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Epiretinal membrane and cataract in a 5-year-old boy with the suspicion of neurofibromatosis type 2

Case report

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Abstract: Different ocular findings have been described in association with neurofibromatosis 2 (NF2). Detailed ophthalmological examination of asymptomatic subjects with a family history of NF2 could help confirm the diagnosis in young patients. We present a case of unilateral cataract and bilateral epiretinal membranes in a 5-year-old boy with a family history of neurofibromatosis 2. The patient was referred to our department with diminished visual acuity bilaterally and an initial diagnosis of cataract in the right eye. Best-corrected visual acuity was 3/19 in the right eye and 3/24 in the left eye (LH charts). On fundus examination, bilateral macular epiretinal membranes were found and confirmed by optical coherent tomography. In view of the ophthalmic signs mentioned above and the history of the patient's father, who suffered from NF2 and died from meningioma and ependymoma, the patient was referred for genetic examination. Seventeen exons of the NF2 gene were tested with negative results. No pathology was found on clinical neurologic examination and magnetic resonance imaging of the brain. Although the patient has not met the criteria for NF2, he is now considered as an asymptomatic subject at risk and observed. Lens opacities with epiretinal membranes in children may be regarded as part of the clinical manifestation of NF2.

Keywords: *Cataract • Epiretinal membrane • Inborn genetic diseases • Neurofibromatosis 2 • Retinal disease*

1. Introduction

According to National Institute of Health the diagnostic criteria for type 2 neurofibromatosis (NF2) include: bilateral eighth cranial nerve tumours (schwannoma) or a family history of NF2, and either a unilateral schwannoma or two of the following: neurofibroma, meningioma, glioma, schwannoma or juvenile posterior subcapsular cataract [1]. Additional criteria include bilateral schwannomas and any two of: meningioma, glioma, neurofibroma, schwannoma and posterior subcapsular opacities, or multiple meningiomas (2 or more) with bilateral schwannomas or any two of: glioma, neurofibroma, schwannoma and cataract [2]. NF2 is a complex disorder demanding a multidisciplinary approach. The cooperation of specialists in neurology, radiology, otolaryngology, genetics and ophthalmology may diminish morbidity and mortality from this disease.

Different ocular abnormalities have been reported in patients with NF2. Patients present with visual symptoms in their childhood, usually before the development of neurological signs and symptoms. The description of posterior capsular lens opacities in NF2 was first published in 1986 [3]. It occurrs at an early age in approximately 85% of NF2 patients. Additionally, the association between combined pigment epithelial and retinal hamartomas (CPERH) and NF2 was confirmed [4]. Epiretinal membranes (ERMs) were also reported in patients with NF2 [5,6]. Both retinal hamartomas and epiretinal membranes are seen in up to one-third of individuals and represent the most common retinal manifestations of NF [6].

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The aim of this paper is to describe the case of a 5-year-old boy who, based on ophthalmic examination, was for the first time considered as a patient at risk of developing type 2 neurofibromatosis and was referred for further evaluation.

2. Material and Methods:

Case report presentation: ophthalmic examination, including optical coherence tomography examination, neurologic examination with magnetic resonance imaging, genetic evaluation.

3. Statistical methods and experimental procedures

None.

4. Case Report

A 5-year-old boy, born at term, was referred to our department with diminished visual acuity bilaterally and an initial diagnosis of cataract in the right eye. Past medical history was otherwise unremarkable. His father died from meningioma and ependymoma of the spinal cord and type 2 neurofibromatosis was diagnosed *post mortem*.

Best-corrected visual acuity was 3/19 in the right eye and 3/24 in the left eye (on LH charts) and his refraction showed astigmatism of +1.25 -2.75 ax40 in the right eye and -2.25 -1.50 ax165 in the left eye (examined after cycloplegia). A central posterior pole cataract was confirmed in the right eye. On fundus examination, epiretinal membranes (ERMs) extending into the macula were found in both eyes. Abnormal straight vessels dragged temporally from the left optic disc were seen. Pigmentation changes with pigmentary mottling in the right eye were also noted. The ERM was transparent in the right eye and translucent, whitish-grey in the left one. It was about two disc diameters in size. Optical coherence tomography (OCT) confirmed the presence of ERMs in both eyes (Figure 1 and Figure 2), but the left ERM was significantly more extensive, with atypical curled edges. The internal limiting membrane in the left macula was slightly wrinkled. No other ocular pathology was detected.

Although the findings of cataract and ERMs in addition to the family history were not diagnostic of NF2, the patient was referred for genetic consultation because of this atypical association. This was his first genetic

Figure 1. Optical coherence tomography of the epiretinal membrane in the right eye.

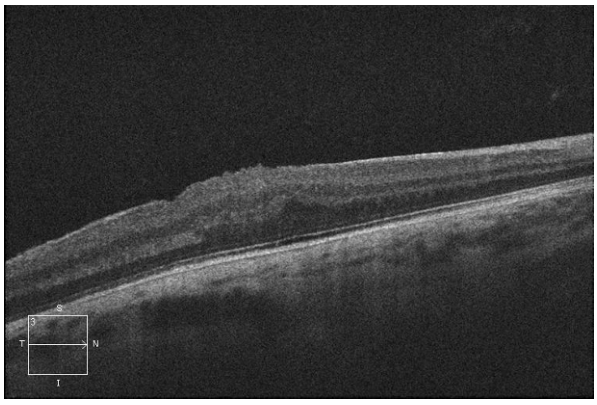
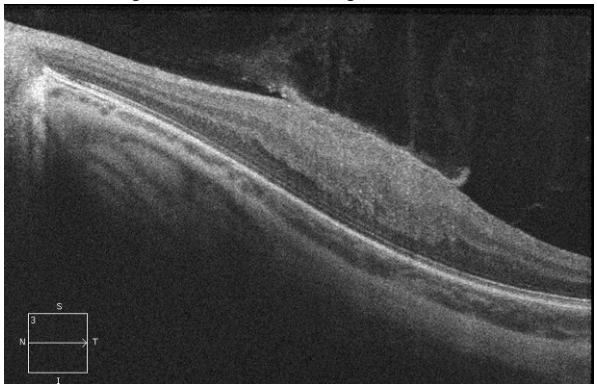


Figure 2. Optical coherence tomography of the epiretinal membrane in the left eye, showing atypical, curled edges with significant macular thickening.



referral despite the early death of his father. Seventeen exons of the NF2 gene (responsible for 27% cases of type 2 neurofibromatosis) tested with MLPA (Multiplex Ligation-dependent Probe Amplification) were normal in our patient. Thus, the genetic examination was negative and could not confirm the disease. However, small point mutations cannot be excluded.

Neurological examination and contrast-enhanced magnetic resonance imaging (MRI) of the brain and spine were performed, but no pathology was found. The patient does not meet the criteria for NF2, but is now considered as an asymptomatic subject at risk and is carefully followed-up.

5. Discussion

In our patient a simultaneous occurrence of cataract and epiretinal membranes was discovered. Although the cataract configuration was typical of a congenital cataract, it could not explain the low visual acuity in both eyes of our patient. The second pathology – epiretinal membranes – may have a different etiology in children and in adults. In adulthood, epiretinal membranes are

often the result of other ocular diseases [6]. We could not find any ocular disorders related to ERM in our patient. Isolated ERMs are unusual in children and probably of congenital origin [6]. Therefore we decided to explore further for associated pathology. Bearing in mind his family history, we performed a literature search and found similar case descriptions.

Despite the congenital nature of most of the ophthalmic findings in NF2 (including NF2-specific ERMs), they may become more symptomatic and enlarge over time [5]. Hence, annual ophthalmoscopy from the age of 2 to12 in patients with NF2 is suggested [1,2]. Bosch found ERMs in 40% of 30 referred patients with NF2 [7]. McLaughlin suggested that dysplastic glial Müller cells may be the major component of NF2-associated epiretinal membranes [8]. Schefler described ERMs in NF2 patients as atypical and unusually thick, with rolled edges extending into the vitreoretinal interface [9]. This description corresponds with our patient's OCT results.

Why is ERM characteristic of NF2? All ocular associations mentioned above reflect embryological pathology of neural crest cells differentiation into the lens, the retinal pigment epithelium and retinal glial cells. The process takes place between the surfaces of the ectoderm and neuroectoderm. Meyers speculated that, in NF2, the neural crest cells at the vitreoretinal junction and in the retina retina, and the lens ectodermal cells, can proliferate abnormally leading to different pathologies, including ERM, retinal hamartoma or cataract, even at early age [6]. Therefore, Meyers suggested that in addition to lens opacities, ERMs and combined pigment epithelial and retinal hamartomas (CPERH) should also be considered as a part of the diagnostic criteria of NF2 in young patients [6]. Additionally, according to Sisk, bilateral ERMs appear to be a marker for a more severe phenotype of NF2 [10]. If ophthalmologists could confirm the association between the prevalence of retinal lesions and the type of the disease, the evaluation of advancement of NF2 would be possible. A possible treatment option for ERM is pars plana vitrectomy with membrane peeling, but in this type of ERM, like in CPERH, the surgery is difficult and associated with complications (delayed-onset rhegmatogenous retinal detachment from peripheral traction and recurrence of ERM) [11]. We could not find any case descriptions of NF2-related ERM treated with vitrectomy.

Our case and literature search lead to the conclusion that, in children or young patients, ERM and lens opacities are rarely unrelated to other ocular disorders and should be considered as congenital lesions, perhaps as part of NF2.

In this specific group, a family history of NF2 should be excluded and neurological evaluation performed, although the diagnosis of NF2 is often difficult. The mutation detection rate in patients with NF2 is about 50%, so the diagnosis is instead based on clinical criteria [1,2]. Therefore, for early diagnosis of this disease, careful evaluation of clinical signs and symptoms play a crucial role. Patients at risk (i.e. with NF2-affected family members) observed in specialized treatment centers have a lower risk of mortality when screened from birth [6]. Screening allows earlier identification and surgical intervention in cases of life-threatening pathology. Serial MRI of the spine and brain with gadolinium contrast is recommended from the ages of 10 to 12 [2,12]. A normal MRI scan at the age of 18 halves the risk of having NF2. A normal scan at the age of 30 indicates that inheritance is unlikely and screening may be ended. According to the results of screening, appropriate advice regarding family planning can be given [1,2]. An important question remains: who should be observed and screened as an at-risk individual?

Our case description suggests that selection of asymptomatic, at-risk patients from a group of healthy NF2 family members could be achieved timely by means of ophthalmic slit lamp examination and, in particular, OCT examination. Although the presented patient has not met the criteria for NF2, he is now carefully followed-up.

6. Acknowledgments

None

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