A case of uveal melanoma under fingolimod treatment in a MS patient (P163)

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Uveal melanoma is a rare cancer having an incidence of 2–8 per million per year in Caucasians. A common genetic abnormality includes loss on the short arm (p) of chromosome 1, involving sphingosine-1-phosphate (S1P) receptor type-1. (Nathan, 2015)
Herewith we describe the development of primary uveal malignant melanoma in a Multiple Sclerosis (MS) patient under fingolimod treatment, an immunosuppressive drug acting via interaction with S1P-receptors (Cohen 2010)

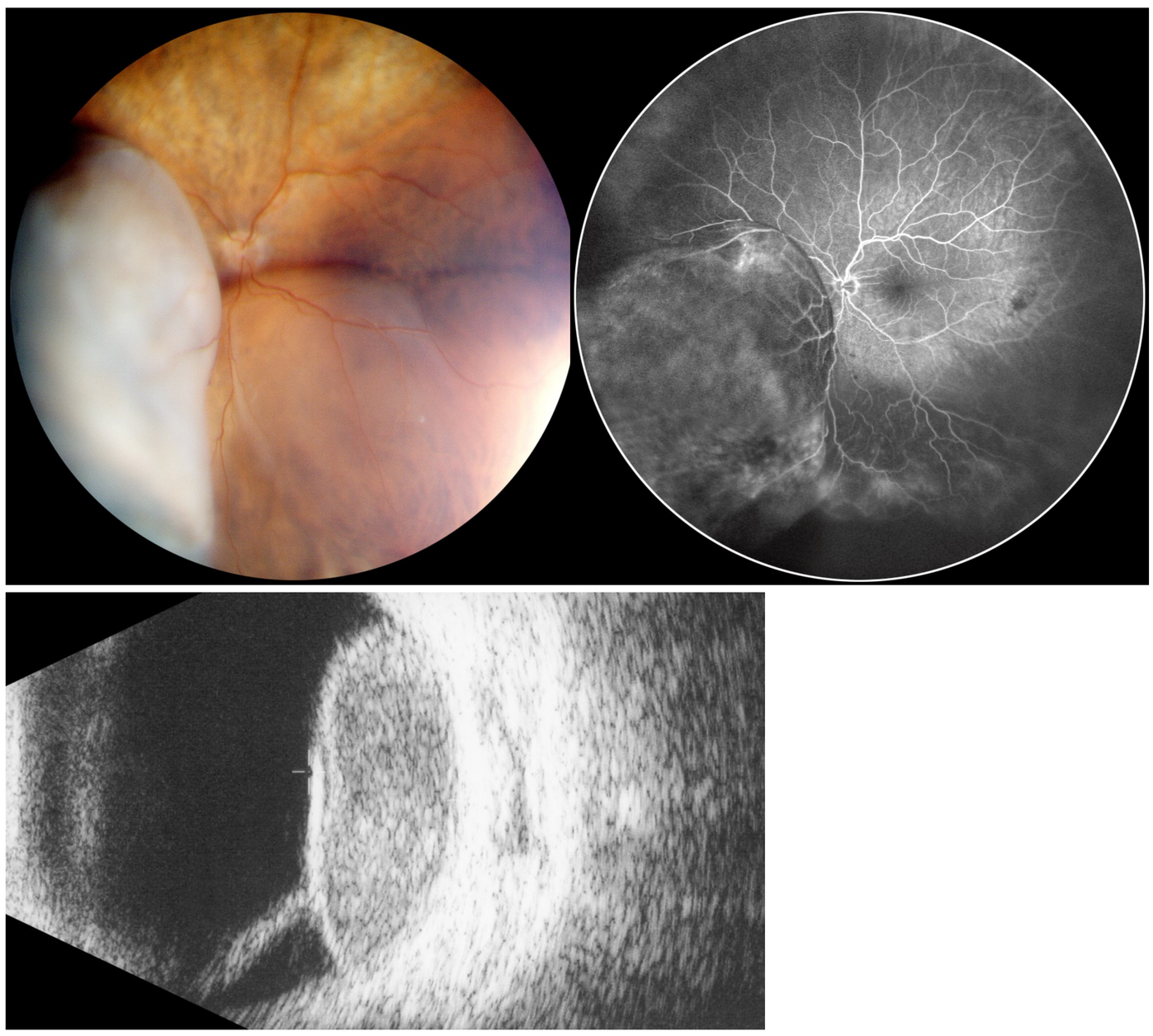

Figure 1. FUNDUS OCULI, FLUORANGIOGRAPHY AND ECHOGRAPHY OF THE UVEAL MELANOMA

CASE REPORT
A 25 years-old woman was diagnosed having highly active relapsing remitting MS in 1993 and then she was consecutively treated with IFNbeta1b, iv mitoxantrone (cumulative dose 112 mg/m^2), iv cyclophospahmide (cumulative dose 4 g/m^2), iv natalizumab (56 infusions) and finally fingolimod since Nov-2012.
On January 2016 she developed blurred vision with large peripheral scotoma of the left eye and on the basis of clinical examination, retinal fluorangiography and brain MRI the diagnosis of uveal melanoma was performed. (Figure 1) Due to the clinical characteristics of the neoplastic mass, that was more than 2 cm in diameter, no biopsy was performed and the patient was promptly treated with photon radiotherapy and intraocular bevacizumab for the presence of perifoveal retinal damage. No clinical, nor laboratory nor radiological evidence of systemic disease was detected. The only recognised risk factor was the presence of light-coloured irides.
Six months later she developed liver metastasis and nivolumab was started.

Fingolimod is an agonist agent for $S1P_1$, but not for $S1P_2$: $S1P_1$ mediates stimulation of cell proliferation whereas $S1P_2$ mediates inhibition of cell proliferation. (Takuwa, 2012)
It can be supposed that in our patient the chronic stimulation of $S1P_1$ receptor induced the internalization of the receptor and then the activation of Gi-mediated pathways of phosphatidylinositol 3-kinase / (PI3K/Akt) and (ERK) that have been described in proliferation of cancer cells, a mechanism that can also be involved in the deletion of chromosome 1p as seen in uveal melanoma. (Watters, 2011)

CONCLUSION
This is the first described case of primary uveal melanoma under fingolimod treatment arising concerns about oncogenic risk of this pleiotropic drug.
A strict clinical follow-up, including at least yearly ophthalmologic examination, is mandatory to minimize long-term risk for fingolimod treated MS patients.

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