*Case Report*

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# Optical coherence tomography significance in managing complex neurofibromatosis 2-related papilledema: Report of a case

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## Summary

This case describes the strong utility of optical coherence tomography in multidisciplinary management of a complex case of type 2 neurofibromatosis.

## Keywords

optical coherence tomography, neurofibromatosis, shunt placement, vision loss, multidisciplinary approach

## Case description

This case describes the strong utility of optical coherence tomography in multidisciplinary management of a complex case of type 2 neurofibromatosis.

Neurofibromatosis 2 (NF2) is an autosomal dominant disorder caused by pathological variants in the *NF2* gene on chromosome 22, encoding neurofibromin-2 or merlin. The estimated prevalence is 1:56,000.[1] Diagnostic criteria for neurofibromatosis 2 were published by Evans et al. in 1992.[2] Patients are predisposed to develop schwannomas, meningiomas and ependymomas. Clinical presentation is heterogeneous, especially in childhood.[3] Symptoms include hearing loss, tinnitus or ataxia, skin marks and lumps, most commonly cutaneous schwannomas and neurological deficits. Visual system involvement is also prominent in neurofibromatosis 2, with optic nerve sheath meningiomas and other optic nerve tumours, epiretinal membrane, lens opacities, combined hamartoma of the pigment epithelium and retina.[4]

In 2007, a 7-year-old girl was referred to the paediatric ophthalmology Unit of Meyer Children's Hospital because of a severe left microphthalmia and glaucoma with uncontrolled intraocular pressure. The right eye was unremarkable. In the left eye, a severe dysgenesis of anterior and posterior segment with the presence of a total retinal detachment was found. In 2011, the patient complained of a progressive hearing loss in the left ear. A magnetic resonance imaging was performed that confirmed the left microphthalmia as well as left optic nerve thickening due to an optic nerve sheath meningioma associated with bilateral vestibular schwannomas and multiple other intracranial schwannomas; on this basis, the diagnosis of neurofibromatosis 2 was made. Genetic investigations did not conclusively find a pathogenic variant in the *NF2* gene. Three years later, an epiretinal membrane was found at the posterior pole in the right eye by means of spectral domain optical coherence tomography (I-Vue, Optovue Fremont, CA) scan as previously reported in other studies.[5] Nonetheless, her best corrected visual acuity remained 20/25. Further magnetic resonance imaging scans showed progressive growth of the intra-cranial schwannomas and the patient received Bevacizumab infusions starting with 5 mg/kg two weekly[6] changing to 7.5 mg/kg every three weeks. In October 2014, right eye papilledema was observed for the first time without visual acuity reduction, nor visual field scotomas, but with evident peripapillary retinal nerve fiber layer thickening from baseline at spectral domain optical coherence tomography scan. Papilledema remitted and relapsed many times until December 2016 without

any visual changes. Magnetic resonance imaging scans did not show any significant change in tumours near the optic pathways and there was no modification of the clinical neurological picture, specifically there were no symptoms of raised intracranial pressure. At the end of 2017, a further relapse of papilledema was noticed without changes in best corrected visual acuity or visual field (Figure 1) and the patient was started on oral acetazolamide 250 mg/die for two months: despite a good compliance to the therapy, the papilledema did not improve and we therefore decided to stop the diuretic treatment. In order to rule out a raised intracranial pressure causing the persistent papilledema, an intracranial pressure monitoring device was implanted. The three days' continuous recordings showed only some short isolated nocturnal peaks of 28 mmHg with tachycardia not consistent with a clearcut high intracranial pressure. During follow-up examinations, the papilledema remained stable until mid 2018 when a new spontaneous improvement was noted. In 2018, Bevacizumab administration was reduced to 5 mg/kg every four weeks for increased proteinuria and worsening of renal function. Serial spectral domain optical coherence tomography controls showed a stable peripapillary retinal nerve fiber layer thickness until the beginning of 2019 when a new relapse was noticed together with reduced vision in right eye and a dropped acuity to 20/32 in the following five months. Bevacizumab interval administration was therefore reduced to every three weeks. After a multidisciplinary consultation with the Manchester neurofibromatosis 2 multidisciplinary team, a magnetic resonance venography was performed to rule out eventual stenosis of dural sinuses due to schwannomas: the dominant right sigmoid sinus and jugular bulb appeared almost completely closed because of a direct compression of a cystic-solid jugular schwannoma (Figure 2). The reduced venous outflow stenosis was correlated with the moderate chronic intracranial hypertension, papilledema and visual failure; intracranial pressure fluctuations could have been related to cycles of venous insufficiency followed by recovery with venous collateralisation. The

**Figure 1.** Upper part: timeline and composite of fundus imaging showing the recurrent–remittent trend of right eye papilledema. Lower part: composite of spectral domain optical coherence tomography imaging of the right optic nerve head according to timeline and fundus images. The lowest row shows details of peripapillary retinal nerve fiber layer trend over time: note that the peripapillary retinal nerve fiber layer thickness is compared with normative database from December 2017 after the patient becomes >18 years old. Timing of the images is reported in the lower left corner of the fundus image: last image shows the resolution of papilledema after ventriculo-peritoneal shunting procedure (see text).

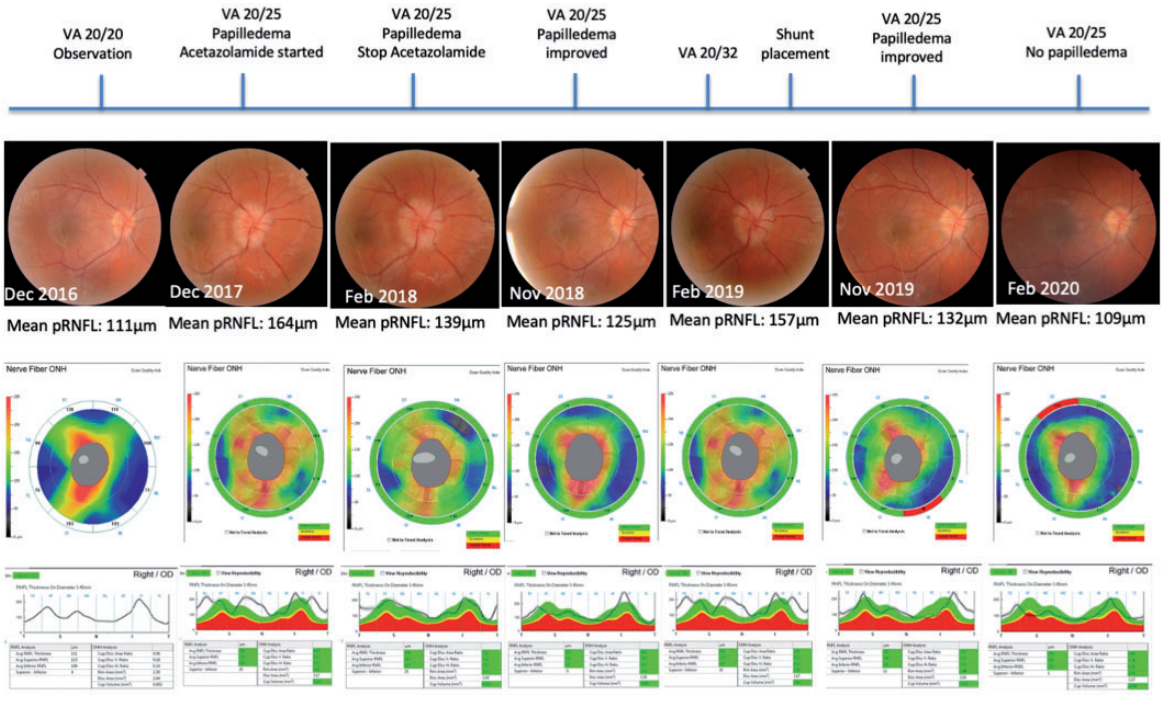
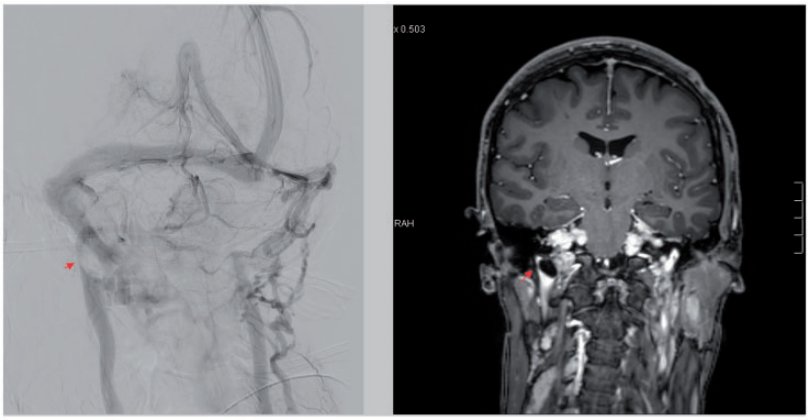


**Figure 2.** Left: catheter angiographic study showing stenosis of the right sigmoid sinus and jugular bulb with oval-shaped compressive filling defect (arrow). Right: magnetic resonance imaging showing cystic formation within the right lower cranial nerve schwannoma (arrow) at the level of the tumour-related venous stenosis demonstrated on venography.




options for management were either stenting the dural sinus or ventriculo-peritoneal shunting to relieve the intracranial pressure. Given the need for long-term anticoagulation therapy after stenting and the continuous deterioration in visual acuity, we preferred the ventriculo-peritoneal shunting as first choice despite normal ventricles because it's a procedure that allows faster and more efficient intracranial pressure control if compared to stenting option. Under image-guidance, a right frontal ventriculo-peritoneal shunt was inserted with Orbis-Sigma valve (OS-II, Integra Life SciencesCorporation®, Princeton, USA). The post-operative period was characterised by a dramatic and immediate improvement of visual function. The peripapillary retinal nerve fiber layer rapidly returned to the baseline values (Figure 1) and best corrected visual acuity progressively restored to 20/25. At last consultation, 10 months after surgery, the patient had good visual acuity with a stable peripapillary retinal nerve fiber layer without papilledema.

In recent years, optical coherence tomography has become a powerful, non-invasive, diagnostic tool in optic neuropathies and brain tumours with optic pathways involvement[7–9] thanks to the detection of change in peripapillary retinal nerve fiber layer thickness and ganglion cell complex-inner plexiform layer,[10] in the paediatric age too. Since the peripapillary nerve fiber layer is strictly related to intracranial pathologies directly or indirectly involving optic pathways,[7] the structural data obtained with this technology and the anatomic quantification of peripapillary retinal nerve fiber layer thickness can make the difference in difficult decision-making procedures.

Neurofibromatosis 2 is a complex hereditary disease usually associated with bilateral vestibular schwannomas and increased risk of multiple central nervous system tumours. Multidisciplinary management and sharing of patients' data with leading research groups are mandatory especially for unusual presentations or challenging tumour locations and related complications. The present case deals with a young patient with neurofibromatosis 2, optic nerve sheath meningioma, unilateral microphthalmos, epiretinal membrane and multiple central nervous system tumours. Systemic Bevacizumab allowed control of the progressive hearing loss due to bilateral vestibular schwannomas.[6] The multiple intracranial schwannomas leading to cerebral venous insufficiency of a dominant sigmoid sinus caused recurrent papilledema and finally visual failure. A prompt resolution of the raised intracranial pressure was achieved by ventriculo-peritoneal shunting to restore visual function and normal peripapillary retinal nerve fiber layer thickness.

Our experience provides many evidences of the dramatic role of spectral domain optical coherence tomography to get a quantitative analysis of the optic nerve head and related intracranial pressure instead of simple qualitative evaluation (Figure 1) as with eye fundus information. Finally, the role of multidisciplinary management supported by the expertise of specialised teams focused on neurofibromatosis 2 is strengthened.

## Availability of data and material

Giacomo Maria Bacci had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

## Declarations

**Competing Interests:** DGE is supported by the all Manchester NIHR Biomedical Research Centre (IS-BRC-1215-20007). All other authors declare no conflicts of interest.

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