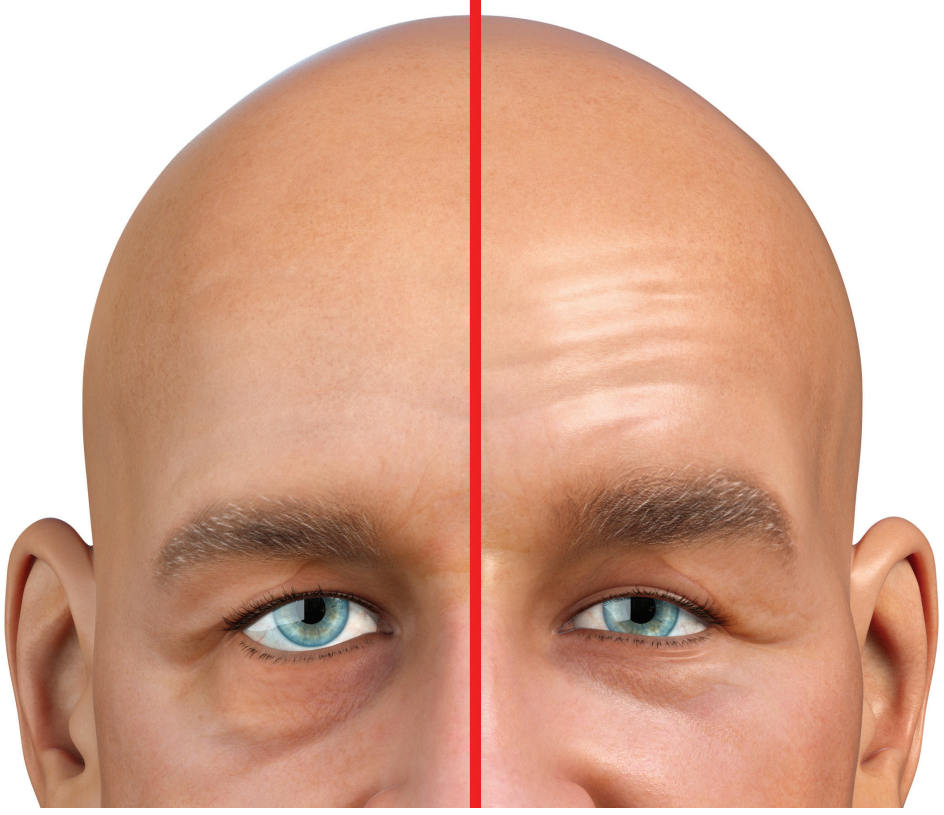
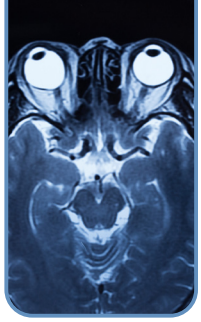
NEURO CASE SERIES





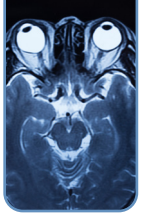
THIRD NERVE PALSY WITH SPONTANEOUS RECOVERY AFTER LYME DISEASE

A complex case retrospectively highlights the management protocol of this condition.

BY JOSEPH HALLAK, OD, PHD, FAAO, AND DANIELLE KALBERER, OD, MBA/HSA, FAAO

Isolated third nerve palsy (TNP) is an oculomotor palsy that typically presents with binocular diplopia, ptosis with or without pain, and ptosis with or without pupil involvement (also known as mydriasis). TNP can be complete, except for the lateral gaze, or incomplete with partial limitation. TNP can further be described as a condition that results in *external ophthalmoplegia*, which implicates ocular muscle involvement in the upper lid on the affected side, and *internal ophthalmoplegia*, which can present with pupil involvement, pupil-sparing, or even relative pupil-sparing.[1]

As a general rule, pupil-sparing TNP triggers a high suspicion of microvascular disease, but does not rule out cavernous sinus syndrome or giant cell arteritis in the elderly. Pupil involvement is very common in the presence of aneurysm, especially along the posterior communicating artery. With the rare exception of a complete pupil-sparing TNP, immediate central nervous system imaging is indicated. Appropriate blood tests are also indicated to check for myasthenia gravis, diabetes, or giant cell arteritis, if suspected.[2] Comanagement with an internist, neurologist, and vascular specialist is imperative. Pain and headache constitute an emergency and dictate immediate specialized attention. Treatment consists of addressing the underlying cause.



DIAGNOSING TNP

The most common cause of pupil-sparing TNP is an ischemic event, especially in the older population. Ischemic causes of TNP, such as diabetes or hypertension, usually improve within 4 to 12 weeks, although resolution at 6 months to 1 year has been noted.[2] Conditions causing inflammation and/or immune reactions can also be a cause.[3]

The prime suspect of partial palsy is a compressive aneurysm at the junction of the internal carotid and the posterior communicating artery. Aneurysms larger than 4 mm are detected with a high degree of accuracy with modern noninvasive neuroimaging when read by neuroradiologists.[4] MRI and magnetic resonance angiography (MRA) are routinely performed with haste in cases of TNP to rule out emergent causes (ie, aneurysm).[1] In the absence of pain or headache, a pupil-sparing partial TNP in an older patient is considered urgent, but not a true emergency. Once the patient is medically stable, the diplopia can be addressed optometrically on a short or long-term basis using patching or prism.

The case presented here is interesting because it is rare. The patient's TNP was a diagnosis of exclusion, and he ended up recovering spontaneously. In addition, this case details the treatment and management plan by a professional optometry and ophthalmology eye care team.

CASE REPORT

A 76-year-old male presented with complaints of binocular diplopia, slight blurred vision, and tearing in his left eye. He reported having a tick bite 2 months prior and that he removed it within 24 hours and self-treated with a 2-week course of oral doxycycline 100 mg twice daily (he was a retired dentist). One month after the exposure, he experienced left leg pain, especially around the knee. He saw his internist at that time and a Lyme titer test was ordered (see *Lyme Disease*), which came back positive (Table). The patient was then evaluated by orthopedics, vascular surgery, and infectious disease specialists, after which tetracycline treatment was instituted for 3 weeks, followed by minocycline maintenance therapy for 1 month (the exact dosages are not known because he saw specialists outside of the hospital system). The patient's additional medical history included benign prostatic hypertrophy, essential tremor, and controlled hypertension. He denied any other neurologic deficits or symptoms of stroke.

Initial Exam Findings

The patient's BCVA was 20/30 OU with no improvement on pinhole. His pupils were normal without afferent pupillary defect, and monocular Ishihara color vision was normal and equal. Partial ptosis of the left upper eyelid was noted, with large exotropia on the contralateral side. Full range of motion was present OU on extraocular motility testing. Slit-lamp examination was within normal limits OU and IOPs were 14 mm Hg OU. Dilated fundus examination was normal, with no remarkable retina findings in either eye. Both cup-to-disc ratios were 0.5 round, and both optic nerves appeared healthy and well-perfused.

Comanagement

The patient was evaluated promptly by a neuro-ophthalmologist, who noted that the patient's BCVAs had "improved" to 20/20 OU. A right exotropia was present in primary gaze and was observed to increase on right gaze. There was also a left hypotropia with slight levator palsy. A tentative diagnosis of partial TNP of the left eye was made, given the ptosis and vertical duction limitation. The patient was scheduled for urgent neuroimaging and spinal tap the next day. The results were normal.

The patient was referred back to optometry 2 weeks later, and at that time, no exotropia or motility deficits were present. Ptosis of the left upper lid had resolved. On binocular testing, a deviation of 15 prism diopters exo posture was measured, and the patient was isophoric. He was diagnosed with convergence insufficiency; however, due to lack of symptoms at that time he chose to be monitored in 6 months rather than consider prism or vision therapy. He noted that rare diplopia due to the convergence insufficiency was self-controllable, as opposed to his short-lived but constant "post Lyme diplopia."

DISCUSSION

In this case, the patient was not diabetic, and his hypertension was well-controlled. He had no other significant

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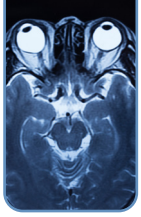
AT A GLANCE

- Isolated third nerve palsy (TNP) typically presents with binocular diplopia, ptosis with or without pain, and ptosis with or without pupil involvement.
- Pain and headache constitute an emergency and dictate immediate specialized attention.
- Treatment consists of addressing the underlying cause.



LYME DISEASE

Lyme disease is an infectious, inflammatory condition caused by *Borrelia burgdorferi* and can present with varying manifestations. The disease is typically contracted within 36 to 48 hours of a tick bite. Lab testing for Lyme disease specifically includes antibody testing against *B. burgdorferi*. However, it takes 4 to 6 weeks for the Lyme titer to show up on the test and immunoglobulin M and G (IgM; IgG) positivity can persist for months to years, even after the infection is cured. Confirmation by Western blot is recommended. If the pathognomonic erythema migrans (bullseye) rash is present or Lyme is highly suspected, a course of antibiotics should be initiated immediately. Doxycycline is typically the preferred regimen.[1]

The chronologic history provided by our patient was difficult to map because he had treated himself, then was seen by specialists outside of the hospital system. Two months after the last optometry evaluation (4 months after the exposure) he still showed IgG and IgM abnormal titer on retest, which is not unusual. A positive Lyme titer can linger for months and cannot be used as an indication of a successful treatment. Ideally, if the disease is suspected and treatment is initiated within a day, the Infectious Diseases Society of America considers 2 to 4 weeks of treatment adequate. However, the International Lyme and Associated Diseases Society advocates long-term treatment based on symptoms because 10% to 20% of patients present with persistent fatigue, joint pain, insomnia, and/or "brain fog."[2]

At one point, our patient experienced fatigue and knee pain. His antibiotic treatment was restarted after consultation with an infectious disease specialist. He was directed to continue antibiotic maintenance therapy until he reported relief from his systemic symptoms.

There are reported cases of Lyme disease with cranial neuropathy. In most of these cases, neurologic symptoms tend to resolve within 1 to 2 months after treatment is initiated.[3] If Lyme-induced cranial neuritis is present, it often shows thickening of the affected segments on MRI.[4] In the case of Lyme disease, however, MRI and MRA may be normal unless there is significant inflammation of the afflicted nerve.[3] The neuroimaging in our case was normal.

Cackett and Weir presented a similar case in which the patient presented with diplopia onset several days prior to facial nerve palsy. The patient was found to have oculomotor nerve palsy initially and developed facial nerve palsy 5 days later. The patient was subsequently found to have positive Lyme serology and was treated with a course of antibiotics and prednisone to resolution. This patient also had normal neuroimaging and made a rapid recovery once treatment was implemented.[3]

It seems that there is a lingering problem for many patients, an intriguing so-called *post-treatment Lyme disease syndrome*. There are various hypotheses that remain unproven. One is that there remains persistent intracellular bacteria that evade treatment; another is that the antigen on the spirochete is inflammatory.[5] Researchers at Johns Hopkins are considering unique gene expressions after Lyme infection that result in metabolic changes and symptoms like that of systemic lupus erythematosus or rheumatoid arthritis. After vascular surgery and infectious disease consultation for our patient, long-term antibiotic treatment was initiated per the International Lyme and Associated Diseases Society.[2]

1. Lyme disease diagnosis and testing. Centers for Disease Control and Prevention. Last reviewed May 21, 2021. www.cdc.gov/lyme/diagnosistesting/index.html. Accessed May 2, 2022.
2. Lyme disease treatment trends. International Lyme and Associated Disease Society. April 25, 2019. www.ilads.org/treatment-trends-for-lyme-disease. Accessed May 2, 2022.
3. Cackett P, Weir C. Oculomotor nerve paralysis and bilateral facial nerve paralysis as presenting signs of Lyme disease. *Neuro-Ophthalmol*. 2002;27:183-186.
4. Savas R, Sommer A, Gueckel F, Georgi M. Isolated oculomotor nerve paralysis in Lyme disease: MRI. *Neuroradiology*. 1997;39:139-141.
5. Feng J, Li T, Yee R, et al. Stationary phase persister/biofilm microcolony of Borrelia Burgdorferi causes more severe disease in a mouse model of lyme arthritis: implications for understanding persistence, post-treatment lyme disease syndrome (PTLDS), and treatment failure. *Discov Med*. 2019;27:125-138.

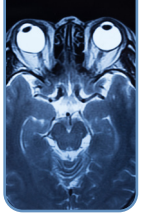


TABLE. Our Patient's Lyme Serology

TEST	RESULT	REFERENCE RANGE
C6 *B. burgdorferi* (Lyme)	6.37 (High)	Neg < 0.91 Equivocal 0.91-1.09 Positive > 1.09
Lyme Ab IgG by WB:		
IgG P93 Ab	Absent	
IgG P66 Ab	Absent	
IgG P58 Ab	Present Abnormal	
IgG P45 Ab	Absent	
IgG P41 Ab	Present Abnormal	
IgG P39 Ab	Present Abnormal	
IgG P30 Ab	Absent	
IgG P28 Ab	Absent	
IgG P23 Ab	Present Abnormal	
IgG P18 Ab	Present Abnormal	
Lyme IgG WB Interpretation	**Positive Abnormal***	
Lyme Ab IgM by WB:		
IgM P41 Ab	Present Abnormal	
IgM P39 Ab	Absent	
IgM P23 Ab	Present Abnormal	
Lyme IgM WB Interpretation	**Positive Abnormal***	

Abbreviations: Ab, Antibody; Ig, Immunoglobulin; WB, Western blot
**Note: According to the Centers for Disease Control, IgM results should be ignored if the patient has been ill for more than 30 days when the test is performed.*[4]

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health issues. Various differential diagnoses were considered. Ptosis from myasthenia gravis was less likely; giant cell arteritis did not rise to that level of suspicion without pupil involvement, unequal visual acuity, abnormal color vision, or optic nerve involvement, etc. The superior rectus and levator palpebrae superioris with pupil-sparing TNP led to a diagnosis of the superior division of pupil-sparing TNP. After due consideration to the differential diagnoses, the TNP was presumed to be related to the Lyme disease diagnosis because the patient reported a positive Lyme titer.

GOOD CLINICAL SENSE + GOOD LUCK

The patient case discussed here should remind practitioners to consider Lyme disease on their list of differentials when confronted with TNP. In this case, prompt care was rendered, but not with great urgency, given the patient's symptoms, timing, age, and previous history. Nonetheless, a seasoned neuro-ophthalmologist still felt the need for more invasive and advanced testing because one can never be sure with a TNP.

Research has shown that aneurysm of the posterior communicating artery can be misinterpreted on imaging, even by experienced radiologists if specific neuroradiology technique is not used; thus, some physicians prefer to re-test at their own institution.[4] The frequently reported ocular signs associated with Lyme disease include inflammation of the optic nerve, uveitis, vitritis, and conjunctivitis. Now we can add partial TNP.[5] It is no surprise that Lyme disease was dubbed a masquerader. Our patient was fortunate to have had a mild case of short duration, followed by good recovery with no lasting sequelae thus far.

The same patient was re-examined by one of the authors (J.H.) 3 years later. A small left hypophoria in his right upper gaze persists, residual of what was noted at the time of the first diagnosis of the superior division of the pupil-sparing TNP. Such sequalae is noncontributory, and the patient reports that he is still practicing home vision therapy for his past preexisting convergence insufficiency and is doing well. ■

1. Ehlers JP, Shah BP. *The Wills Eye Manual: office and emergency room diagnosis and treatment of eye disease*. Philadelphia: Lippincott Williams & Wilkins; 2008:231-234.
2. Keane JR, Ahmadi J. Most diabetic third nerve palsies are peripheral. *Neurology*. 1998; 51:1510.
3. Chou PY, Wu KH, Huang P. Ptosis as the only manifestation of diabetic superior division oculomotor nerve palsy: a case report. *Medicine*. 2017;96(46):e8739.
4. Elmalem VI, Hudgins PA, Bruce BB, et al. Underdiagnosis of posterior communicating artery aneurysm in noninvasive brain vascular studies. *J Neuroophthalmol*. 2011;31:103-109.
5. Zaidman GW. The ocular manifestations of Lyme disease. *Int Ophthalmol Clin*. 1993;33(1):2-22.

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