

## NEOVASCULAR GLAUCOMA AS PRESENTING FEATURE OF OCULAR LEPTOSPIROSIS – A CASE REPORT

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### ABSTRACT

**Background:** Leptospirosis is a waterborne zoonosis, commonly found in tropical countries with heavy rainfall. Leptospirosis poses a diagnostic challenge due to its diverse clinical features that range from prodromal symptoms to multiorgan failure. Most cases of leptospirosis are under diagnosed due to its biphasic nature of presentation. We report a rare case of ocular leptospirosis presenting as unilateral neovascular glaucoma.

**Materials and Methods:** A case report.

**Result:** A 54-year-old gentleman who was previously well presented with right eye generalized progressive blurring of vision for one-month duration. One month later, he experienced right eye pain and redness. His right vision was of perception of light while the left vision was 6/6, with high intraocular pressure of 54 mmHg and positive relative afferent pupillary defect. A provisional diagnosis of right eye neovascular glaucoma secondary to panuveitis was made. Infective screening showed positive Anti-leptospiral immunoglobulin M (IgM). Oral Azithromycin was commenced for 6 weeks and oral prednisolone 1mg/kg was added after a week of oral antibiotics. On subsequent follow-up, his vision had gained to hand movement vision.

**Conclusions:** The awareness of the spectrum of these clinical manifestations may assist clinicians in making a timely diagnosis and instituting successful treatment. Understanding the specificity and sensitivity of enzyme-linked immunosorbent assay (ELISA) test in diagnosis of leptospirosis infection should be highlighted in handling cases with tropical fever or idiopathic panuveitis. Long-term follow-up is required to detect the late complications of leptospirosis. Azithromycin is another viable option for treatment of ocular leptospirosis.

**Keywords:** Leptospirosis, ocular leptospirosis, neovascular glaucoma, panuveitis

## 1.0 Introduction

Leptospirosis, or Weil's disease, is a waterborne zoonosis caused by spirochetes, *Leptospira interrogans*. It is the most widespread zoonosis in the world.<sup>1</sup> This bacterium is a thin, spiral-shaped, motile, gram negative bacilli. Transmission is through infected animals, mainly rodents via direct or indirect contact from water contaminated by urine from the infected animals, mainly rodents.

Most cases of leptospirosis remain under diagnosed due to its wide spectrum of clinical manifestations. Its presentation mimics other tropical countries' diseases such as dengue fever, viral hepatitis, viral haemorrhagic fever, typhoid and malaria.<sup>2</sup> Clinical features range from asymptomatic to multiorgan failure, involving the respiratory, neurological, haematological, gastroenterological, nephrological, ocular and cardiovascular system. Weil's disease is the most severe form of leptospirosis with high fatality rate.<sup>3-4</sup>

The disease has a biphasic presentation. The acute phase happens after inoculation of the spirochetes into intact oral mucosal or abraded skin. Haematogenous spread occurs rapidly due to the high motility of the spirochetes. Spread to various organs cause an acute febrile phase that lasts about a week. The second phase begins when the host immunity responds to remove the spirochetes out of the host tissue via urine. However, spirochetes that remain in immune-privileged sites such as eye and brain<sup>5</sup> will escape from being phagocytosed. In addition, the autoimmune response will be activated resulting in influx of inflammatory mediators into the anterior chamber of the eye.<sup>7</sup> Direct invasion and antibodies influx into anterior chamber can damage the ocular structure causing cell death and toxicity.<sup>7</sup> Chu KM et al has proved the existence of leptospiral Deoxyribonucleic Acid (DNA) in the anterior chamber by performing Polymerase Chain Reaction (PCR) analysis and postulate that the spirochetes may direct cause pathogenic response to the eye in the active phase.<sup>6</sup> Previous studies<sup>8-11</sup> have found and reported spirochetes having virulence factors such as haemolysin, sphingomyelinase C, and proteins that resemble function of Platelet-activating factor Acetylhydrolase (PafAH), von Willebrand factor type A domain (vWa), and paraoxonase (pon). Ren S-X et al<sup>8</sup> proposed that presence of PafAH, vWa, pon may be responsible to the pathogenesis of small vessel endothelium damage during the infection. Pathogenesis of leptospirosis is still not well understood as its protean manifestation involved multiorgan damage. Here, we report a rare case of leptospirosis presenting as unilateral neovascular glaucoma.

## 2.0 Materials and Methods

A case report.

## 3.0 Result

### 3.1 Case

A 54-year-old gentleman who was previously well presented with right eye generalized progressive blurring of vision for one-month duration. One month later, he experienced right eye pain and redness. The right eye pain was associated with headache but there was no nausea, vomiting or eye discharge. This was the first episode of red eye and it was preceded by fever and myalgia for a week. However, there was no history of jaundice, rashes, loss of weight or appetite and ocular trauma. He lived in a village house adjacent to the jungle. Pre-morbidly, his vision was good and equal in both eyes.

On examination right vision was of perception of light in two quadrants while the left vision was 6/6. There was a positive relative afferent pupillary defect in the right eye. Anterior segment examination found no jaundice conjunctival, subconjunctival haemorrhage or chemosis. There were circumcorneal injection, hazy cornea, multiple fine keratic precipitates and presence of moderate anterior chamber inflammation with no hypopyon. The pupil was mid-dilated with 360° of rubeosis iridis (**Figure 1**) and posterior synechiae from 9-12 o'clock. Intraocular pressure of the right eye was 54 mmHg. Gonioscopy of the affected eye revealed neovascularization of the angles with presence of peripheral anterior synechiae.

Right fundus revealed dense vitritis with membranous vitreous clumps obscuring the optic disc (**Figure 2A**). The optic disc was pallish with overlying a clump of vitreous. There was minimal vitreous haemorrhage temporal to the optic disc, however, there was no disc neovascularization and no new vessels elsewhere. There was presence of multiple small choroiditis along the inferotemporal arcade with absence of vasculitis, retinitis, tortuous vessel, retinal or choroidoretinal scars. The examination of the left eye was unremarkable. Systemic examination was also unremarkable.

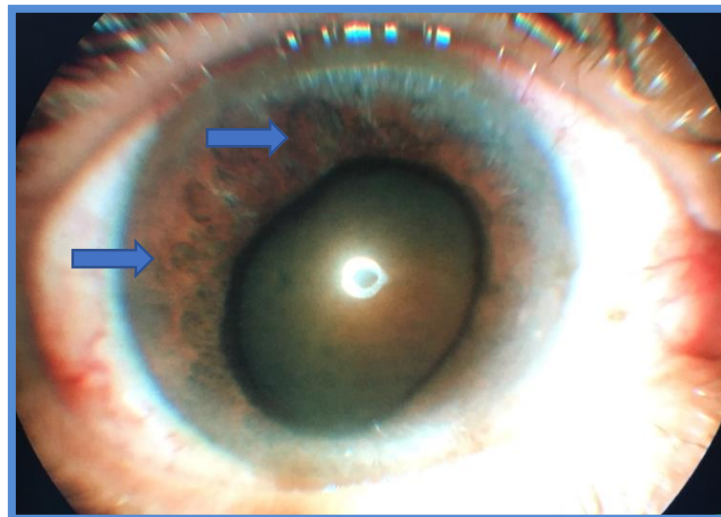
A provisional diagnosis of right neovascular glaucoma secondary to panuveitis was made. Infective cause of panuveitis was suspected in view of possibility of indirect contact with wild rodents as he was staying in remote area adjacent to the jungle. Besides, he also presented with a short duration of fever and myalgia which pointed us toward infective causes of panuveitis. Thus, blood investigations to screen for infective causes such as syphilis, toxoplasmosis and leptospirosis were taken, together with full blood count, erythrocyte sedimentation rate, renal profile, and liver function tests were done. Nevertheless, he was also screened for connective tissue disease and tests such as rheumatoid factor and antinuclear antibodies were requested.

Symptomatic treatment was instituted while waiting for the laboratory results. Intraocular lowering agents such as oral acetazolamide, timolol and dorzolamide were commenced. Empirically, oral azithromycin 500 mg once daily and topical moxifloxacin was started.

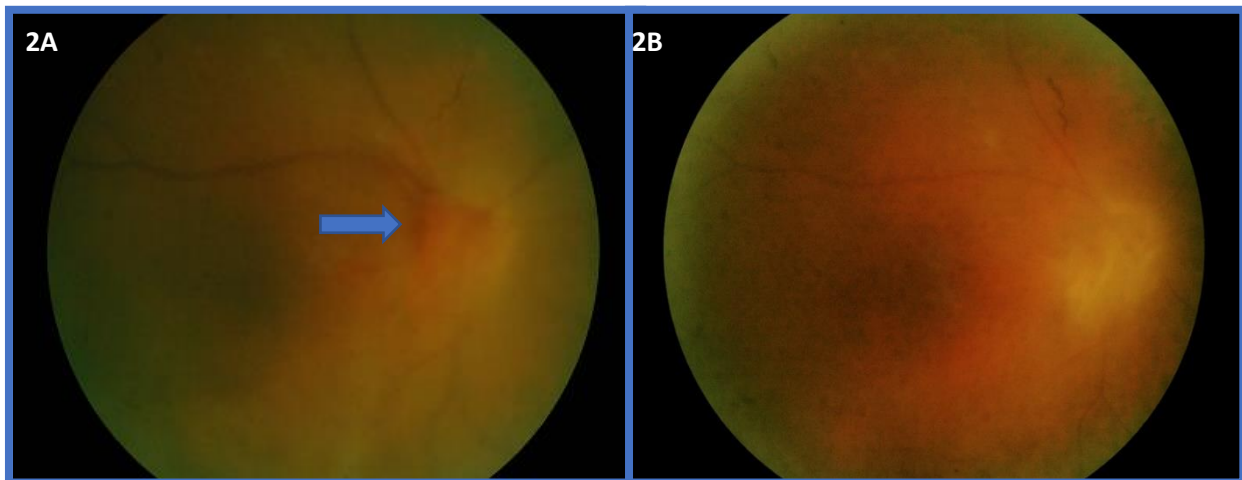
Topical steroids were also given to reduce the inflammation. He underwent panretinal photocoagulation therapy to the right eye.

Anti-leptospiral immunoglobulin M (IgM) was detected via ELISA testing. All other investigations were normal. Based on the investigation results, we revised our diagnosis to neovascular glaucoma secondary to ocular leptospirosis. Oral Azithromycin was commenced for 6 weeks. Oral prednisolone 1mg/kg was added after a week of oral antibiotics in view of dense vitritis.

On completion of 4 weeks of treatment, the right vision improved to hand movements and there was regression of his rubeosis iridis. His intraocular pressure reduced to 23 mmHg and fundus showed reduction in vitritis and vitreous clumps (**Figure 2B**). However, subsequent follow-up of this patient was not possible as he defaulted follow-up and was not contactable.



**Figure 1:** Right eye showed mid-dilated pupil with presence of rubeosis over 360 degrees (blue arrow).



**Figure 2A:** Right fundus at presentation showing dense vitritis with membranous vitreous clumps obscuring the optic disc with minimal vitreous haemorrhage (arrow) at temporal part of the optic disc

**Figure 2B:** Right fundus at 2 months review showing reduction of vitritis and vitreous clumps.

#### 4.0 Discussion

Typical leptospirosis is defined as a febrile illness with any other classic clinical manifestation such as icterus, arthralgia, myalgia, hepatitis, spontaneous bleeding from viscera and acute kidney injury.<sup>12</sup> Ocular leptospirosis is rare and is grouped under atypical<sup>12</sup> manifestation of leptospirosis as it may not have the classic clinical features of leptospirosis. Its ocular manifestations can be found in both acute and immune phase.<sup>2</sup> Features of acute phase are subconjunctival and retinal haemorrhage, retinal vasculitis, papillitis and hard exudates.<sup>13</sup> About 92% of the patient presented with subconjunctival haemorrhage.<sup>14</sup> Uveitis is typically seen in the immune phase presenting during the 2<sup>nd</sup> to 4<sup>th</sup> week of illness,<sup>2</sup> but it can also occur in both phases.<sup>2</sup> Uveitis in ocular leptospirosis normally presents with non-granulomatous keratic precipitates,<sup>2</sup> anterior vitreous cells, patchy perivasculitis,<sup>2</sup> dense vitritis,<sup>2</sup> and membranous vitreous over the optic disc.<sup>5</sup> Jaundice and conjunctival chemosis are pathognomonic features of severe systemic leptospirosis.<sup>2</sup> Our patient presented with features of dense vitritis. A study by Rathinam SR,<sup>5</sup> found that vitreous inflammation in ocular leptospirosis was severe compared to others infective posterior uveitis. Furthermore, it has been reported that panuveitis is the most common presentation of uveitis with good visual prognosis.<sup>15</sup> Six common ocular features commonly seen in ocular leptospirosis include anterior chamber cells, vitreous opacities, papillitis, vasculitis, bilateral panuveitis, and lack of visual deficit.<sup>4</sup> This helps differentiate ocular leptospirosis from others infective uveitis.

Unfortunately, our patient presented with neovascular glaucoma with poor vision as the initial presentation which is a very rare ocular leptospirosis complication. A study by Rathinam et al<sup>5</sup> described that vascular occlusion and neovascularization are typically not seen in ocular



leptospirosis.<sup>2</sup> Furthermore, neovascular glaucoma has a grave visual prognosis. To the best of our knowledge, there have been no reported cases of severe ocular manifestation due to leptospirosis without concurrent systemic involvement.

Our patient was treated with oral Azithromycin and laser panretinal photocoagulation was performed. Azithromycin has a broad spectrum of antimicrobial covering both gram positive and negative. It is known for its capability to penetrate the ocular-aqueous barrier reaching to the anterior chamber.<sup>16</sup> In addition, it has less side effect and patient is more compliance to daily dose of administration.<sup>17-18</sup> Both Griffith et al<sup>19</sup> and Ghouse et al<sup>20</sup> has demonstrated the efficacy of oral azithromycin in treating human leptospirosis in comparison with other convention drugs for leptospirosis treatment such as penicillin and cephalosporin group of antimicrobials. Hence, it became our antibiotic of choice. Besides, clinical signs of this case found overlaps with those of ocular toxoplasmosis with panuveitis. By administrating azithromycin empirically, it will act as double edge sword to combat both these infections, while waiting for infective screening reports. Steroid therapy has found to be effective in securing the good visual outcome by reducing the intraocular inflammation caused by the leptospirosis,<sup>21</sup> thus, we commenced steroid therapy in this case to reduce the dense vitritis.

Early detection of leptospiral disease pose a diagnostic challenge as isolation of organism is often difficult during the initial phase. In addition, blood culture is not favoured due to long culture duration. ELISA testing aided the diagnosis in our patient. It has been found that antibody production is the hallmark for second phase and IgM can be detected as early as first week of infection.<sup>22-23</sup> It is found that ELISA detects IgM as early as day 6 to 8 days after the onset of infection. Detection is earlier compared to Microscopic Agglutination test (MAT).<sup>23-24</sup> Cumberland et al<sup>25</sup> demonstrated that the sensitivity of ELISA in detecting IgM using the antigen of nonpathogenic *Leptospira biflexa patoc* strain, is 52% in the initial phase which increased to 89% and 93% in second acute-phase and convalescent phase respectively.<sup>25</sup> In contrast, sensitivity using MAT is 41% during the first week and only found positive after day 10 of onset, but, increased sensitivity on 2<sup>nd</sup> week onward and further increased to 96% during the 4<sup>th</sup> week.<sup>25</sup> Interestingly, the specificity for MAT was slightly higher than ELISA at 94%<sup>25</sup> as its able to identify the infecting serogroup, thus the cost for operating MAT is higher as its requires expertise to interpret the findings. On the other hand, polymerase chain reaction (PCR)<sup>24,26</sup> is more sensitive and specific compared to ELISA in acute phase but it is expensive. It can detect leptospiral DNA as early as 5-10 days of onset which is almost the same timing as ELISA.<sup>24</sup> Thus, ELISA rapid kit has gained popularity in endemic regions assisting in timely diagnosis. It does not require trained laboratory clinician to interpret the findings and the cost of the kits is relatively cheaper compared to both PCR and MAT.

Close supervision for signs and symptoms of uveitis and optic neuropathy should be emphasized to the physician as the latent phase of ocular manifestation can extend up to 4 years<sup>2</sup> after the systemic infection. Any symptoms such as reduced near vision, light brightness and colour saturation should raise the red flag for early ophthalmology referral.

## 5.0 Conclusions and recommendations

Thorough and detailed clinical assessment remain the main tools in diagnosing this rare entity of leptospirosis. Awareness of the specificity and sensitivity of ELISA test in diagnosis of

leptospirosis infection should be highlighted in handling cases with tropical fever or idiopathic panuveitis, as many cases of leptospirosis still under diagnosed. Long-term follow-up is required to detect the late complications of leptospirosis. Azithromycin is another viable option for treatment of ocular leptospirosis.

## Declaration

The authors have no conflicts of interest to declare.

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