

Neurosyphilis Manifesting With Bilateral Adie's Pupil: A Case Report

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Case report

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Abstract

Background Pupillary abnormalities play an important role in identification of neurosyphilis. Among them, Argyll Robertson pupil is most typical and has been mentioned in many reports and studies. However, papers about Adie's pupil associated with neurosyphilis are extremely rare. In the present study, we report a case of patient with bilateral Adie's pupils as isolated manifestation of neurosyphilis. Case presentation we describe a 58-year-old retired Chinese woman with bilateral Adie's pupils. Further evaluation revealed serologically positive for Treponema pallidum particle agglutination (TPPA), chemiluminescence immunoassays (CLIA) and rapid plasma regain (RPR) test (1:16). The Cerebrospinal fluid (CSF) examination revealed pleocytosis, elevated protein, and positive RPR (1:2), TPPA and CLIA. Final diagnosis of Adie's pupils associated with neurosyphilis was made and other possible causes were excluded. Cephalosporin was used for treatment due to penicillin allergy. Despite effective anti-syphilis treatment, her pupils remained unchanged. Conclusions Adie's pupil can be caused by neurosyphilis and is one of the most important pupillary changes in early neurosyphilis. Our study further underscore the necessity of syphilis screening in patients with Adie's pupil due to further treatment consideration.

Background

In recent years, the rapidly increased incidence of syphilis leads to a significant increase in the number of neurosyphilis worldwide (1, 2). Neurosyphilis can occur during any stage of syphilis and cause various neurological and psychiatric symptoms, even life-threatening if untreated (3, 4). As the disease progresses, the rate of treatment failure increases (4). To make early identification and diagnosis of neurosyphilis, pupillary abnormalities, as important clinical manifestations and signs of neurosyphilis, play an essential role (5, 6). Among them, Argyll Robertson (AR) pupil is most typical and has been mentioned in many reports and studies (7). However, information about Adie's pupil associated with neurosyphilis is limited. In the present study, we described a rare case of neurosyphilis presenting with bilateral Adie's pupils as the only manifestation.

Case Presentation

A 58-year-old retired Chinese woman presented with a 1-month history of mydriasis. She stated that she was found enlarged pupils during her annual routine medical examination a month ago. Nevertheless, she had visual fatigue sometimes but denied blurred vision, diplopia or history of ocular trauma. The physical examinations (PE) at that time revealed that the patient's bilateral pupils were enlarged and unreactive to light. The ophthalmologist advised her to refer to the neurology department for further examinations without giving any treatment. On admission, PE revealed that her right pupil was 5 mm in diameter, and the left pupil was 6 mm in diameter, both pupils were unreactive to light. The corrected visual acuity was 5/16 in the left eye, and 5/8 in the right, with normal intraocular pressure in both eyes. Blunt responses of both pupils was noted on near response. However, extraocular movements were normal without eyelid ptosis. 0.125% Pilocarpine was administered in both eyes, and both pupils were constricted obviously after 30 minutes (Fig.1). The patient exhibited normal muscle strength and muscle

tension in all extremities with normal reflexes. No pathological reflex could be induced. Her past medical history and family history were unremarkable. She denied the history of hypertension, diabetes mellitus, ocular trauma, surgery and blood transfusion.

The routine laboratory tests were normal, including blood routine, blood sugar, glycosylated hemoglobin, human immunodeficiency virus (HIV) antibody, etc. However, the serum rapid plasma regain (RPR) test was positive in a 1:16 titer. The serum *Treponema pallidum* particle agglutination (TPPA) and chemiluminescence immunoassays (CLIA) was also positive. A lumbar puncture was carried out after an informed consent form was signed. The intracranial pressure was 110 mmH₂O. Cerebrospinal fluid (CSF) was clear and colorless. CSF examination demonstrated a protein level of 626mg/L, white blood cell count 38×10⁶/L (89% lymphocytes and 11% neutrophil) and normal glucose and chloride. CSF-TPPA and CLIA test were positive with CSF-RPR positive in a 1:4 titer. Results of brain Magnetic Resonance Imaging (MRI) and Diffusion Weighted Imaging (DWI) were unremarkable. The patient was diagnosed with neurosyphilis and treated with intravenous ceftriaxone 2 g daily for 14 days due to penicillin allergy. After three months of follow-up, the serum-RPR and CSF-RPR turned to negative, and the CSF examination showed normal protein level and cell count. However, her pupils remained unchanged. But the visual fatigue had improved.

Discussion And Conclusions

Adie's pupil, also known as Tonic pupil or Adie's tonic pupil, is characterized by enlarged pupil, disappeared light reflex under ambient light, slow contraction under bright light in dim environment and tonic re-dilation when the light removes (8). Moreover, the convergence is slow, and the accommodation reflex is attenuated (8). In addition, Adie's pupil is sensitive to diluted pilocarpine with an optimum concentration of 0.125% and constrict remarkably to its administration, but normal pupil or AR pupil will remain indifferent (9-11). It is generally believed that Adie's pupil is a characteristic pupillary change of Holmes-Adie syndrome (HAS), which is absence of deep tendon reflexes and usually idiopathic and more common in young women (8). However, the occurrence of Adie's pupil in neurosyphilis appears to be far from exceptional. Reviewing previous researches, we found that about 8-17% of the Adie's pupils is caused by syphilis (12). It could onset either unilaterally or bilaterally and could extend from a single pupil to both pupils with time (13, 14).

We evaluated many possible conditions that may lead to the pupillary changes in our patient, and finally confirmed the diagnosis of Adie's pupil caused by neurosyphilis. In this patient, the pupillary changes were consistent with the characteristics of the Adie's pupil: bilateral pupil dilated, light reflex disappeared, and the convergence reflex was slow. Bilateral pupils were sensitive to diluted pilocarpine, consistent with the cases reported in previous literatures (8, 12, 15, 16). The evaluation revealed serum positive of CLIA, TPPA and RPR (1:32) test. The CSF examination revealed pleocytosis, elevated protein, and positive RPR (1:2), TPPA and CLIA. Neurosyphilis was diagnosed according to the guidelines proposed by the American Centers for Disease Control (CDC) in 2015 (17). Other causes of pupil abnormality were

excluded, include HAS, diabetic ophthalmoplegia, localized ocular traumas and intracranial space-occupying lesions.

Growing evidence suggests that pupillary abnormalities are important clinical manifestations and signs of neurosyphilis. Nearly half of the patients with neurosyphilis could present with pupil changes (14). Despite the most typical pupillary change of neurosyphilis is AR pupil, which manifests as bilateral miosis, lack of light reflex but brisk constriction with accommodation reflex, it mainly exists in late neurosyphilis such as Tabes Dorsalis and dementia paralytica (14, 15, 18). On the contrary the Adie's pupil onsets early in neurosyphilis, and may even be the first clinical sign or the only performance of neurosyphilis (12). Therefore, the Adie's pupil changes could be more important than AR pupil in the identification of neurosyphilis, especially early neurosyphilis. Patients with Adie's pupil usually present with mild symptoms, such as blurred vision, visual fatigue or can even be asymptomatic. Abnormalities can be found during PE or when patients themselves look in the mirror.

Parenterally Penicillin G administration is recommended for treating patients in all stages of syphilis, including neurosyphilis (17, 19). For patients who are allergic to penicillin, cephalosporin can be used as an alternative treatment (17, 20). For patients with unilateral Adie's pupil, timely anti-syphilis treatment may promote partial or complete recovery of the pupil (13, 15, 21). However, when the disease progresses and extends to bilateral pupils, the pupils remain unchanged after effective treatment (12, 16). Therefore, for patients presented with Adie's pupil, it should warrant an evaluation of neurosyphilis timely due to further treatment consideration.

In conclusion, Adie's pupil is one of the most important pupillary changes in neurosyphilis, it can occur in early neurosyphilis and deserves more attention. For patients with Adie's pupils, the possibility of neurosyphilis should be considered, and syphilis screening should be carried out in time. Our studies further underscore the need for syphilis screening for patients with abnormal pupil changes.

Abbreviations

AR: Argyll Robertson; **CDC:** Centers for Disease Control; **CLIA:** chemiluminescence immunoassays; **CSF:** Cerebrospinal fluid; **DWI:** Diffusion Weighted Imaging; **HAS:** Holmes-Adie syndrome; **HIV:** human immunodeficiency virus; **MRI:** Magnetic Resonance Imaging; **PE:** physical examinations; **RPR:** rapid plasma regain; **TPPA:** *Treponema pallidum* particle agglutination.

Declarations

Ethics approval and consent to participate

This research was performed in accordance with the Declaration of Helsinki and approved by the ethics committee of the First Affiliated Hospital of China Medical University. The patients gave written informed consent prior to obtaining the data.

Consent for publication

The consent to participate was obtained from the patient in a written informed consent form including the consent for the publication of all the personal, medical details and images.

Availability of data and materials

All data are presented in the manuscript. There are no additional data.

Competing interests

The authors declare that they have no competing interests.

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Not applicable.

Authors' Contributions

YZ contributed to the concept, drafting and reporting of the case. JJ, ML and ML contributed the reporting and revising the report. XS revised the report. All authors read and approved the final manuscript.

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Figures

Figure 1

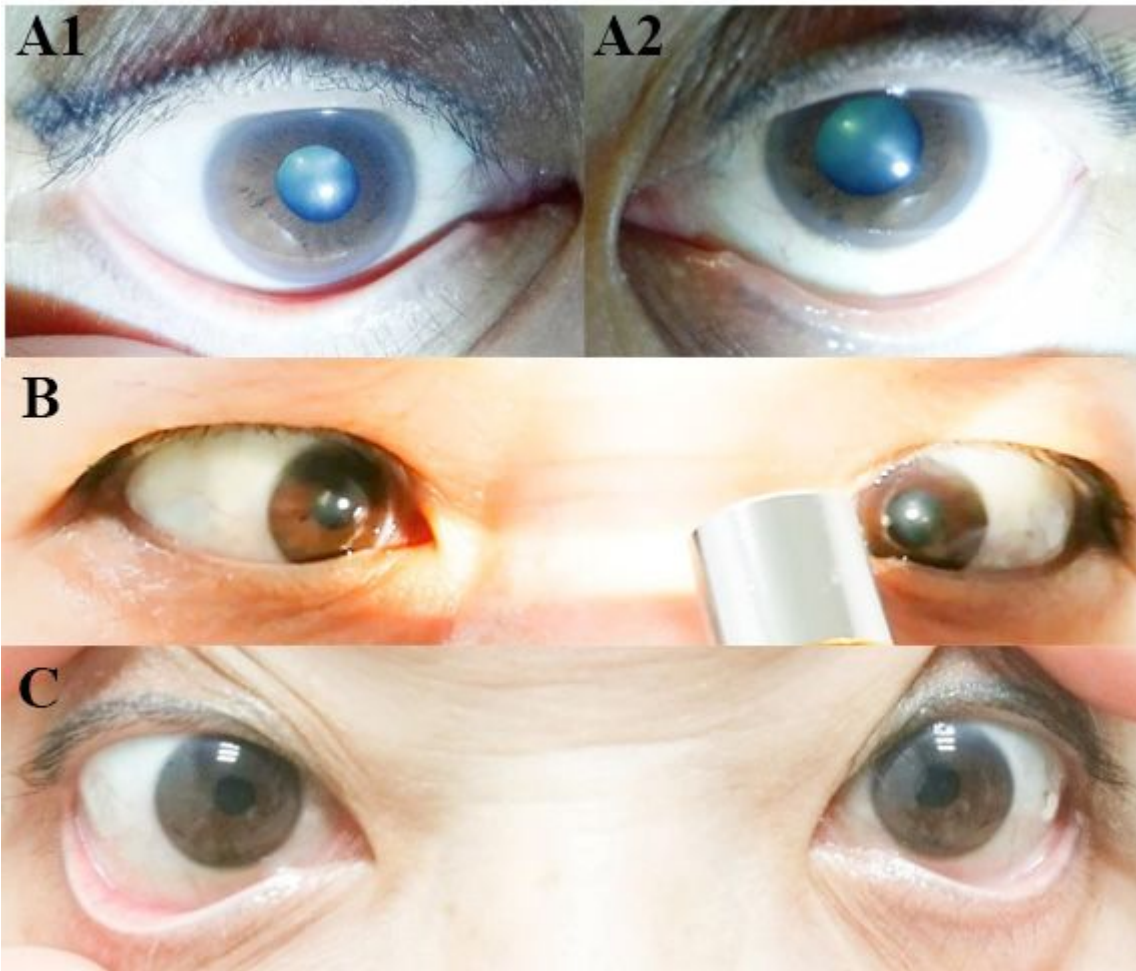


Figure 1

Bilateral pupil dilated without contraction under light stimulation, left pupil $D \approx 6.0\text{mm}$, right pupil $D \approx 5.0\text{mm}$ (A1: right eye, A2: left eye); Pupils contraction was attenuated in near reflex (B); After instillation of diluted pilocarpine (0.125%), both pupils showed marked constrictions (left pupil $D \approx 3.5\text{mm}$, right pupil $D \approx 2.5\text{mm}$ (C). (D: diameter).

Figure 2

A 58-year-old retired Chinese woman with unremarkable past medical history and family history, denied history of hypertension, diabetes mellitus, ocular trauma, surgery and blood transfusion.

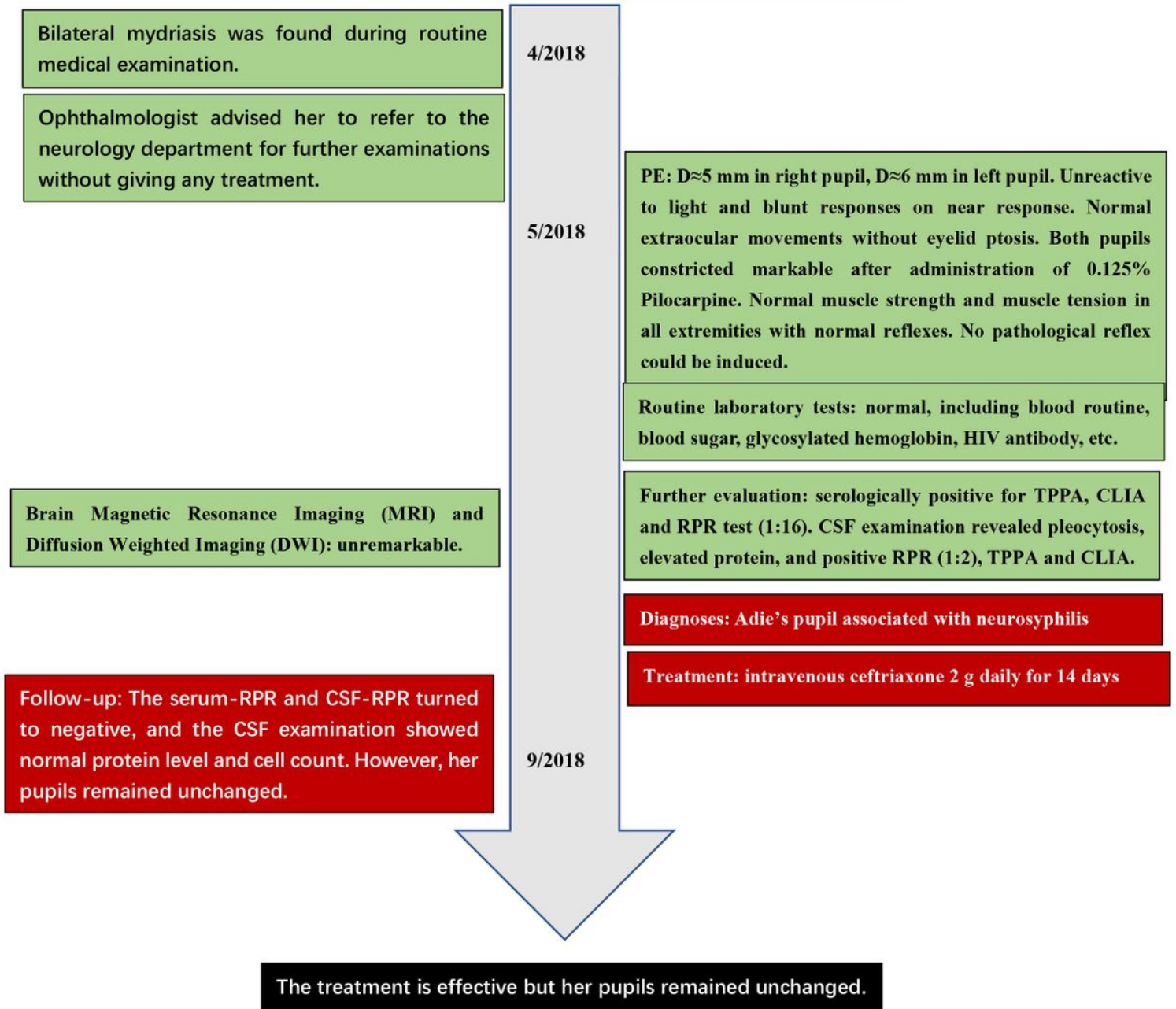


Figure 2

Timeline.

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