THE OCCURRENCE OF AN INFLAMMATORY-DEMYELINATING DISEASE IN TWO PATIENTS WITH NEUROFIBROMATOSIS TYPE 1.

Virgilio E, Vecchio D, Naldi P, Lucchi F, Comi C, Cantello R.
Multiple Sclerosis Center, Department of Neurology, University of Piemonte Orientale (UPO), Novara, Italy

BACKGROUND and OBJECTIVE

Neurofibromatosis type 1 (NF1) is an autosomal dominant disease, related to NF1 gene point mutations on chromosome 17, involving skin, peripheral and central nervous systems (CNS). Multiple sclerosis (MS) is the most common acquired CNS demyelinating disease. NF1 and MS apparently do not share any known etiopathological mechanism.
We report two unrelated patients with co-occurrence of NF1 and CNS demyelinating disorder: case 1 with secondary progressive MS; case 2 with recurrent retrobulbar optic neuritis (ON).

CASE 1

58-year-old man with previous juvenile clinical diagnosis of NF1 and genetic confirmation at the age of 53.
History and examination: at 56 years old progressive paraparesis, lower limbs paresthesias and mild bladder dysfunction.
He described previous episodes of sensory and motor symptoms with remissions.
Brain and Spinal MRI: multiple T2 and FLAIR white matter and corpus callosum lesions (suggestive for MS, not for "unidentified bright objects" (UBO) specific for NF1), not enhancing *(figure 1)*.
Spinal MRI (one year later) two new dorsal demyelinating lesions without contrast enhancement *(figure 2).*
Lumbar puncture: oligoclonal bands (pattern II) in CSF.
Blood test, autoimmunity, trombophilia screening and infectious serology: normal
Diagnosis: *secondary progressive MS.* EDSS 4. No disease modifying therapies (DMT) was started due to active GI neoplastic lesions.
Follow up:
- his motor and sensory deficit improved during his first year of follow up with progression of gait difficulties
- no evidence of MS disease activity at MRI.

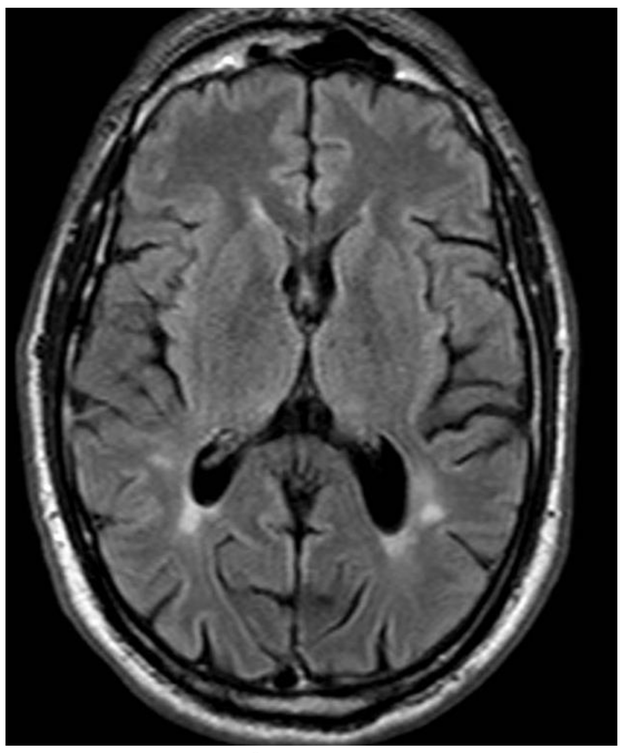

figure 1
FLAIR brain MRI

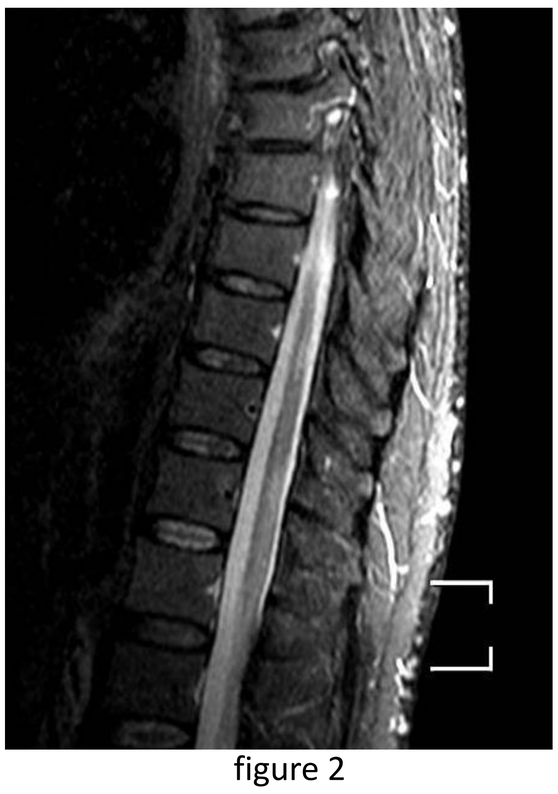

figure 2
STIR spinal MRI

CASE 2

28-year-old man with a diagnosis of NF1 at the age of 18.
History and examination: at 21-year-old unilateral loss of vision in the left eye treated with steroid with complete recovery (no further investigations). At 28 years old a second episode of left ON. New treatment with steroids with incomplete recovery (small central scotoma).
Visual evoked potentials: prolonged latency of P100 in the left eye.
Brain MRI: normal (no optic nerve glioma) *(figure 3)*.
Spinal MRI giant spinal neurofibroma extended from L2 to L5.
Lumbar puncture: not performed due to giant spinal neurofibroma.
Blood test, autoimmunity, trombophilia screening and infectious serology : normal
Diagnosis: *recurrent demyelinating ON*.
EDSS1. No DMT was started.
Follow up:
- for four years he didn't develope any dissemination in space for his demyelinating condition.
- four years later, he died for a left hemispheric glioblastoma multiforme *(figure 4).*

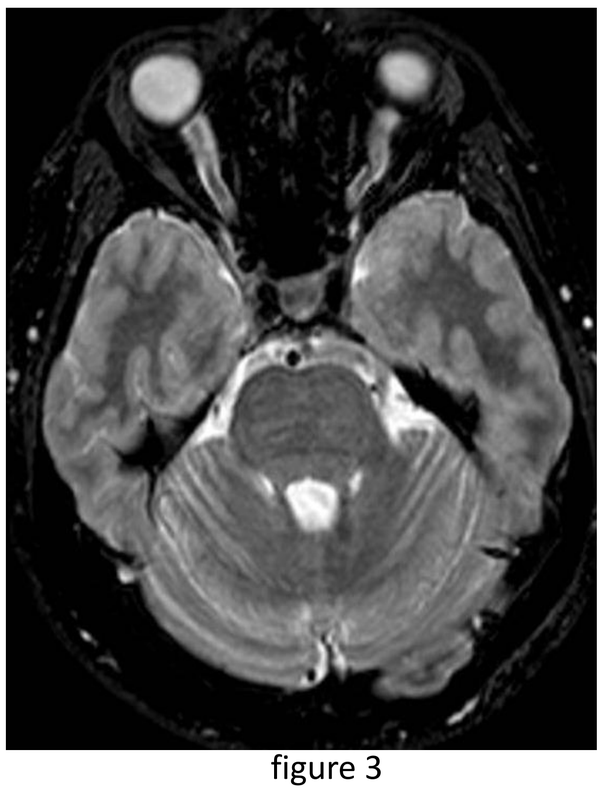

figure 3
T2/W brain MRI

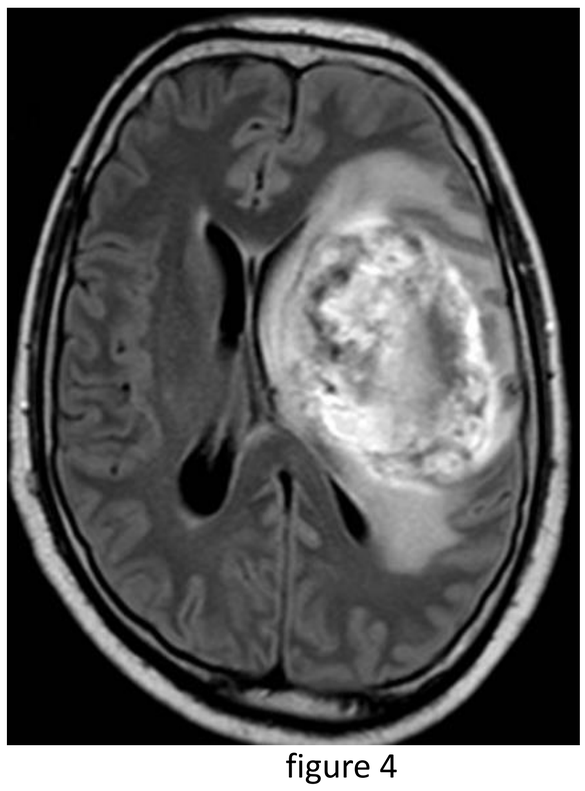

figure 4
FLAIR brain MRI

DISCUSSION AND CONCLUSION

We presented two cases of co-occourence of NF1 and MS, rarely previously reported in literature. Nowaday 20 cases, mostly with primary progressive MS have been described. Even if these two disorders do not seem to be related, several hypothesis have tried to find a link between NF1 and MS. In particular:

- neurofibromin's suppressor gene function is not only expressed on Schwann cells but also on other cell types including cells of the immune system and this loss of regulation could favour an autoimmune response to CNS myelin.
- oligodendrocyte myelin glycoprotein gene (OMgp), involved in myelination and axonal survival, is located on intron 27b of NF1 gene and if alterated may promote MS demyelination. However OMgp mutation seems not sufficient to explain the development of inflammatory disease.

Increasing the number of report of co-occurence of NF1 and MS could help clinicians to better understand connection between these two diseases.; nevertheless this co-occurence opens new questions, in particular regarding DMTs and their use in patients with an increased risk of tumors such as NF1 patients. Further datas are needed.

REFERENCES

1 Mohebi N et al. Relapsing remitting multiple sclerosis in an Iranian patient with neurofibromatosis type I. Neurology International 2015; 7:5966
2 Pipatpajong H, Phanthumchinda K. Neurofibromatosis Type I Associated Multiple Sclerosis. J Med Assoc Thai 2011; 94 (4): 505-10.
3 Billiet T, et al. Characterizing the microstructural basis of "unidentified bright objects" in neurofibromatosis type 1: A combined in vivo multicomponent T2 relaxation and multi-shell diffusion MRI analysis. NeuroImage: Clinical 4 (2014) 649–658

SIN, XLVIII CONGRESSO NAZIONALE, NAPOLI 14-17 OTTOBRE 2017