Clinical Case Report

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# A case report of hepatitis B related optic neuritis treated with plasma exchange

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**Abstract**

**Introduction:** There are few studies focusing on Binocular hepatitis B related optic neuritis (HB-ON) and associated therapies are still limited. We present a case of HB-ON which has been cured with therapeutic plasma exchange (TPE).

**Patient concerns:** The patient was diagnosed as acute hepatitis B in hepatology and got a rapid loss of binocular visual acuity (2/100 in the right eye and no light perception in the left eye) after the onset.

**Diagnosis:** Hepatitis B related optic neuritis.

**Interventions:** Methylprednisolone and therapeutic plasma exchange.

**Outcomes:** The treatment of high dose methylprednisolone was not curative. After 5 TPE sessions, the patient's best corrected visual acuity (BCVA) returned to 20/20 in the right eye and finger counting (FC)/40 cm in the left eye. One month later, the visual acuity increased to 5/100 in the left eye.

**Conclusion:** This is the first case in which we used TPE to cure HB-ON. Also, it can demonstrate the relationship between HB-ON and immunopathogenesis. The case may provide an effective method for the treatment of hormone invalid and disabled ON in clinical practice.

**Abbreviations:** ADEM = acute disseminated encephalomyelitis, AQP4-Ab = aquaporin-4 antibody, AVH-B = acute viral hepatitis B, BCVA = best corrected visual acuity, CHB = chronic hepatitis B, CHB-AE = chronic hepatitis B with acute exacerbation, CNS = central nervous system, CNS-IDD = central nervous system inflammatory demyelinating diseases, CSF = cerebrospinal fluid, EHD = extrahepatic diseases, FC = finger counting, FERG = flash-electroretinogram, FVEP = flash-visual evoked potentia, GBS = Guillain-Barré syndrome, HB-ON = hepatitis B related optic neuritis, HBsAg = hepatitis B surface antigen, HBV = hepatitis B virus, IVMP = intravenous high-dose methylprednisolone, MS = multiple sclerosis, NLP = no light perception, NMOSD = neuromyelitis optica spectrum disorders, OCB = oligoclonal band, OCT = optical coherence tomography, ONTT = Optic Neuritis Treatment Group, RAPD = related afferent pupillary defect, RNFL = retinal nerve fiber layer, TPE = therapeutic plasma exchange.

**Keywords:** extrahepatic diseases, hepatitis B, optic neuritis, plasma exchange

## 1. Introduction

People (approximately 2 billion) infected by hepatitis B virus (HBV) account for one-third of the world population.[1] China has a hyperendemic for HBV and about 8% of the population is hepatitis B surface antigen (HBsAg) positive.[2] Although HBV primarily affects hepatocytes, it also shows that it can cause complications in other organs such as joints, muscles, central nervous system (CNS) and kidneys. Neurological disorders combined with hepatitis B include mononeuritis multiplex and CNS abnormalities in general, while few reports are available on optic neuritis (ON) as an extrahepatic diseases (EHD)

The management of acute ON followed the suggestion of the Optic Neuritis Treatment Group (ONTT). An intravenous high-dose methylprednisolone (IVMP, 1.0 g) was administered for 3 to 5 days, and then gradually tapered off.[3] Although most acute central nervous system inflammatory demyelinating diseases (CNS-IDD) resolve spontaneously or are corticosteroid-responsive, about 5% of those are refractory to steroids, necessitating rescue therapy.[4] For HB-ON, IVMP may not be applicable, especially in the active stage of HBV replication. According to previous research,[4] plasma exchange (PE) has been confirmed as an effective treatment for some steroid-refractory attack of CNS-IDDs such as multiple sclerosis (MS), neuromyelitis optica spectrum disorders (NMOSD), monophasic ON and acute disseminated encephalomyelitis (ADEM). This has similar pathogenesis with HB-ON. In the following, we present a case of HB-ON cured by PE.

## 2. Case report

Medical history: A 26-year-old male complained of headache and orbital pain after an acute hepatitis B. He presented a sudden binocular hypopsia combined with color vision changes. Three

Editor: N/A.

The authors declare that they have no competing interests.

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Medicine (2019) 98:18(e15432)

Received: 30 November 2018 / Received in final form: 25 March 2019 / Accepted: 2 April 2019

http://dx.doi.org/10.1097/MD.0000000000015432

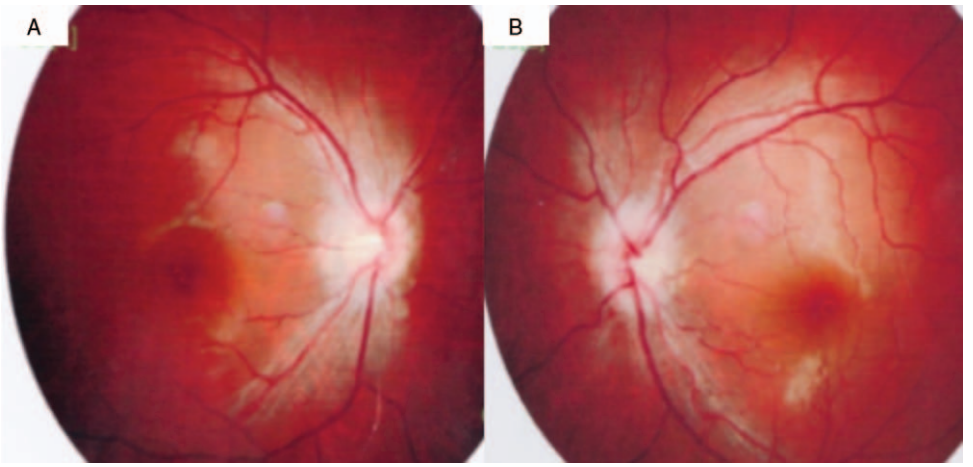


**Figure 1.** A and B: Fundus examination showed binocular optic disc swelling.

days after the onset, the visual acuity decreased to 2/20 in both eyes. Fundus examination showed binocular optic disc swelling (Fig. 1A and B). The patient was treated by methylprednisolone (1 g/day for 3 days) in another hospital and tapering off. Fifteen days after the onset, the vision dropped to 2/100 in the right eye and no light perception (NLP) in the left eye. Related afferent pupillary defect (RAPD) was positive in the left eye, the optic disc in both eyes looked pale and they are accompanied with the blurred edge. Orbital MRI revealed that the left optic nerve extended thickening. Long T2 signals were found in the intraorbital segment, intracanalicular segment and intracranial segment of the left eye and intraorbital segment of the right eye, which showed slight enhancement (Fig. 2A and B). Flash-visual evoked potential (FVEP) revealed a delay of the latency and a decrease of amplitude in both eyes. Flash-electroretinogram (FERG) found no abnormality. Visual field showed a diffuse defect in the left eye and a peripheral defect in the right eye. A disc swelling and thickening of the retinal nerve fiber layer (RNFL) showed in optical coherence tomography (OCT).

Laboratory examination: Laboratory tests showed positive results in serum HBsAg, HBeAg, HBcAb, and HBsAb; the level of serum HBV-DNA determination was 1.08E+7 IU/mL; serum plasma antithrombin III level was low (70%); liver functions tests showed slightly abnormal; erythrocyte sedimentation rate, serum levels of C-reactive protein and autoantibodies profile test were normal. Lumbar puncture showed the opening pressure was 194 mm$H_2O$. The cerebrospinal fluid (CSF) sample was acellular, the protein level was 217.8 mg/L and the glucose level was 3.9 mmol/L. Aquaporin-4 antibody (AQP4-ab, known as NMO-IgG) and oligoclonal band (OCB) in both serum and CSF showed negative.

Treatment: 5 sessions of TPE were carried out in every other day, and 20 units of plasma volume were exchanged for each

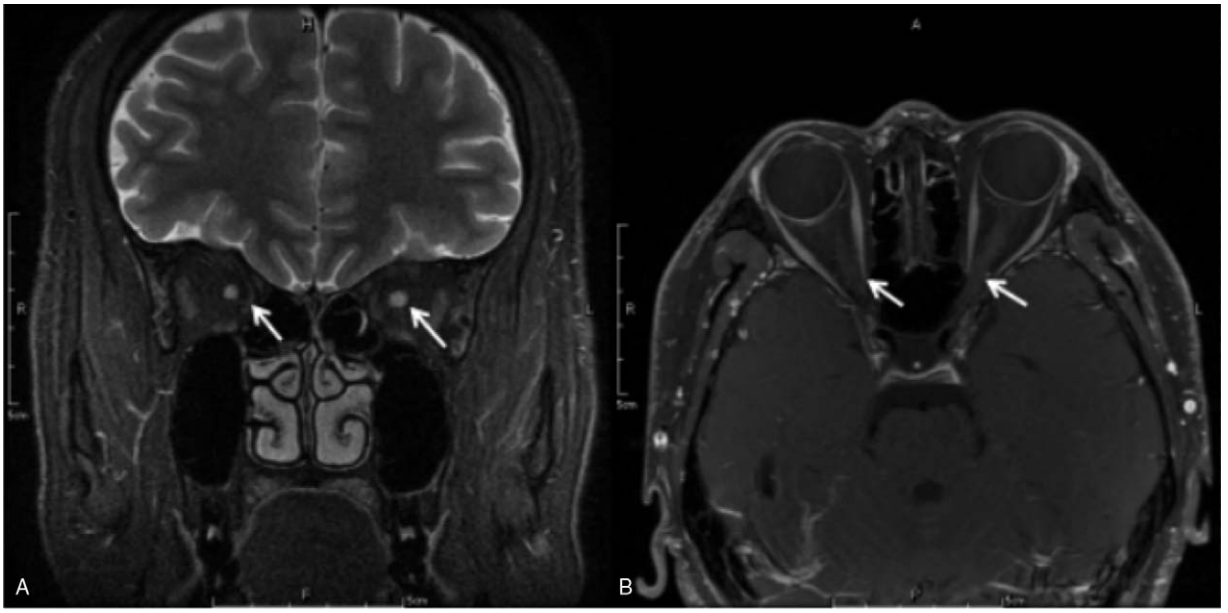


**Figure 2.** A: coronal scan, B: horizontal scan. Orbital MRI revealed long T2 signals in the intraorbital segment, intracanalicular segment and intracranial segment of left eye and intraorbital segment of right eye, meanwhile showed slight enhancement.

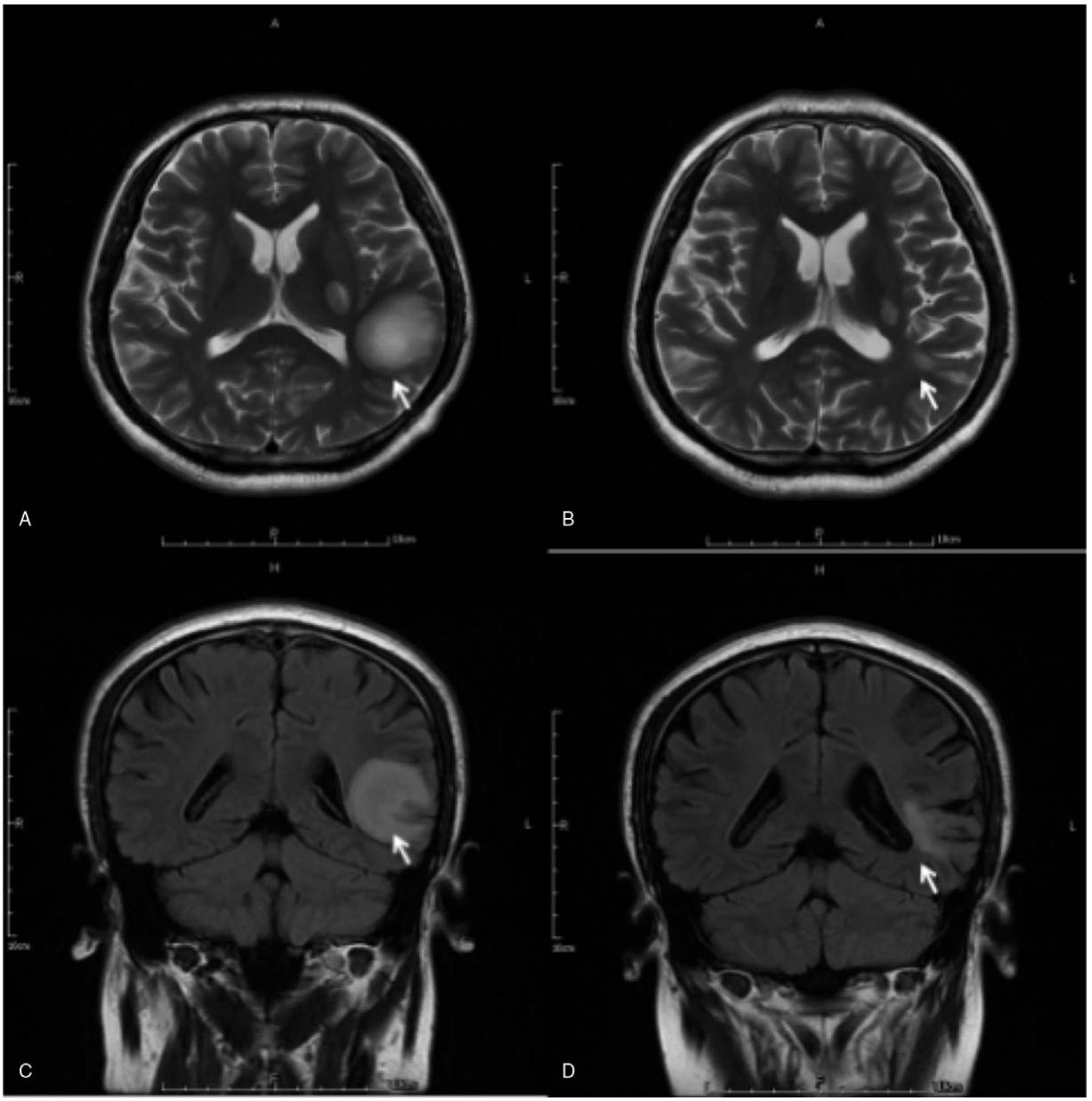


**Figure 3.** A: horizontal scan, C: coronal scan. Brain MRI showed multiple oval T2 signals in left basal ganglia region and left temporal lobe. The larger lesion which located in the left temporal lobe was 3.8 × 3.6 × 3.3 cm in size and showed incomplete annular enhancement. B: horizontal scan, D: coronal scan, 3 months after treatment.

session. After TPE, the level of serum HBV-DNA determination fell to 1.66E+6 IU/mL, the BCVA rose to 20/20 in the right eye and FC/40 cm in the left eye. One month after TPE, the BCVA of left eye increased to 5/100 and elevated to 8/20 four months later.

Unfortunately, 3 months after being discharged, the patient got a sudden appearance of dyslexia, hypomnesis and motor aphasia accompanied with a progressive sensory and motor deficit on the right side of the face and body. Laboratory tests showed that positive results were seen in serum HBsAg, HBeAb, HBcAb, and HBsAb; level of HBV-DNA determination dropped to 2.45E+1 IU/mL in serum and <20 IU/mL in CSF. Anti-GQ1b antibody, anti-GD1b antibody and anti-GM1 antibody in serum and CSF were negative. All other tests were normal. Brain MRI showed multiple oval long T1 and T2 signals in left basal ganglia region and left temporal lobe. Longer T2 signal could be found in the center of lesion, which was known as "fried egg sign." The larger lesion which was located in the left temporal lobe was 3.8 × 3.6 × 3.3 cm in size and showed incomplete annular enhancement (Fig. 3A and C). The visual field showed right lower quadrant defect in both eyes, which revealed significant improvement. Other ophthalmologic examinations showed no obvious changes.

A systemic high-dose corticosteroids treatment (1000 mg for 5 days, 500 mg for 3 days, 240 mg for 3 days and then changed to the oral administration) was given to the patient timely and took mycophenloate mofetil tablets (500 mg 2/day) orally at the same time. The patient's condition improved after hormonotherapy and almost returned to normal in the review of 3 months (Fig. 3B and D) and 1 year.

The study was approved by the PLAGH ethics committee, the ethical approval number was S2017–093–01. We obtained informed consent from the patient and his family.

## 3. Discussion

Optic neuritis combined with hepatitis B has been rarely reported, mainly including ON combined with chronic hepatitis B (CHB)[5] and HBV vaccination,[6] ON combined with acute hepatitis B or acute exacerbations of chronic hepatitis B have not been reported so far. In our case, the patient suffered an acute visual loss with eye pain and the RAPD in the left eye after hepatitis B. There was also a visual field defect and abnormal VEP. Meanwhile, slight enhancement could be found on orbital MRI. Other compressive, vascular, toxic, metabolic, infiltrative, and hereditary explanations were ruled out and other ocular diseases that may lead to vision loss were also ruled out, which meet the requirement of the ONTT[7] and the Chinese consensus on ON diagnosis.[8] AQP4-antibodies and OCB of the patient in serum and CSF showed negative, which can exclude NMO and MS basically, although about 30% of NMO cases are seronegative especially combined with HBsAg positive.[9] Moreover the positive findings of HBsAg, HBeAg, HBcAb, HBsAb, and the high level of HBV-DNA in serum (1.08E + 7 IU/mL) manifest the replication and infectivity of HBV.[10] Based on previous reports, HBVDNA levels are lower in acute viral hepatitis B (AVH-B) than in chronic hepatitis B with acute exacerbation (CHB-AE) and an undetectable HBVDNA is more likely to be seen in AVH-B than in CHB.[11] Kumar et al found low levels of HBVDNA <5.0 pg/mL (141,500 copies/mL) in 96% of AVH-B, while in patients with CHB-AE, the HBVDNA was >5.0 pg/mL ($P < .001$).[12] Therefore, according to our previous studies,[5] the diagnosis may be the CHB-AE related ON, but actually we cannot distinguish CHB-AE and AVH-B clearly. Eventually, we diagnosed the disease as HB-ON. There is no clear diagnostic criteria agreed on internationally so we named it HB-ON. In most clinical cases, we could not find the relationship between the ON and the HB, and they are mainly diagnosed as ON combined with HB. In this way, the patient suffered from a visual loss and an inflammatory lesion in the brain follow after an AHB, which confirmed the direct relationship between them. We would practice our theory on more cases for further confirmation.

ON combined with CHB-AE, as extrahepatic manifestations of acute HBV infection, may have the similar pathogenesis with other CNS-IDDs. The pathogenesis of acute HBV-related CNS-IDDs caused by whether the virus itself or an immune-mediated reaction works is uncertain. It has been established in the literature that the mechanism of Guillain-Barré syndrome (GBS) is direct assault or perhaps a vasculitis-related insult to the myelin sheath.[13] In this case, the patient suffered a CNS-IDDs which was combined with a lower HBV-DNA determination in CSF. It indicated that an immune-mediated reaction played a pivotal role.

It is known that TPE is an effective treatment in neurologic diseases whose autoimmunity plays an important role in the pathogenesis.[14] It appears to be effective in patients with CNS-IDDs who do not recover after IVMP treatment, such as the treatment of NMO. Plasmapheresis is becoming the preferred standard rescue therapy for NMO when high-dose IVMP treatment elicits only a weak response.[15] The patient received a steroid hormone aggressive therapy (methylprednisolone 1 g for 3 days and maintained with oral corticosteroids for one month) but had no effects, so we chose TPE as a preferred treatment according to the Guidelines on the Use of Therapeutic Apheresis in Clinical Practice-Evidence Based Approach from the Writing Committee of the American Society for Apheresis.[16] Although CHB-AE related ON has not been mentioned in any of its recommendations, it has the similar pathogenesis with the diseases mentioned above, which provides the theoretical basis for treating HB-ON by PE. Previous reports showed a rapid melioration in 33% to 37% of patients involving CNS-IDDs after TPE and the percentage elevated to 50% recently,[17] especially 50% to 67% in NMO patients.[18] We found an immediate visual improvement following TPE in our case which has been confirmed.

The efficacy of plasmapheresis may be due to the removal of circulating autoantibodies and other immunologically active substances (e.g., complement and cytokines) from the blood.[19] The treatment of PE, which could lead a considerable decrease in the harmful antibodies of the blood, suggested a protective effect of myelin sheath. However, this protection is impermanent. We also think the recurrence of CNS-IDDs may be related to the short-term therapeutic effects of PE. After PE, the effect of hormone on patients' recurrent lesions improved significantly, which provided the indirect evidence of the correlation between HBV and ON. Furthermore, the coexist of autoimmune antibody reduced the hormone therapy effect.

Previous studies suggest that the highest PE response rate was observed among patients receiving PE within 20 days from attack onset[20] and visual improvement may continue beyond the initial PLEX treatment phase. The visual acuity of patient increased to 5/100 one month later and 8/20 four months later in the left eye. After 1 year's follow-up, the condition of the patient remained stable and had good eyesight.

Through this case, the therapeutic effect of PE to HB-ON has been proved, which can provide a new method for clinical treatment.

## Acknowledgments

Thanks to the blood transfusion department for their help in plasma exchange.

## Author contributions

**Data curation:** Jie Zhao.
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**Supervision:** Da Teng, Shihui Wei.
**Writing – review & editing:** Mo Yang.

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