Acquired and progressive myelinated retinal nerve fibers in neurofibromatosis type 1

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Acquired myelinated retinal nerve fibers (MRNF) is rare. The reported cases occur after optic disk injuries. We describe a case of a patient with neurofibromatosis type 1 and bilateral optic pathway glioma, who after 3 years' follow-up developed unilateral MRNF. Optical coherence tomography of the optic nerve disclosed progressive increased thickness and hyper-reflectivity of the peripapillary retinal nerve fiber layer associated with the myelinization process. Although the patient remains asymptomatic, myelinization continues to progress.

Myelinization of the visual pathways normally begins centrally at the lateral geniculate body, and at 7 months' gestational age, progresses anteriorly and terminates at the lamina cribrosa. The processes is generally complete at about 3 months after birth.[1] The mechanisms by which myelinization ends at the lamina cribrosa are not clearly understood.[2] Occasionally, myelinization may extend into the optic disk and the retinal nerve fiber layer (RNFL).[2,3] Congenital retinal myelinization is not uncommon, occurring in 0.6%-1.0% of the population as an isolated developmental anomaly. Congenital myelinated retinal nerve fibers (MRNF) most commonly do not progress.[1,2] MRNF appear as gray-white well-demarcated patches with frayed borders along the RNFL that obscure the underlying retinal vessels.[4] Patients with MRNF may be completely asymptomatic or may have significant visual defects; the majority of cases are incidentally diagnosed in asymptomatic, healthy children by ophthalmoscopy.[1] Visual function can be affected, especially in those with marked myopia, amblyopia, and strabismus.[4,5]

Acquired retinal myelinization is exceptionally rare and occurs after optic nerve injuries. Reported cases are associated with optic disk drusen,[6,7] optic nerve glioma,[3,6] ocular trauma, and surgical intervention for increased intracranial pressure.[7] This case report describes a patient with unilateral acquired MRNF in context of bilateral optic pathway glioma associated with neurofibromatosis type 1 (NF1).

Case Report

A 2-year-old boy with a recent diagnosis of NF1 was referred to Hospital de Santa Maria, Lisbon, Portugal, for ophthalmologic evaluation. On examination, visual acuity was 20/20 in the right eye and 20/40 in the left eye, with no significant refractive error. There was left eye ptosis due to a periorbital mass involving the left upper eyelid, with no ocular motility restriction. No Lisch nodules were present at that time. Dilated fundus examination revealed temporal pallor of the right optic disk. Magnetic resonance imaging (MRI) with contrast disclosed bilateral optic nerve gliomas, with prechiasmatic extension on the right, and a left orbital plexiform neurofibroma involving the upper eyelid, lacrimal gland, lateral rectus muscle, and temporal muscle.

The patient started amblyopia treatment with 4 hours patching of the right eye, and visual acuity in the left eye improved to 20/20. Due to clinical stability of the glioma and neurofibroma, with no major visual defects, no treatment was initiated, and the patient was evaluated routinely every 4 months. Three years after the initial visit, visual acuity remained 20/20 in each eye, although a relative afferent pupillary defect was present in the right eye. The left eyelid neurofibroma had mildly enlarged. Lisch nodules were present on both eyes. Fundus examination of the right eye disclosed a new finding—white patches along the RNFL in the temporal superior and temporal inferior peripapillary areas.

RNFL imaging over the period 2012-2018 using spectral domain optical coherence tomography (Heidelberg Spectralis; Heidelberg Engineering version 5.3, Heidelberg, Germany) disclosed marked hyper-reflectivity and increased thickness of this layer in the temporal superior and temporal inferior sectors (Figure 1). RNFL thickness increased over this time span in the temporal superior sector from 129 μm to 242 μm, in the temporal inferior sector from 128 μm to 192 μm, and in the nasal superior sector from 79 μm to 96 μm (Table 1). Posterior shadow due to medium to high reflective echoes caused by myelin makes it difficult to evaluate the inner and outer retina.

Mild thinning of the RNFL was present in the temporal sector in 2012 (54 μm) and in 2013 (58 μm), most probably due to optic atrophy caused by the glioma, although in subsequent years the thickness of the RNFL increased because of acquired myelinization and had probably masked this thinning. The same finding was found in the nasal sector in 2015 (44 μm) and in 2016 (43 μm) but disappeared in 2017 and 2018. The only change over 7 years' follow-up has been increased myelinization; examination has been otherwise stable.

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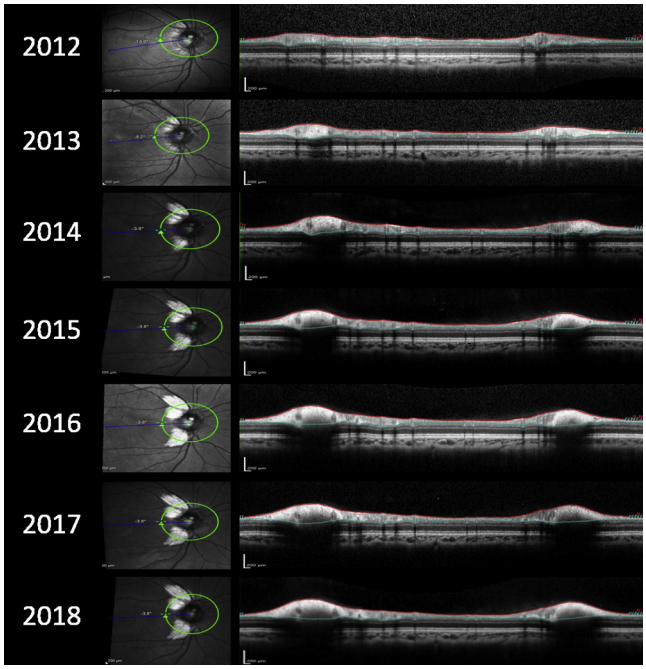

FIG 1. Red-free images of the optic nerve and corresponding optical coherence tomography scans of the right eye showing the presence and expansion of myelinated retinal nerve fibers from 2012 to 2018 in a patient with optic pathway glioma (optic nerve and prechiasmal lesion).

Table 1. Progression of retinal nerve fibre layer (RNFL) thickness, 2012-2018

	RNFL thickness, μm						
Year	MT	TS	TI	T	N	NS	NI
2012	79	129	128	55	52	79	79
2013	81	165	123	54	48	87	67
2014	95	204	150	58	51	108	81
2015	97	209	163	59	44	111	90
2016	102	220	177	65	43	116	86
2017	109	228	190	69	48	122	97
2018	113	242	192	74	51	125	96

I, inferior; *MT*, mean thickness; *N*, nasal; *S*, superior; *T*, temporal. Note increased thickness more prominent in the temporal-superior, temporal inferior, and nasal superior sectors.

Discussion

The pathophysiology of MRNF is not completely understood, although it is thought that it results from an abnormal migration of oligodendrocyte-like cells into the retina prior to the development of the barrier function of the lamina cribrosa (congenital cases). Histological studies show no apparent deficits in the lamina cribrosa in congenital forms of MRNF.[4] In acquired cases it is thought that the disease process is caused by an abnormal dislocation of oligodendrocyte-like cells into the retina due to temporary loss of the barrier function of the lamina cribrosa.[5] Prakalapakorn and colleagues[7] hypothesized that the conditions associated with acquired MRNF may also lead to an insult to the optic nerve, which might result in a reactive microgliosis restarting the myelinization process.[7]

In our case it is likely that the optic nerve glioma disrupted the lamina cribrosa structure, leading to a reactivation of oligodendrocytes, which in turn caused the axonal remyelinization that extended into the retina. Although optic nerve glioma was present in both eyes, on the right side the tumor had larger dimensions, possibly explaining why the MNRF only developed in the right eye. According to the MRNF classification system,[8] our case presents type II, with myelination occurring contiguous to the optic disk and in both temporal arcades. The association between the progression of MRNF and optic nerve glioma in the context of NF1 has been previously reported by Parulekar and colleauges.[3]

Aside from ocular fundus examination for monitoring these patients, OCT is a valuable tool to measure the changes in RNFL thickness and to consider future changes that could occur in the adjacent retina. OCT features of congenital MRNF have been described as increased reflectivity and thickness in the area of the MRNF. These characteristics are responsible for a posterior cone of shadowing, as noted by Salvatore and colleauges,[9] and for the sudden termination of structures posterior to the hyperreflective RNFL, as detailed by Saxena and Jain.[10]

Our findings in this case of acquired MRNF were similar to those described previously for congenital MRNF. There was progressive increased thickness and reflectivity of the RNFL adjacent to the temporal arcades, and these changes led to progressive back shadowing, resulting in difficulties in measuring RNFL thickness.

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