NEUROFIBROMATOSIS TYPE 1 ASSOCIATED WITH MULTIPLE SCLEROSIS:

a case series with focus on neuro-ophthalmological findings

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BACKGROUND

The co-occurrence of neurofibromatosis type 1 (NF1) and multiple sclerosis (MS) is a rare condition, with only 43 cases reported in the literature to date [1]. Epidemiological data from the French National Referral Centre for Neurofibromatosis suggest a slightly increased tendency to develop MS in individuals carrying NF1 mutations [2]. In this report, we describe two patients affected by both diseases, emphasizing neuro-ophthalmological findings of this rare comorbidity.

PATIENT 1 (34-year-old woman) presented with **acute bilateral visual loss**. Her past medical history was notable for a one-week episode of left lower limb clumsiness two years earlier and the development of urinary urgency six-month prior to hospital admission. Ophthalmological evaluation demonstrated **bilateral reduced visual acuity** (OD 3/10, OS 2/10), **optic disc temporal pallor** on fundoscopy (*Figura 1*), **inferior visual field defects**, **bilateral optic atrophy** at Optical Coherence Tomography (OCT) (*Figura 2*) and **Lisch nodules** on slit lamp. Physical examination showed café-au-lait spots, bilateral ankle clonus and Babinski sign. Brain and spine magnetic resonance imaging (MRI) disclosed periventricular, brainstem and cervical (C4-C5, C7) demyelinating white matter (WM) lesions, while cerebrospinal fluid (CSF) analysis revealed intrathecal Immunoglobulin G (IgG) synthesis, supporting MS diagnosis. Brain MRI also revealed right optic tract glioma (*Figura 3*) and unidentified bright object (UBO) in the right globus pallidus (*Figura 4*). Genetic analysis identified a pathogenic missense NF1 gene mutation (exon 33, c.3461 A>T; p.Asn1154Ile).

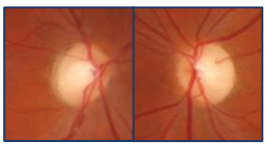

Figura 1.

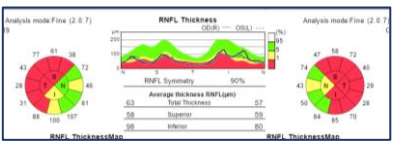

Figura 2.

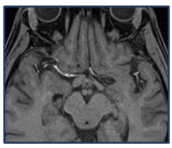

Figura 3.

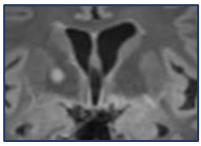

Figura 4.

PATIENT 2 (49-year-old man) was referred for **left eye blurred vision**; visual field study demonstrated **bilateral supero-temporal defects (OD>OS)** (*Figura 1*). Brain MRI disclosed right optic nerve glioma (*Figura 2*), optic chiasm atrophy and peritrigonal WM signal alteration. Fundoscopy showed **right optic disc diffuse pallor and left optic disc temporal pallor** (*Figura 3*); OCT demonstrated **right optic diffuse atrophy and left optic band atrophy (temporal and nasal quadrants)** (*Figura 4*). Dermatological examination revealed café-au-lait spots and neurofibromas. Genetic analysis identified a pathogenic NF1 gene heterozygous deletion (exon 47, c.7037_7040delATAG, p.Asp2346ValfsTer49). A follow-up brain MRI revealed right optic nerve thickening with sheath contrast-enhancement, while spine MRI showed a C3 contrast-enhancing lesion compatible with neurofibroma (*Figura 5*) and a D7 lesion suggestive of demyelination. Both subsequent brain MRIs demonstrated new demyelinating supratentorial WM lesions, with contrast-enhancement in one, allowing MS diagnosis despite negative CSF analysis.

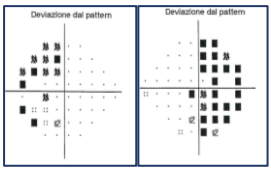

Figura 1.

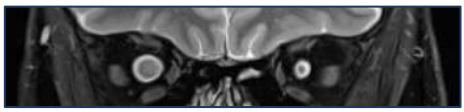

Figura 2.

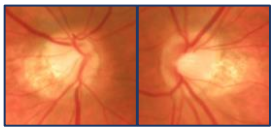

Figura 3.

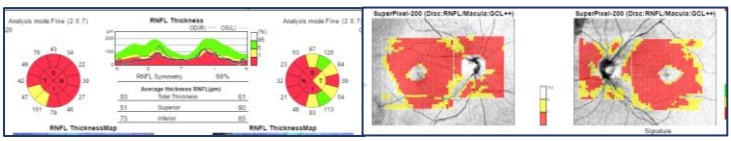

Figura 4.

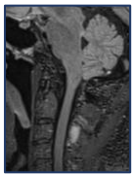

Figura 5.

CONCLUSIONS

This case series highlights the rare coexistence of NF1 and MS, which should be considered in patients presenting typical NF1 MRI (especially optic pathway gliomas) and dermatological features in association with classical MS features. Possible hypotheses put forward for this association are the localization of the oligodendrocyte myelin glycoprotein gene within NF1 intron 27b, neurofibromin 1 expression in oligodendrocytes, abnormal Schwann cell proliferation and exposure to peripheral myelin antigens in NF1, potentially triggering cross-reactive autoimmune CNS demyelination [3].

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