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Case Report Open Access

# Ocular Findings of Neurofibromatosis 2: A Case Study

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## Abstract

We report a case, from China, of neurofibromatosis 2 with notable ocular lesions, a unilateral cataract, and optic nerve meningiomas. The 24-year-old patient was diagnosed as neurofibromatosis type 2 based on his bilateral vestibular schwannoma and intraspinal tumors, but he also had some important clinical features of neurofibromatosis type 1, such as skin tumors and "cafe-au-lait" macules. He noticed that his left lens had become gradually more opaque over the past two years, and could only perceive light at the time of the study. Phacoemulsification, intraocular lens implantation, posterior capsulotomy and anterior vitrectomy were performed on this patient to manage the cataract and ruptured posterior capsule. Following surgery, the patient could count fingers at a 30cm distance from his eyes. Optic nerve meningiomas existed in both orbits in different sizes. Early surgery interventions are important for neurofibromatosis patients with ocular symptoms to restore vision.

Neurofibromatosis is an autosomal dominant disease resulting from a mutation in the tumor suppressor gene. It is generally classified into two distinct disorders: type 1 neurofibromatosis (NF 1, von Recklinghausen's disease) and type 2 neurofibromatosis (NF 2). Both types are characterized by multiple neoplasias. Ophthalmic signs include, but are not limited to, juvenile cataracts, retinal hamartomas, and epiretinal membranes as discussed in the literature. Here we report a rare case of neurofibromatosis type 2 with clinical features of type 1 who had evidence of both a unilateral cataract and optic nerve meningiomas in China.

## Case Report

This Chinese patient was 24 years old, with no family history of neurofibromatosis. He felt feeble, with a history of numbness for 6 weeks in both legs. Gradually, he lost the ability to walk by himself. Urinary urgency and incontinence often occurred. An MRI scan of his cervical, thoracic, and lumbar spinal cord revealed several intraspinal tumors, which suggested neurofibromatosis [1,2] (Figure 1). When the patient was a young boy, many plaques ("cafe-au-lait" macules) and tumors (epidermal and subcutaneous) were noticed all over his skin and scalp (Figure 2). Several skin tumors were removed and histopathologically confirmed as dermatofibromas. At the age of 17 years old, he began to notice hearing loss in both ears. A cranial MRI revealed several masses on both acoustic nerves and the right trigeminal nerve (Figures 3A and 3B). Therefore, the young man was finally diagnosed as neurofibromatosis type 2 by the department of neurosurgery based on his bilateral vestibular schwannoma and intraspinal tumors according to the clinical diagnostic criteria of NF 2 by NIH [3].

He stated that vision in his left eye consisted of light perception only (since he was a child), and that his vision has remained the same for over 20 years. However, he had noticed (obviously) that his left lens had become opaque over the past two years. He had never been exposed to ocular trauma or cataractogenic agents, such as glucocorticoids or phenothiazines. His cranial MRI scan also indicated one tumor on his right lateral rectus muscle and another small one on left optic nerve (Figures 3C and 3D).

This patient agreed to a series of ophthalmological examinations to evaluate the indication for cataract surgery. His right visual acuity was 0.6, while his left visual acuity was only light perception. His intraocular pressures were, respectively, 18.5 mmHg (OD) and 14.5 mmHg (OS). Slit lamp microscopy and anterior segment photography clearly revealed left lens opacities with partial lens absorption (Figure 4A). Because his left lens was severely opaque, and most of the cortex was absorbed and organized, his left fundus could not be observed in total, despite pupillary dilation (Figure 4B). Ultrasonic examination of the left eye showed vitreous opacification and posterior scleral staphyloma. ERG examination (left eye) showed a lower amplitude wave, suggesting that the retinal cone cells were in a dysfunctional status. The flash-VEP examination showed lower wave amplitude, which reflected the impaired visual pathway. In spite of that, the patient chose to have the phacoemulsification operation and intraocular lens implantation.

During surgery, rupture of the posterior capsule occurred after hydrodissection. It suggested that perhaps it was a congenital posterior polar cataract. The organized lens capsule was removed and an anterior vitrectomy was performed. Following this, the residual cortex inside the peripheral capsule was extracted (as much as possible) by I/A aspiration of the phacoemulsification apparatus. An intraocular lens (ZCB00, 14.0D) was then implanted at the ciliary sulcus. The operation was performed successfully, and on the day following the operation, the patient could count fingers at a 30cm distance from his eyes. Slit lamp examination showed a transparent and clear pupillary zone with little remaining cortex around the peripheral capsule (Figure 5C). Left fundus photography and fluorescein angiography (FFA) suggested high myopic changes and papillopathy (Figure 6).

## Discussion

Neurofibromatosis type 2 results from a mutation in the NF2 tumor suppressor gene on chromosome 22q12. This disorder is characterized by vestibular schwannomas, spinal cord schwannomas, meningiomas, and ependymomas [4-6] It occurs in one out of every 25,000 live births [7]. These patients often present with hearing loss or difficulty walking due to the schwannomas in the central nervous system. NF 1 is the most common phakomatosis, occurring in 1 of 5000 [4]. Skin tumors and "cafe-au-lait" macules are the features of type 1 neurofibromatosis.

With the increasing knowledge of neurofibromatosis, more attention is paid to the ocular manifestations of this disease. Through

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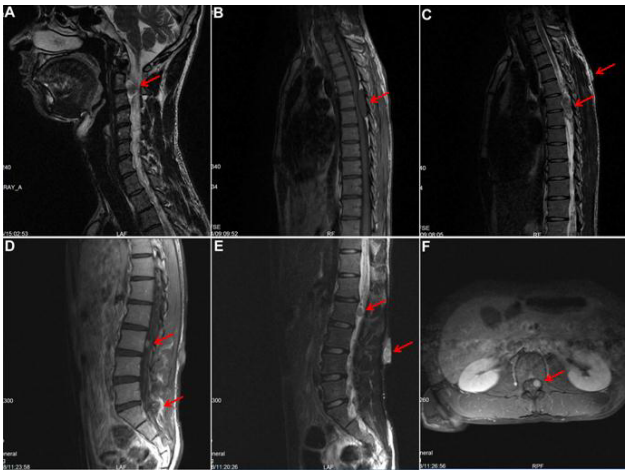

**Figure 1:** MRI scan of the spinal cord showing several intraspinal masses. (A) Sagittal T2-weighted MRI showing a dumbbell-shaped abnormally low signal in the right intervertebral foramen at the C2-3 level, approximately 13 mm × 15 mm × 15 mm in size. (B) Sagittal T1-weighted MRI and (C) Sagittal T2-weighted MRI showing a dumbbell-shaped abnormal intraspinal mass in the right intervertebral foramen at the T5-6 level, approximately 37 mm × 12 mm × 40 mm in size. The epidural mass was then excised and confirmed as a schwannoma by a pathologist. (D) Sagittal T1-weighted MRI, (E) Sagittal T2-weighted MRI, and (F) Transverse T1-weighted MRI showing multiple nodules in the lumbar vertebral canal. The largest was approximately 11 mm × 9 mm × 8 mm in size at the L2 level. Oval-shaped masses on both sides of the spine at the L5-S1 level are also visible, approximately 31 mm × 18 mm in size. A 31 mm × 10 mm oval subcutaneous mass is also shown on the back at the L3 level.

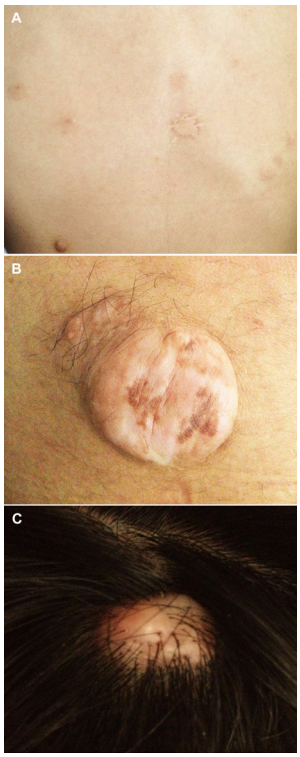

**Figure 2:** Skin plaques and tumors. (A) Scattered “cafe-au-lait” macules are visible on the epidermis of the back. (B) The biggest skin tumor is approximately 4cm in diameter at the waist. (C) A protuberant tumor is even seen on the scalp.

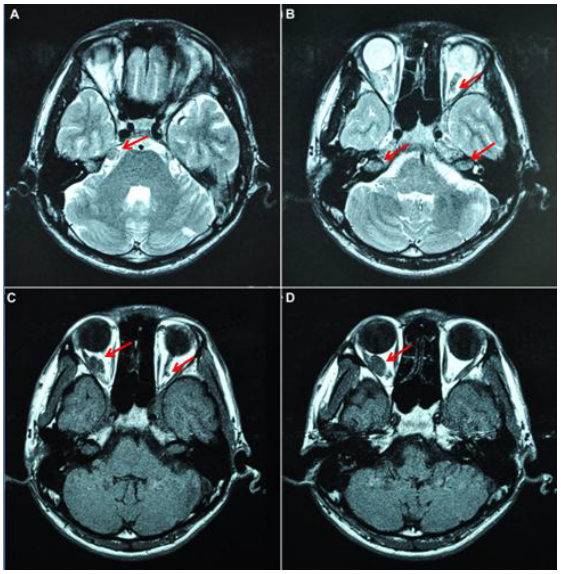

**Figure 3:** Transverse MRI scan showing several cranial masses. (A) A nodule is shown in the right trigeminal area. (B) A widened internal auditory canal tube suggests bilateral vestibular schwannomas. (C) A small tumor close to the left optic nerve is seen. (D) A fusiform mass in the lateral rectus of the right orbit compresses the neighboring optic nerve.

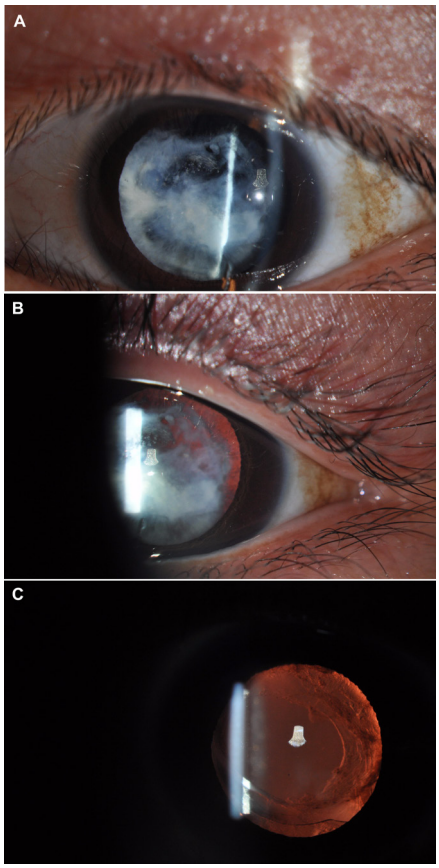

**Figure 4:** Anterior segment photography. (A) A slit camera showed heterogeneous white cortical opacities of the left lens (mostly absorbed). (B) Partial fundus was visible through the dilated pupil. (C) Retro-illumination reveals the transparent intraocular lens after the phacoemulsification operation.

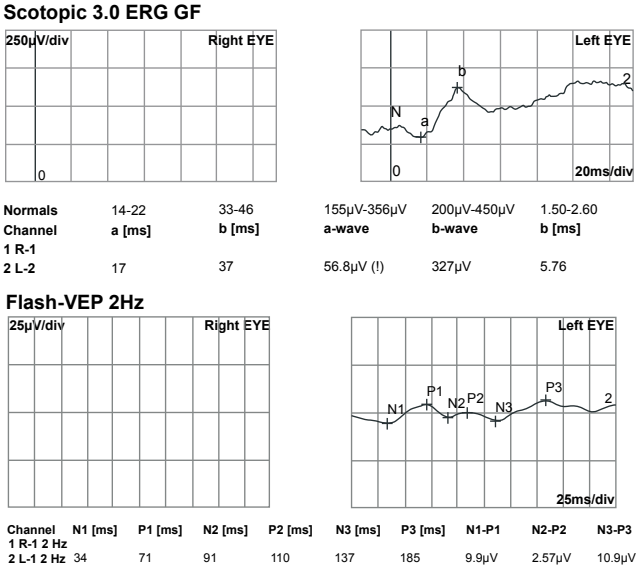


**Figure 5:** ERG and Flash-VEP examination (ROLAND CONSULT Color Ganzfeld Q450C). Scotopic 3.0 ERG examination (left eye) showed lower wave amplitude, suggesting that the retinal cells are in a dysfunctional status. Flash-VEP examination was also performed to the left eye of the patient because of his bad visual acuity, showing lower wave amplitude.

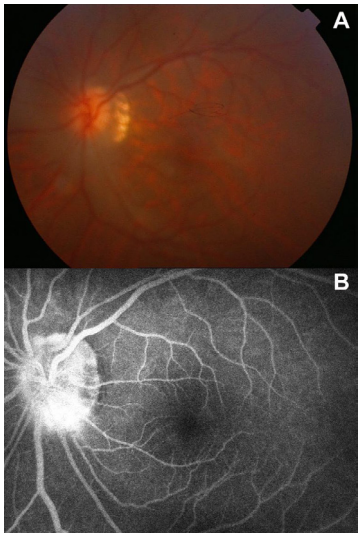


**Figure 6:** Left fundus photography and fluorescein angiography after the phacoemulsification operation. (A) Fundus photography showing a leopard retina with a crescent surrounding the temporal part of the disc. (B) FFA (fundus fluorscein angiography) showing an unclear disc with a small amount of fluorescein leakage.

literature review, we summarized the ocular findings in type 2 neurofibromatosis as listed in Table 1. Unfortunately, some of the signs are limited to case reports, with a lack of occurrence data based on population studies. Lens opacities are the only ocular signs which were incorporated into the diagnostic criteria of type 2 neurofibromatosis, but were not reported in NF 1.

The patient with typical signs of neurofibromatosis also had cataracts and optic nerve meningiomas at the same time. Both of these

| Location | Disorder |
|---|---|
| Cornea | Corneal opacity [1] |
| | Corneal pigmentation [2] |
| | Neurotrophic keratopathy [3] |
| sclera | Intrascleral schwannoma [3] |
| Lens | Cataract [1,3-9] |
| Iris | Lisch nodules/ Melanocytic hamartoma [4,10,11] |
| Glaucoma [10] | |
| Retina | Epiretinal membrane [1,3,6,12-14] |
| | Retinal hamartoma [1,5,6,12,15] |
| | Optic disc glioma [16] |
| | Retinal detachment [1,12,17] |
| | Dragged disc syndrome [18] |
| | Retinal microaneurysm [6] |
| | Retinal haemangiomas [19] |
| | Fibrotic maculopathy [20] |
| Optic nerve | Optic sheath meningioma [21] |
| | Secondary optic nerve atrophy caused by tumor [1] |
| | Optic schwannoma [18] |
| | Optic perineural calcification [20] |
| Refractive error | Amblyopia [1,4,7,18] |
| | Myopia [22] |
| | Hyperopia [22] |
| Eye movement | Strabismus [1,7,22] |
| | Nystagmus [22] |
| | Ptosis [12] |

**Table 1:** Ocular findings of neurofibromatosis type 2.

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types of lesions contributed to his visual deficiency despite cataract surgery. Cataracts are important markers for diagnosing NF-2, with an occurrence frequency of 38-81% [1,8,9]. Most sufferers have lens opacities located in the posterior subcapsular or capsular regions, while some are located in the peripheral cortical region of the lens [8-10]. Only 10-25% of them needed surgical intervention to restore vision [6]. The special points of the lens pathology on the patient we report here were that most of the lens cortex was absorbed, which resulted in a flat appearance of the lens. During the operation, the posterior capsule was found to be ruptured with organization and opacity.

Lenses develop from the epidermal ectoderm during the embryonic period, which is also the origin of the surface epithelium. Lens opacities and skin fibromas may be the common results of developmental defects in the epidermal ectoderm. Baser et al. analyzed the genotype-phenotype correlations for cataracts in NF-2 patients and found that the relative risk of cataracts is lower in somatic mosaics, people with large deletions or new/undiscovered mutations, and the onset of signs occurs at ages >20 years old [11]. The NF-2 gene product, schwannomin or merlin, may have extended roles in the development of the lens, vitreous humor, and retina [12]. Merlin is closely related to the ezrin/radixin/moesin proteins, which link the plasma membrane-cytoskeletal interface [13]. Merlin is able to stabilize adheren junctions at the sites of cell-cell contact. McLaughlin et al. described small groups or individually displaced lens cells anterior to the posterior lens capsule, and within the posterior lens cortex, by autopsy and microscopic observation [2]. She suggested that NF-2-deficient posterior lens vesicle cells couldn't vertically elongate to form primary lens fiber cells, due to abnormal adherence junctions, and therefore accumulate in front of the posterior capsule [2]. A merlin deficit may also be one of the possible explanations underlying abnormal lens cell adherence and cataractogenesis.

The other ocular lesions presented in this patient were tumors of both orbits. However, according to the MRI images, these two tumors seemed to be, in essence, "different" (Figure 3). The most probable pathological type of tumor is the optic nerve sheath meningioma (ONSM), according to the most common types and the slow progress of the patient's impaired vision, although we cannot obtain pathological evidence [4,14]. An optic nerve meningioma would interfere with vision and even cause progressive visual loss, visual field defects, proptosis, and upgaze restrictions at an early age [4,6]. This case provided further evidence that optic nerve meningiomas may develop in NF2 patients, and that they originate from the loss of the normal genes responsible for regulating the growth of neural tissues.

It is reported that ocular signs appear at 5.6 years old, on average, compared with 14.1, 20.6, and 25.7 years old for skin abnormalities, other CNS tumors, and vestibular schwannomas [12]. Ragge et al. found that the first presenting sign was ocular in 10% of NF-2 patients [12]. Therefore, it is important to pay attention to ocular signs at an early age in neurofibmatosis patients in order to preserve good visual quality by administering the proper treatment, such as cataract extraction at an early age. If necessary, orbital tumors should also be removed surgically. In a word, early explicit examination and therapy for neurofibromatosis patients must be highlighted.

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None of the authors has a financial or proprietary interest in any materials or methods mentioned.

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