cases or in our case as an immune reconstitution reaction. Tb-IRIS although is rare but can occur following administration of anti-tuberculous drug regimen. Through examination and investigations needed to exclude other life or visual treating conditions before starting any immunomodulatory treatment to reduce mortality and morbidity related to this condition and fasten recovery.

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Declaration

The authors declare that the above has not been published or submitted for publication in any other journal. There is no conflict of interest on this article.

Authors contribution

The 1st and 2nd author involved directly in the managementg of the patient . The 1st author prepared the manuscripts with supervision of 2nd and 4rd author. The 3rd author provide consultation with regards to the imaging studies.

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