Buckle, M., Majid, M. A., Lee, R., & Steeples, L. R. (2017). Full-thickness macular hole: a rare complication of *Borrelia burgdorferi* neuroretinitis. *BMJ Case Reports*, *2017*, [219019]. https://doi.org/10.1136/bcr-2016-219019

TITLE OF CASE

Full-thickness macular hole: A Rare Complication of *Borrelia burgdorferi* neuroretinits

SUMMARY ***Up to 150 words summarising the case presentation and outcome***

Borrelia burgdorferi is a known infective cause of neuroretinitis. We present a case of *Borrelia burgdorferi* neuroretinitis complicated by macular hole in a 22 year old man. The neuroretinitis was managed with early high dose intravenous corticosteroid and oral antibiotic. The macular hole was managed with macular hole surgery after intraocular inflammation had resolved.

BACKGROUND ***Why you think this case is important***

Our patient presented with acute and severe, sight threatening neuroretinitis and we describe our clinical decision to treat early with high dose intravenous corticosteroid, despite strong suspicion of an infective aetiology. Prompt corticosteroid treatment was deemed necessary in view of significant optic nerve involvement and secondary macular oedema, and had a favourable outcome suggesting there is a role for this treatment in our experience.

Macular hole formation in posterior uveitis is infrequently reported[1]. Macular hole has been reported in four cases of *Bartonella* neuroretinitis[2-5] but has not been previously reported in *Borrelia* neuroretinitis and our case therefore presents a unique complication of this condition.

CASE PRESENTATION ***Presenting features, medical/social/family history***

A 22 year old man presented to our uveitis service with a sudden, painless vision loss in his right eye. He described a preceding prodromal illness with pyrexia, sore throat and cervical lymphadenopathy. His vision was 6/60 right and 6/5 left. Colour vision was significantly impaired in the right, and normal in the left. The left eye was normal. The right eye had a relative afferent papillary defect with very mild vitritis, significant optic nerve swelling with secondary macular oedema, and the clinical appearance of macular folds (Figure 1a). Macular folds are a recognised sign in optic nerve swelling. Optical coherence tomography (OCT) demonstrated macular sub- and intra-retinal fluid (Figure 1a). Fundus fluorescein angiography demonstrated optic nerve early hyperfluorescence and progressive leakage (Figure 2). There was no vasculitis or focal lesions of the choroid or retina. The visual loss was attributable to optic nerve inflammation and and secondary macular oedema.

He recalled possible tick bites, in France, in the preceding 3-months. There was no history of *erythema migrans* or visible bites. Full medical examination was unremarkable including no other neurological signs.

INVESTIGATIONS ***If relevant***

Borrelia IgM was equivocal and IgG was positive (ELISA C6 EIA and Western blot). Syphilis serology (treponemal and non-treponemal), *Toxoplasma* IgG and IgM, and HIV testing were negative. Inflammatory markers were elevated (ESR 15, CRP 28). There was no history of previous *Mycobacterium tuberculosis* (TB) and no known TB contacts. The patient had undergone BCG vaccination and had no clinical features suggestive of active TB. There was no evidence of tuberculous granuloma of the optic nerve or specific uveitis consistent with intra-ocular TB. Serum ACE, chest radiograph and brain MRI

were normal. *Bartonella* serology was not performed; this is no longer routinely available in the UK.

DIFFERENTIAL DIAGNOSIS ***If relevant***

Unilateral neuroretinitis was diagnosed and the initial differential diagnosis included *Borrelia burgdorferi*, *Bartonella henselae*, *Toxoplasma gondii* and *Treponema pallidum* infection.

TREATMENT ***If relevant***

In view of the clinical presentation, *Bartonella* and *Borrelia* were considered the most likely infectious causes. Negative *toxoplasma* and syphilis serology results were received before *Borrelia* serology results and we elected to start treatment to treat marked visual loss. Empirical therapy with oral doxycycline (100mg BD) was commenced simultaneously with intravenous methylprednisolone (1gm daily for 3 days), followed by oral prednisolone (40mg OD) was commenced. Oral doxycycline is an established empirical treatment in infectious neuroretinitis, providing appropriate antimicrobial action for both *Bartonella* and *Borrelia*. High dose systemic corticosteroid was considered necessary to treat significant optic nerve inflammation. There was rapid response, with progressive reduction of neuroretinitis.

OUTCOME AND FOLLOW-UP

The vision improved to 64 and 66 letters at two and four weeks respectively. However, at 4 weeks, a full thickness macular hole was evident (Figure 1b). Repeat *Borrelia* IgG and IgM were strongly positive in keeping with recent infection. A 3-month course of oral doxycycline was given, following microbiologist consultation. Corticosteroids were tapered and discontinued after 10 weeks. There was no evidence of spontaneous hole closure by 1 weeks and macular hole surgery was performed with *pars plana* vitrectomy, internal limiting membrane (ILM) peel and gas tamponade. Three months later the vision was 6/9.5 and the macular hole was closed. There was persistent but reducing shallow subretinal fluid (Figure 1c).

DISCUSSION ***including very brief review of similar published cases***

We treated this patient on an individual basis and elected to treat with high-dose corticosteroid therapy because of the degree of visual impairment at presentation. This was agreed with our local microbiology service. Our report highlights a favourable visual outcome with this approach. However, we do not recommend this as a specific treatment for any patient with neuroretinitis and positive *Borrelia* serology. Rather we recommend patients are treated on an individual basis and all treatment decisions made in conjunction with microbiology advice. In such patients it is important to consider other differentials and exclude these, such as syphilis or *toxoplasma*, before proceeding with high dose corticosteroid therapy.

Macular hole formation in posterior uveitis is infrequently reported[1]. Macular hole has been reported in four cases of *Bartonella* neuroretinitis[2-5] but has not been previously reported in *Borrelia* neuroretinitis. *Borrelia burgdorferi* is a spirochaete bacteria transmitted by the *Ixodes* tick. The pathophysiology of macular hole formation in uveitis is poorly understood and may be caused by one or more of: irregular inflammatory contraction of the pre-macular vitreous[2]; antero-posterior traction; tangential forces caused by epiretinal membrane (ERM) or ILM contraction or intraretinal weakening caused by cystic changes[1]. In this case, there was no evidence of posterior vitreous detachment (PVD) or ERM. However, abnormal hyaloid forces interacting with disrupted intra- and sub-retinal anatomy likely contributed.

The appropriate timing of surgery in this condition is not clear. We recommend adequate control of inflammation and optic nerve swelling before surgical intervention. Furthermore, spontaneous macular hole closure has been reported in some patients with underlying inflammatory pathology[1]. Induction of PVD and ILM peel may be difficult and harmful in the context of significant serous detachment. An excellent visual outcome was achieved in this particular case after prompt medical treatment and appropriate surgical intervention once inflammatory activity had resolved.

LEARNING POINTS/TAKE HOME MESSAGES ***3 to 5 bullet points***

- Macular hole formation can complicate posterior uveitis and neuroretinitis including *Borrelia* neuroretinitis and is an important causes for reduced central vision in such patients
- Early high-dose systemic corticosteroid therapy with appropriate antibiotic therapy can achieve favourable visual outcomes and good visual recovery in this condition.

REFERENCES ***Vancouver style (Was the patient involved in a clinical trial? Please reference related articles)***

1. Bonnin N, Cornut PL, Chaise F, Labelle E, Manificat HJ, Feldman A et al. Spontaneous closure of macular holes secondary to posterior uveitis: case series and a literature review. *J Ophthalmic Inflamm Infect* 2013;3: 34.

2. Albini TA, Lakhanpal RR, Foroozan R, Holz ER. Macular hole in cat scratch disease. *Am J Ophthalmol* 2005;140: 149-51.

3. Donnio A, Jean-Charles A, Merle H. Macular hole following *Bartonella henselae* neuroretinitis. *Eur J Ophthalmol* 2008;18: 456-8.

4. Alternan MA, Young BK, Eggenberger ER, Kaufman DI. Macular hole: A rare complication of ocular bartonellosis. *J Neuroophthalmol* 2013;33: 153-4.

5. Seth A, Raina UK, Thirumalai S, Batta S, Ghosh B. Full-thickness macular hole in Bartonella henselae neuroretinitis in an 11 year old girl. *Oman J Ophthalmol* 2015;8: 44-6.

Figure captions

Figure 1: Right eye colour photographs at (a) presentation demonstrating gross optic nerve swelling and serous macular detachment; (b) 6-weeks later with reduced optic nerve swelling and evolution to a macular star and (c) at latest follow up (post-operatively) resolution of optic nerve swelling and macular serous fluid. OCT images are superimposed and show (a) massive serous macular detachment and intra-retinal fluid; (b) development of full thickness macular hole and (c) macular hole closure with persistent sub-retinal space.

Figure 2: Right eye fundus fluorescein angiography at presentation. Left hand image shows early optic nerve hyperfluorescence; right hand image shows progressive leakage with masking by serous detachments superior to the nerve and extending extensively within the macular area.

PATIENT'S PERSPECTIVE

I first noticed something wrong with my eye when I woke up one morning. The vision in my right eye was subtly but noticeably affected at the centre of my vision by what seemed like a small dot. At first I wasn't very concerned and decided it was likely to be just a scratch on my lens that would disappear with time. After a few days the dot had grown progressively in size until it was a large grey smudge that covered my entire central vision. It was at this point that I sought medical attention. I had not history of medical problems and had never before had any reason to believe that my health would be at risk. A couple of days before the onset of my visual problems I had had a fever and an achey feeling in my bones which lasted for just over a night. In hindsight this seems to be the point at which the issues started. I was aware of Lymes disease, especially as my

parents live in a rural region of France where ticks abound. I had always taken care to make sure I didn't have any ticks on my after going for a walk and had never spotted one on me. Once it was determined that the cause was likely to be Lymes and not neurologically related I felt a lot calmer with what was happening to my eye. Once I had started taking medication the grey cloud that obscured my vision started to shrink quite rapidly. The cloud itself was quick to go but it took a good while longer before my right eye could see any detail reliably without too much warping and poor light sensitivity getting in the way. It was all quite easy to go through as I never felt any pain in my eye at all. The harder part was keeping my head face-down after surgery to heal the macular hole that had formed from the swelling in my optic nerve. Keeping my head down during sleep was incredibly difficult, but it all proved to be more than worth it for the gains I made in vision afterwards. Now, almost a year after my operation, I rarely notice my right eye as being very different to my left. It's only if I directly compare the two that I notice that it has a harder time at making out letters or objects at long distance. I feel very fortunate that I was so close to a hospital that was well equipped to deal with my condition, as well as one staffed by doctors and nurses who were so incredibly warm and reassuring. Although I was told to expect a cataract within a year or so of surgery, I still haven't noticed any sign of any yet! I will probably get one at some point down the road, but it's hard not to feel as if it will never come after the amount of good luck that I've had so far.