



Tubercular Optochiasmatic Arachnoiditis: A Case Report with Current Therapeutics and Management

Satish Swain¹  Akansha Didwania¹ Abhishek Anand² Upendra Baitha¹

¹ Department of Medicine, All India Institute of Medical Sciences, New Delhi, India

² Department of Neurology, All India Institute of Medical Sciences, New Delhi, India

Address for correspondence Upendra Baitha, MBBS, MD, Department of Medicine, All India Institute of Medical Sciences, 4th Floor Teaching Block, Ansari Nagar, New Delhi 110029, India (e-mail: drupendraraj14@gmail.com).

Libyan Int Medical Univ J 2023;8:3–7.

Abstract

Central nervous system tuberculosis (CNS TB) involves the brain parenchyma, meninges, and spinal cord. The primary pathology in CNS TB includes thick basal exudates leading to intense meningeal inflammation, vasculitis, and hydrocephalus. When these exudates and inflammation predominantly involve the structure in and around suprasellar cistern region, it results in a condition called optochiasmatic arachnoiditis (OCA). OCA is one of the cataclysmal complications of CNS TB, leading to vision loss. A previously healthy young woman came to our center with the complaints of low-grade fever, headache, weight loss, and visual obscuration. For further evaluation, she underwent lumbar puncture, and based on cerebrospinal fluid analysis, she was diagnosed with CNS TB and was promptly started on antitubercular therapy along with steroid. A contrast-enhanced magnetic resonance imaging of the brain and orbit showed OCA. For OCA, she was given pulse-dose dexamethasone along with intrathecal hyaluronidase with which there was marginal improvement in vision. Management of OCA can be very challenging with unsatisfactory response. Many agents such as pulse steroid, intrathecal hyaluronidase, thalidomide, tumor necrosis factor alpha inhibitors, and cyclophosphamide have been used with inconsistent results. We have also done a review of the literature for the current evidence and newer therapeutics available for the management of OCA.

Keywords

- ▶ optochiasmatic arachnoiditis
- ▶ CNS tuberculosis
- ▶ steroid
- ▶ tuberculosis

article published online
April 20, 2023

DOI <https://doi.org/10.1055/s-0043-1768222>.
ISSN 2519-139X.

© 2023. The Author(s).

This is an open access article published by Thieme under the terms of the Creative Commons Attribution License, permitting unrestricted use, distribution, and reproduction so long as the original work is properly cited. (<https://creativecommons.org/licenses/by/4.0/>)
Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

ملخص المقال باللغة العربية

التهاب العنكبوتية السلي - تقرير حالة مع العلاجات والعلاجات الحالية

المؤلفون:

Satish Swain¹, Akansha Didwania¹, Abhishek Anand², Upendra Baitha¹

Department of Medicine, All India Institute of Medical Sciences, New Delhi 1

Department of Neurology, All India Institute of Medical Sciences, New Delhi 2

المؤلف المسؤول: Upendra Baitha البريد الإلكتروني- drupendraraj14@gmail.com

يشمل مرض سل الجهاز العصبي المركزي (CNS TB) كل من النسيج الحشوي للدماغ (البرنشيمة) والسحايا والحبل الشوكي. وتعتبر التهاب العنكبوتية البصري (OCA) مضاعفة كارثية لسل الجهاز العصبي المركزي مما يؤدي إلى فقدان البصر.

جاءت شابة كانت تتمتع بصحة جيدة في السابق إلى مركزنا وهي تشكو من انخفاض درجة الحرارة والصداع وفقدان الوزن وتعتيم بصري. ولمزيد من التقييم خضعت المريضة لثقب قطني، واستناداً إلى تحليل السائل الدماغي الشوكي تم تشخيص مرض السل في الجهاز العصبي المركزي، وبدأ على الفور العلاج المضاد للسل بمجموعة الستيرويد. ولمزيد من البحث قمنا بإجراء الرنين المغناطيسي لمدار الدماغ الذي أظهر التهاب العنكبوتية البصري. بالنسبة لسل الجهاز العصبي المركزي، تم إعطاء المريضة جرعة نبضية من ديكساميثازون جنباً إلى جنب مع هيالورونيداز داخل القراب، هذا العلاج سبب تحسن هامشي في الرؤية.

في الغالب يكون علاج سل الجهاز العصبي المركزي صعباً للغاية مع نسبة استجابة غير مرضية. تم استخدام العديد من الطرق مثل الستيرويد النبضي، والهيالورونيداز داخل القراب، والثاليدوميد، ومثبطات عامل ألفا للنخر الورمي، وسيكلوفوسفاميد مع نتائج غير مرضية. هذه المقالة راجعت أدبيات الأدلة الحالية والعلاجات الأحدث لسل الجهاز العصبي المركزي.

الكلمات المفتاحية: سل الجهاز العصبي المركزي، التهاب العنكبوتية البصري، هيالورونيداز داخل القراب، ديكساميثازون، فقدان البصر

Introduction

Central nervous system tuberculosis (CNS TB) is a form of extrapulmonary TB primarily involving the brain parenchyma (tuberculoma and abscess), meninges (meningitis), and spinal cord (spinal tuberculoma and arachnoiditis). The exact prevalence of CNS TB is not known, but it is estimated to be around 1 to 5% of total TB cases. Initially, *Mycobacterium* bacilli acquired by inhalation of aerosol droplets colonize the macrophages in the alveoli and later, via hematogenous dissemination, establish themselves in the brain or meninges as tuberculous foci/tubercles (Rich focus).¹ The rupture of Rich focus into the subarachnoid space is the key in the development of CNS TB. The clinical picture of CNS TB is a result of an intense inflammatory reaction to the tubercular bacilli leading to thick basal exudates, vasculitis, and hydrocephalus. All forms of CNS TB are associated with high incidence of mortality and long-term disability.² Optochias-

matic arachnoiditis (OCA) is one of such catastrophic complication of tuberculous meningitis (TBM) leading to irreversible vision loss unless intervened timely. Rapid diagnosis and prompt initiation of antitubercular therapy (ATT) are of paramount importance to prevent complications in TBM.

Case Presentation

A woman in her early 20s presented to us with the complaints of low-grade fever and holocranial headache for 2 months. The patient also gave a history of visual obscuration in both the eyes for the last 20 days. On further probing, there was a history of loss of appetite with a weight loss of around 6 kg over the last 1 month. The patient was admitted for further evaluation. On general examination, she was conscious but confused, with a heart rate of 74 beats per minutes and blood pressure of 122/78 mm Hg. On

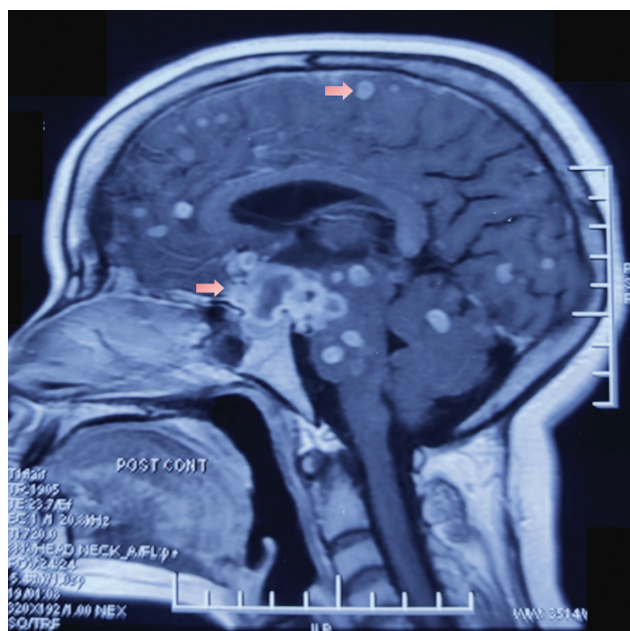


Fig. 1 Contrast-enhanced MRI of the brain (sagittal section) showing multiple conglomerated ring-enhancing lesions (red arrow) along with basal exudates in perisylvian and basal cisterns.

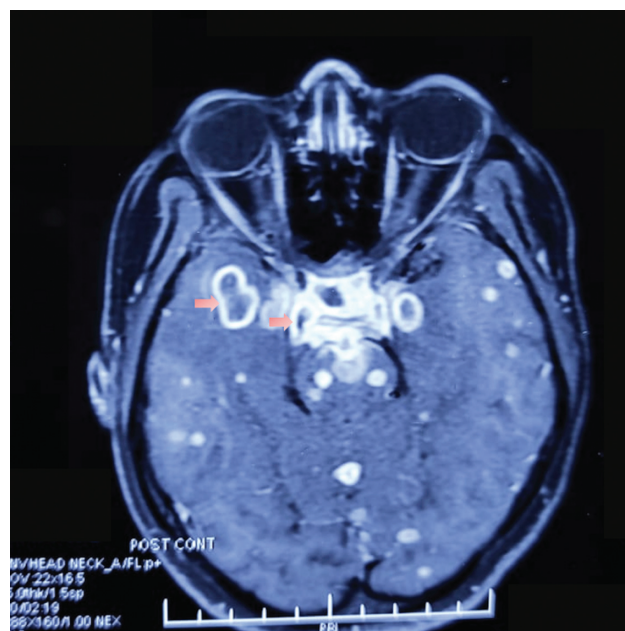


Fig. 2 Contrast-enhanced MRI of the brain (axial sections) showing lesions in perichiasmatic region and lesions in bilateral frontal, parietal, temporal, and occipital lobe (red arrows).

systemic examination, both her pupils were sluggishly reacting to light with absent perception of light on the left eye, and she could only perceive hand movement on her right eye. She was also not able abduct the left eye. Rest of the systemic examinations were within normal limits. There was no known contact history of tuberculosis and she had an unremarkable past medical history.

With this clinical background of fever and headache for more than 4 weeks, the differential diagnosis of chronic meningitis was made. To further delineate the pathology and to investigate into the vision loss, a contrast-enhanced magnetic resonance imaging (MRI) of the brain and optic nerve was conducted, which showed few conglomerated ring-enhancing lesion with intense basal exudates and perichiasmatic enhancement (–Figs. 1 and 2) highly suggestive of OCA.

Her hematological and biochemical parameters were under normal limits except an elevated erythrocytic sedimentation rate of 50 mm/hour. A bedside fundus examination was done, which did not reveal any papilledema; hence, we went ahead with lumbar puncture for cerebrospinal fluid (CSF) analysis. CSF showed a total cell count of 240 cells/ μ L with 80% lymphocytes and 20% polymorphs; protein was elevated (274 mg/dL) with a sugar of 50 mg/dL (with a corresponding blood glucose of 126 mg/dL). CSF for Gram stain, KOH, and Ziehl–Neelsen stain did not reveal any organism. Bacterial and fungal cultures of CSF were also sterile. CSF adenosine deaminase was elevated (14.5 IU/L) and later CSF GeneXpert was also positive (with rifampicin being sensitive). Viral marker (human immunodeficiency virus) for the patient was negative.

After confirming the diagnosis of TBM, the patient was promptly initiated on weight-based ATT (isoniazid, rifampicin, pyrazinamide, levofloxacin) with intravenous (IV)

steroid (dexamethasone). However, due to intense inflammation and presence of OCA, we planned for stepping up of the immunosuppression. After discussion with the neurologist and infectious disease team, pulse-dose steroid (methylprednisolone 500 mg IV) was initiated and given for 5 days. Gradual improvement in vision was observed on day 6 following the initiation of methylprednisolone. A single dose of intrathecal hyaluronidase (ITH) 1,500 IU was also given.

The patient remained admitted for 14 days in hospital. There was a very little improvement in vision (with perception of light on the left eye becoming positive) with the therapy. The patient was discharged on ATT and tapering doses of dexamethasone. We had planned for weekly ITH for the patient but the patient was lost to follow-up.

Discussion

OCA is one of the devastating complications of TBM. It involves the optochiasmatic region, which predominantly consists of suprasellar cistern and includes the major intracranial vessels and their anastomotic channels, the optic nerves, chiasm, and infundibular stalk.³ OCA results from intense meningeal inflammation along with thick basal exudates in this region. These exudates encase the optic nerve and the optic chiasma, leading to vasculitis and infraction. OCA may also develop as a paradoxical reaction after initiating ATT.⁴ Incidence of OCA varies between 8 and 15% among TBM patients. It presents with visual impairment, which is insidious in onset and gradually progressive (rarely acute onset). Vision loss is usually severe, which may be unilateral or bilateral with impaired pupillary response to light.⁵ MRI with contrast is a reliable method for diagnosis and demonstrates perichiasmatic enhancement with hypertrophy of chiasma and cisternal segments of the

optic nerves. Confluent enhancing lesions in the suprasellar cistern in the chiasmatic region have also been reported.³ Treatment of OCA is challenging and the response is not satisfactory. As in CNS TB, patients with OCA should be promptly initiated with ATT in combination with oral/IV steroids. Other treatment modalities that have been used with some success include pulse steroid, ITH, thalidomide, tumor necrosis factor alpha (TNF- α) inhibitors, and microsurgical decompression. We did a review of literature exploring the role and efficacy of different therapeutics used in the management of OCA. We enumerate the same in the following.

Pulse Steroid

A Cochrane systemic review in 2016 by Prasad et al has shown the mortality benefits of steroid in TBM, but the role of high-dose or pulse steroid in OCA is still unexplored.⁶ Steroid reduces the inflammatory mediators (such as interleukin-12, interferon gamma), which are responsible for OCA. It also modulates the matrix metalloproteinase, which plays a key role in the pathogenesis of TBM.⁷ There are no prospective studies or controlled trials that have looked into the efficacy of steroid (dose and duration) in OCA. Many authorities favors using methylprednisolone pulse (250–1,000 mg/day) for 3 to 5 days followed by tapering dose of steroid in OCA.⁸

Intrathecal Hyaluronidase

Evidence for the use of ITH in OCA has been limited to two small case series and multiple case reports. Hyaluronidase breaks down glucosaminidase bonds of hyaluronic acid and other mucopolysaccharides of the extracellular matrix, thus preventing organization of the exudates. Gourie-Devi and Satish had use ITH as an adjuvant therapy for OCA; in the study cohort, visual improvement was seen in three out of seven patients.⁹ However, this study was done back in 1980, where patients had received streptomycin, isoniazid, and thiacetazone as antitubercular drugs. In a recent retrospective review published in 2020 by Samal et al, 11 patients with OCA were given adjuvant ITH at a dose of 1,500 IU once a week for 10 weeks. Complete to partial visual improvement was seen in all patients.¹⁰ With these promising results, the role of ITH should further be explored in prospective randomized controlled trials. Hyaluronidase is inexpensive and an easily available drug and thus can be tried routinely as an adjuvant in clinical settings.

Thalidomide

Thalidomide is another immune-modulating agent that has been tried in OCA. It decreases the levels of TNF- α , which is the key mediator in OCA, in a dose-dependent manner. An initial randomized controlled trial on thalidomide by Schoeman et al was prematurely discontinued owing to serious adverse effect and death in the thalidomide arm. This was later attributed to the high dose of thalidomide (24 mg/kg/day) used in the trial.¹¹ In the subsequent years, using lower doses of thalidomide (3–5 mg/kg/day) has shown clinical benefits in OCA. The largest cohort of such patients was

published by van Toorn et al in 2021. Thirty-eight pediatric patients with life-threatening CNS TB (including OCA) were given adjunctive thalidomide therapy. Satisfactory outcome was seen along with complete recovery of vision in all OCA patients.¹² Thalidomide could be an excellent choice for OCA but has to be used with caution owing to its narrow therapeutic index and teratogenic nature. The optimal duration of therapy is unknown and depends on clinical and radiological response.

TNF- α Inhibitors

TNF- α inhibitors has been used in paradoxical reactions/immune reconstitution inflammatory syndrome, which is refractory to steroid or other immunosuppressant. The use of infliximab (5 mg/kg, three doses) in OCA has been limited to a handful of case reports, which have shown optimistic response without any adverse effect.¹³ TNF- α inhibitors may be used with cautions in refractory cases.

Cyclophosphamide

Cyclophosphamide has been tried with success in arachnoiditis involving the spinal cord and optic nerve/chiasm refractory to other modalities of treatment. In a small case series of four patients by Goyal et al, IV cyclophosphamide was used at a dose 500 mg/m² once a month for four consecutive months. Significant clinical and radiological responses were seen in all patients.¹⁴ Currently, a randomized controlled trial is underway to further explore the role cyclophosphamide in refractory arachnoiditis in CNS-TB.¹⁵

Although these drugs have shown efficacy in the management of OCA, none of them has been rigorously tried in controlled trials. The overall prognosis remains poor, and without treatment, it leads to irreversible vision loss. Poor outcome is seen when OCA is associated with multiple cranial nerve palsy, high CSF protein, female gender, and younger age of presentation.⁵ Currently, it is difficult to voice the efficacy of one agent over another due to lack of comparative studies, but we strongly believe that early diagnosis and prompt initiation of therapy has a better outcome. Selecting an agent should be based on the clinical profile, past medical history, adverse agent of the drug, and, most importantly, discretion of the treating physician.

Conclusion

Presence of OCA in patients with CNS TB has a serious therapeutic as well as prognostic implication. The treatment of OCA has remained a challenge and is generally unsatisfactory. Although steroids are most commonly used agents, recently tried drugs such as TNF- α inhibitors and cyclophosphamide have shown better results in nonrandomized trials. Early detection and prompt initiation of therapy is the key.

Ethics Approval

This study does not require ethics approval as it is a case report. Consent has been taken from the patient directly.

Author Contribution

S.S., A.D.: conceptualization. S.S., A.D., A.A., U.B.: involved in patient management. All authors contributed to the drafting of the initial manuscript. S.S. and U.B. proofread and reviewed the manuscript.

Funding

None.

Conflict of Interest

None declared.

Reference

- 1 Be NA, Kim KS, Bishai WR, Jain SK. Pathogenesis of central nervous system tuberculosis. *Curr Mol Med* 2009;9(02):94–99
- 2 World Health Organization. Global tuberculosis report 2021. Accessed April 23, 2022 at: <https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2021>
- 3 Garg RK, Paliwal V, Malhotra HS. Tuberculous optochiasmatic arachnoiditis: a devastating form of tuberculous meningitis. *Expert Rev Anti Infect Ther* 2011;9(09):719–729
- 4 Sinha MK, Garg RK, Anuradha HK, Agarwal A, Parihar A, Mandhani PA. Paradoxical vision loss associated with optochiasmatic tuberculoma in tuberculous meningitis: a report of 8 patients. *J Infect* 2010;60(06):458–466
- 5 Gourie-Devi M. Optochiasmatic arachnoiditis and neurotuberculosis: prognostic indicators and therapeutic strategies. *Neurol India* 2010;58(05):714–715
- 6 Prasad K, Singh MB, Ryan H. Corticosteroids for managing tuberculous meningitis. *Cochrane Database Syst Rev* 2016;4(04):CD002244
- 7 Rohlwick UK, Walker NF, Ordonez AA, et al. Matrix metalloproteinases in pulmonary and central nervous system tuberculosis—a review. *Int J Mol Sci* 2019;20(06):1350
- 8 Anupriya A, Sunithi M, Maya T, et al. Tuberculous optochiasmatic arachnoiditis. *Neurol India* 2010;58(05):732–735
- 9 Gourie-Devi M, Satish P. Hyaluronidase as an adjuvant in the treatment of cranial arachnoiditis (hydrocephalus and optochiasmatic arachnoiditis) complicating tuberculous meningitis. *Acta Neurol Scand* 1980;62(06):368–381
- 10 Samal P, Elavarasi A, Kumar A, et al. Intrathecal hyaluronidase in tubercular arachnoiditis: the unexplored adjuvant. *Infect Dis Clin Pract* 2020;28:230–233
- 11 Schoeman JF, Springer P, van Rensburg AJ, et al. Adjunctive thalidomide therapy for childhood tuberculous meningitis: results of a randomized study. *J Child Neurol* 2004;19(04):250–257
- 12 van Toorn R, Solomons RS, Seddon JA, Schoeman JF. Thalidomide use for complicated central nervous system tuberculosis in children: insights from an observational cohort. *Clin Infect Dis* 2021;72(05):e136–e145
- 13 Santin M, Escrich C, Majòs C, Llaveria M, Grijota M, Grau I. Tumor necrosis factor antagonists for paradoxical inflammatory reactions in the central nervous system tuberculosis: case report and review. *Medicine* 2020;99(43):e22626
- 14 Goyal V, Elavarasi A, Kumar A, et al. Cyclophosphamide therapy as an adjunct in refractory post-tubercular arachnoiditis. *Indian J Tuberc* 2022;69(03):325–333
- 15 ClinicalTrials.gov. Cyclophosphamide in the treatment of refractory proliferative arachnoiditis in CNS tuberculosis. Accessed March 23, 2022 at: <https://clinicaltrials.gov/ct2/show/record/NCT04620772>