RESEARCH LETTER

A Case of Tertiary Syphilis with Unilateral Pupillary Abnormality

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To the Editor,

Syphilis is a sexually transmitted infection (STI) caused by the spirochete *Treponema pallidum* and is divided into distinct stages (1). The infection can progress into tertiary syphilis, which is a rare systemic disease that can impact the skin, internal organs, central nervous system (CNS), and bones (1). Before the advent of antibiotics, syphilis was a significant threat in Europe. The symptoms of tertiary syphilis were widely recognized, and abnormalities in the pupils were a dreaded sign of the disease (2, 3). We present a case of tertiary syphilis presenting with pupillary abnormalities (**Fig. 1**).

A 50-year-old male visited an STI clinic after a former partner tested positive for *Chlamydia trachomatis*. He reported no symptoms, and the latest sexual contact was 3 weeks earlier and with a woman, but he reported having had MSM contacts decades earlier. The patient tested positive for syphilis with a positive INNO-LIA® syphilis score (Fujirebio) (treponemal test) and a rapid plasma reagin (RPR) of 8. The duration of the infection was unknown because the patient had never been tested for syphilis, and the most recent partner tested negative for syphilis. One month before the STI screening, the patient noticed an abnormality in his pupil and consulted an optometrist, his general practitioner, and an acute ophthalmology department. None of them suspected syphilis, and he was sent home without suspicion of serious illness.

Given the uncertain duration of the infection and unexplained differences in pupil size, involvement of the CNS was anticipated at the STI clinic, leading to a lumbar puncture. The initial cell count showed 27x10^6/L nucleated cells (reference < 5x10^6/L) and slightly elevated protein levels of 0.66 g/L (reference 0.15–0.5 g/L), and WR was 4 in the cerebrospinal fluid. The intrathecal *Treponema pallidum* antibody index was 37 and 0 for Immunoglobulin (Ig) G and IgM, respectively (reference < 3). The cerebrospinal fluid was also investigated for *Borrelia burgdorferi*-specific antibodies, and the results were negative. The patient was treated with intravenous benzyl-penicillin, at a dosage of 4 million units 6 times daily for 14 days. He was staged with tertiary syphilis, and treatment was extended with intramuscular administration of 2.4 million units of benzathine penicillin G twice at 1-week intervals. During admission, he was evaluated by an ophthalmologist who found anisocoria with a dilated left pupil, non-reactive to light but reactive on accommodation, so-called "light-near dissociation", and no signs of nervus oculomotorius paralysis; these findings were compatible with Argyll Robertson pupil, a sign of tabes dorsalis (4–6). Another ophthalmologist re-evaluated the patient and found a discreet tonic reaction, and Adies' tonic pupil was also considered. No definitive pupil abnormality was identified; however, the finding was attributed to internal ophthalmoplegia.

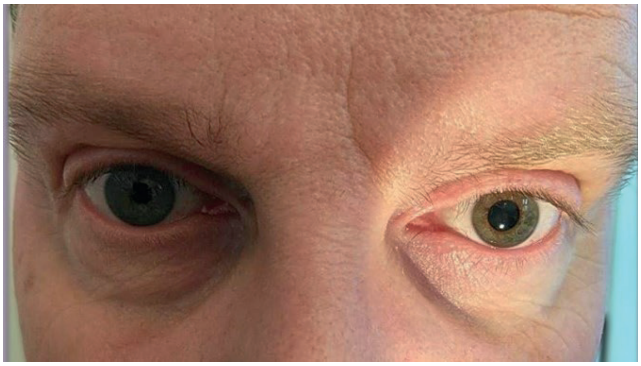

Fig. 1. A 50-year-old man with left pupil anisocoria. The pupil was unresponsive to light but responsive to convergence.

The patient also reported concentration difficulties, sharp pain in his lower limbs, as well as brief episodes of chest pain. Additionally, he reported having transient left-sided peripheral facial paralysis 6 years ago. Neurological examination demonstrated only the already diagnosed anisocoria with light-near dissociation. The Montreal Cognitive Assessment (MoCA) test showed only subtle cognitive impairment with affected recall and word mobilization. Magnetic resonance imaging of the cerebrum showed no conclusive pathology but minimal unspecific gliosis. Computed tomography of the aorta showed a slightly ectatic ascending aorta 3 cm from the aortic valve, but was otherwise normal, and transthoracic echography of the heart was normal. At the 3-month follow-up, the patient reported that the lancinating pains in the lower limbs and the chest pains had ceased following antibiotic treatment. He had unchanged unilateral anisocoria with light-near dissociation. The RPR was 2, an acceptable four-fold decrease.

Neurological involvement can occur in all stages of syphilis, but tabes dorsalis is a consequence of late neurosyphilis and usually occurs 15–30 years after the initial infection (7). It is caused by a degeneration of

the nerves in the dorsal columns of the neural tract, and symptoms include paraesthesia of the lower limbs, diminished reflexes, dementia, loss of coordination, urinary incontinence, and pupillary abnormalities with light-near dissociation (8). Argyll Robertson pupil is defined as unequal, irregular or miotic pupils that do not react to intense light but react normally to convergence accommodation (light-near dissociation) in an eye that is not blind (4, 5).

Tertiary syphilis is now primarily a historical condition, which can lead to misdiagnosis. In this case, the diagnosis was confirmed by intrathecal IgG production and tabes dorsalis symptoms. This case report emphasizes the need for early diagnosis and treatment to prevent irreversible complications, such as pupillary abnormalities, and highlights the necessity for proactive STI screening in individuals with known risk factors.

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