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CASE REPORT

Frontiers in Ophthalmology

Bilateral Congenital Mydriasis in A Patient with Family History of Dilated Pupils

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Introduction

When encountering a fixed bilateral mydriasis a palette of differential diagnosis should come to mind. From a low conscious patient in an emergency setting to a casual finding in an outpatient clinic, the context in which a bilateral fixed mydriasis presents is crucial for its management and significance to the patient's life. Is it of recent presentation or does the patient have a long history of photophobia and old photographs that proves its chronicity? Assessing family history and any associated systemic manifestation, as well as identifying the dysfunctional eye and/or neurological structures through pharmacological tests and images should guide us to the definite diagnosis. Most of the causes of congenital dilated pupils can be confirmed with a genetic workup if the responsible gene is known. We present a case of a patient with a bilateral congenital mydriasis due to a probable aplasia of the iris sphincter muscle, and a strong family story suggestive of X pattern inheritance.

Case Report

We report a case of a 59-years-old woman who attended due to family history of glaucoma and long story of photophobia. Five years before this consult she had cataract surgery done in both eyes due to posterior subcapsular cataracts, at another center. Personal and family history was questioned. She reported that both her mother and daughter had dilated eyes just like hers, all her siblings are females, and she has no sons. She denied any cardiac or intestinal disease, ocular trauma or recent pharmacological dilatation. Old photographs showed the same mydriasis she presented in consult. Months before she was seen by the neurology department due to multiple episodes of intense headaches. A brain and orbit magnetic resonance imaging (MRI) were performed but no organic damage was found. Serological analysis and immune markers were unremarkable. Cerebrospinal fluid analysis was also negative. The patient was discharged with the diagnosis of tension-type headaches. Distance vision was 20/20 in both eyes. Ocular motility exam was normal. No nystagmus was noted. Direct and consensual pupillary light reflexes were absent in both eyes. There was no respond to accommodation. At the slit lamp examination bilateral fixed mydriatic pupils was observed (Figure 1). Pupil diameters were 8mm. Intraocular pressure was of 18mmHg in both eyes. Funduscopic examination and optical coherence tomography (OCT) of the posterior pole were unremarkable. The anterior segment OCT (AS-OCT) evidenced a dilated pupil with a smooth iris surface suggestive of hypoplasia of the iris sphincter muscle (Figure 2). 1% cyclopentolate, 0.125% and 2% pilocarpine eye tests were performed and no response was noted. There was a slight response to phenylephrine drops. PAX6, ELP4, ACTA2 and TRIM4 genes were studied, but no pathological findings were reported. Based on all these findings, the diagnosis of bilateral congenital mydriasis with a probable X-linked dominant inheritance was established. After one-year of follow-up, no ocular or systemic changes were observed.

Discussion

Congenial mydriasis is an exclusion diagnosis in patients with bilateral fixed dilated pupils since birth. This condition, being so rare, should only be considered after considering the most urgent and common differential diagnosis for dilated pupils. Family history, old photographs and discarding any associated systemic abnormalities are a must when considering this diagnosis.

The workup of these kinds of patients should be aimed first to discard neurological reasons such as midbrain lesions, preganglionic or postganglionic parasympathetic damage (PPD). PPD manifest itself as a tonic pupil syndrome (TPS). Although usually unilateral, TPS can lead to a bilateral mydriasis in which the accommodation is spared in contrast to the congenital mydriasis were neither light response nor accommodation are present [1]. Toxic conditions should also be assessed (antidepressants, recreational drugs,

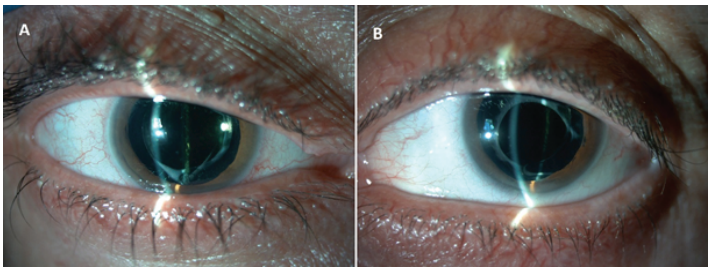

Figure 1. *Slit lamp photographs showing fixed dilated pupils in OD (A) and OS (B)*

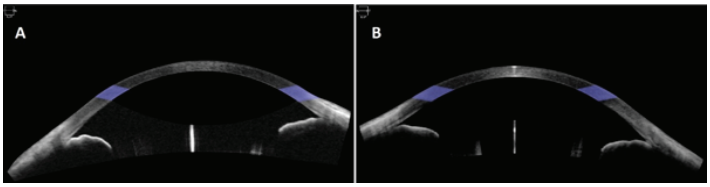

Figure 2. *AS-OCT shows hypoplasia of iris sphincter and dilated muscles in OD (A) and OS (B)*

Parkinson drugs, etc.), as well as any systemic morbidities that can manifests with mydrasis (schizophrenia, hyperthyroidism, migraine) [2].

Pharmacological tests should be performed to note the response of the pupil to adrenergic and cholinergic agents [3]. Absence of response to a cholinergic agent suggests low cholinergic sensitivity and/or aplasia of the pupil sphincter muscle and could rule out a central or peripheral cause of pupilloparesis and/or denervation supersensitivity, as the reported case [4].

Bilateral congenital mydriasis is a rare condition, described as fixed dilated pupils from birth due to aplasia of the iris sphincter muscle. It presents with lack of pupillary constriction to both light and accommodation. The dilator muscle is usually present [5]. Some studies suggest the use of anterior segment OCT as a diagnostic method to evaluate the iris-iris sphincter muscle complex. It is generally bilateral, and most of the patients are female. The pattern of inheritance is autosomal dominant or X-linked dominant incompatible with life in male gender. The exact responsible gene for this condition remains unknown [6].

One of the most studied and reported differential diagnosis for this condition has been the multi-systemic smooth muscle dysfunction syndrome (MSSMD) due to the X linked dominant mutation of the ACTA2 gene. In this syndrome the most notorious manifestations are bilateral mydriasis at birth, patent ductus arteriosus and gastrointestinal problems [7]. Our patient exhibited none of these findings, ruling the MSMDS out.

Another differential diagnosis in patients with large pupils since birth and family history of glaucoma is incomplete aniridia. In this diagnosis, there is a dysgenesis of multiple eye structures, including the iris, related to autosomal dominant inherited mutations in the PAX6, ELP4 and/or TRIM4 genes. Mutations in the PAX6 gene are present in 94% of patients with incomplete aniridia [8]. These patients usually have very low vision, as of less than 20/100, due to concomitant foveal hypoplasia. In all of the published cases, the response to sympathetic and parasympathetic agents was none [9].

In this case, taking into account the highly suggestive pattern of X-linked inheritance, good vision, absence of the mentioned gene mutations, slight response to mydriatic agents and no other significant findings other than the large pupils, inclined us to the diagnosis of bilateral congenital mydriasis.

Conflict of interest declaration

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and /or publication of this article.

Statement of consent

Written informed consent was obtained from patient to publish findings and images presented in this manuscript

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References

1. Gräf MH, Jungherr A. Congenital Mydriasis, Failure of Accommodation, and Patent Ductus Arteriosus. *Arch Ophthalmol*. 2002; 120: 509-510.
2. Kurtul B, Ozer P, Cağlar A, Kabatas E. Bilateral congenital mydriasis in a child case. *Türk Pediatri Arşivi.* 2016; 51: 176-177.
3. Goktas A, Goktas S. Bilateral Tonic Pupils in the Absence of Pupillary Cholinergic Supersensitivity. *Neuroophthalmology*. 2011; 35: 12-14.
4. Reyes MA, Garcia M, Perez D. Midriasis congénita bilateral a propósito de un caso. *Arch. Soc. Canar. Oftal*. 1986-1998; 9: 81-83.
5. Kaeser PF, Kawasaki A. Disorders of pupillary structure and function. *In Neurol Clin.* 2010; 28: 657-677.
6. Roulez FM, Faes F, Delbeke P, Van Bogaert P, Rodesch G, et al. Congenital fixed dilated pupils due to ACTA2- multisystemic smooth muscle dysfunction syndrome. *J Neuroophthalmol*. 2014; 34: 137-143.
7. Regalado ES, Mellor-Crummey L, De Backer J, Braverman AC, Ades L, et al. Clinical history and management recommendations of the smooth muscle dysfunction syndrome due to ACTA2 arginine 179 alterations. *Genet Med.* 2018; 20: 1206-1215.
8. Robinson DO, Howarth RJ, Williamson KA, van Heyningen V, Beal SJ, et al. Genetic analysis of chromosome 11p13 and the PAX6 gene in a series of 125 cases referred with aniridia. *Am J Med Genet A*. 2008; 146A: 558-569.
9. Syrimis A, Nicolaou N, Alexandrou A, Papaevripidou I, Nicolaou M, et al. Aniridia due to a novel microdeletion affecting PAX6 regulatory enhancers: case report and review of the literature. *J Genet.* 2018; 97: 555-562.

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