# Bilateral diffuse uveal melanocytic proliferation: Report of a rare ocular paraneoplastic syndrome

## La prolifération bilatérale mélanocytaire uvéale diffuse : Un syndrome paranéoplasique rare

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**RÉSUMÉ**

La prolifération bilatérale mélanocytaire uvéale diffuse est un syndrome paranéoplasique rare dans lequel la cécité bilatérale est causée par un épaississement choroïdien, un décollement séreux rétinien et une cataracte rapidement évolutive. De multiples néoplasies ont été associées à la prolifération bilatérale mélanocytaire uvéale diffuse, mais le cancer ovarien chez la femme et les cancers du poumon et du pancréas chez l'homme restent les plus fréquents. Le mécanisme sous-jacent semble être lié à un facteur endogène qui régule la prolifération des mélanocytes uvéaux. Nous présentons le cas d'un homme de 75 ans atteint d'une prolifération bilatérale mélanocytaire uvéale diffuse associée à un adénocarcinome pulmonaire.

**Mots clés :** Prolifération bilatérale mélanocytaire uvéale diffuse - Mélanocytes - Tumeur maligne - Rétinopathie paranéoplasique.

**SUMMARY**

Bilateral diffuse uveal melanocytic proliferation is a rare paraneoplastic disorder where bilateral blindness is caused by uveal thickening, serous retinal detachment, and rapid cataract formation.

Several different malignancies have been associated with bilateral diffuse uveal melanocytic proliferation, but ovarian carcinoma in women and lung and pancreatic carcinoma in men are the most common.

The underlying mechanism is thought to be related to a an endogenous factor wich regulates the proliferation of uveal melanocytes.

We present the case of a 75-year-old man with bilateral diffuse uveal melanocytic proliferation secondary to pulmonary adenocarcinoma.

**Keywords :** Bilateral diffuse uveal melanocytic proliferation - Melanocytes - Malignancy - Paraneoplastic retinopathy.

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## INTRODUCTION

Bilateral diffuse uveal melanocytic proliferation (BDUMP) is a rare ocular paraneoplastic syndrome described by Machemer in 1966. The underlying tumor typically presents as a visual disturbance and causes diffuse bilateral proliferation of melanocytes in the uveal tract leading to subsequent destruction of the retina and retinal pigment epithelium (1,2).

Patients often present with bilateral progressive visual impairement, and diagnosis can precede detection of the primary malignancy by months to even years in some cases.

The fundoscopic changes are characterized by the presence of both pigmented and amelanotic uveal melanocytic tumors, diffuse thickening of the uveal tract, exsudative retinal detachments and multiple round or oval red patches at the level of the retinal pigment epithelium (RPE) with specific patterns of hyperfluorescence on fluorescein angiography (1). These changes are associated to rapidly progressive cataract.

## CASE REPORT

A 75-year-old man presented in our department complaining of persisting bilateral visual disturbances 5 months after cataract surgery. His medical history was significant for pulmonary adenocarcinoma treated with radiotherapy and chemotherapy.

On presentation, his visual acuity was 1/20 in both eyes. Slit-lamp examination revealed a normal anterior chamber in both eyes. With dilation, the 2 in-the-bag intra ocular lenses were transparent.

Funduscopic examination revealed bilateral multiple, diffuse, subretinal grey lesions (fig. 1a) that with fluorescein angiography appeared as a mosaic of hyperfluorescent spots with late pinpoint leakage in a giraffe-like pattern (fig. 1b,1c).

Optical coherence tomography revealed bilateral diffuse areas of irregularities and thickening of the retinal pigment epithelium layer, with associated subretinal fluid and increased chroroidal thickness (fig. 2).

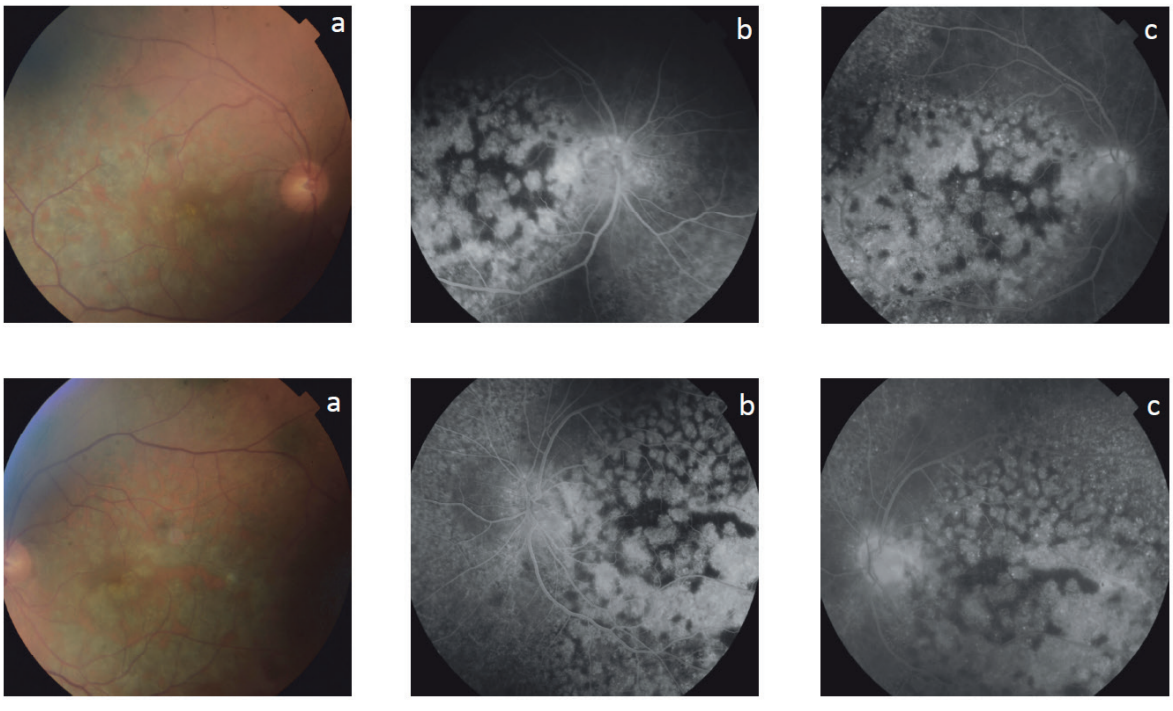


**Figure 1 :** Color photography and fundus fluorescein angiography. Right and left eye
(a) Color photography; Early (b) and late (c) fundus fluorescein angiography. Note the characteristic mosaic with hyperfluorescent patches and late pinpoint leak

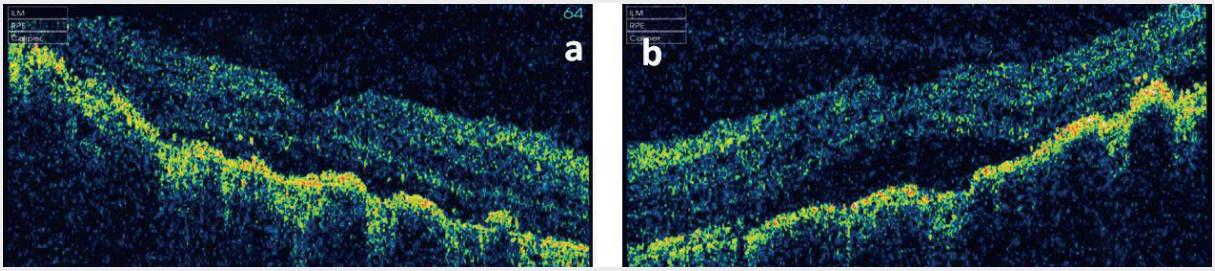


**Figure 2 :** Time domain optical coherence tomography (OCT) : (a) Right eye ; (b) Left eye. Note the diffuse areas of irregularities and thickening of the retinal pigment epithelium layer, with associated subretinal fluid.

The history of lung adenocarcinoma, associated to the clinical presentation and the imaging findings suggested the diagnosis of BDUMP. No treatment was indicated because of the poor general condition of the patient.

## DISCUSSION

BDUMP is a rare paraneoplastic disorder, with a little more than 50 cases reported in the literature. The mean age at diagnosis of BDUMP is approximately 63 years, there are no gender predilections and death usually occurs within 24 months (3).

As ocular symptoms and signs often precede the onset of systemic problems, early recognition of this condition by an ophthalmologist may have an impact on patient morbidity and mortality (2). In the case described here, the diagnosis of the primary lung cancer was made before specific ocular changes were identified.

The clinical features to be aware of include precipitous bilateral visual loss in a person over 50 years of age, bilateral cataract and bilateral serous retinal detachment. Vision decline has been attributed to destruction of photoreceptors and underlying RPE, serous retinal detachments, and, later, cataracts (2).

Systemic carcinomas reported with BDUMP are ovarian, lung, gall bladder, cervical, uterine, kidney, pancreatic, breast, esophageal, and colorectal cancers. They may also be associated with melanocytic proliferation in other tissues (2,4). Our patient had lung cancer.

Gass et al described five cardinal signs related to BDUMP : multiple round, red patches at the level of the retinal pigment epithelium, a striking pattern of multifocal areas of early hyperfluorescence corresponding with these patches, proliferation of choroidal nevus-like lesions as well as diffuse thickening of the uveal tract, exsudative retinal detachment, and rapidly developing cataract (1). In addition glaucoma, dilated episcleral vessels, iridocyclitis, shallow anterior chamber, ciliary body cysts, and iridodonesis have been reported (5).

Our case developed the 5 cardinal signs including bilateral cataract, subretinal fluid, increased choroidal thickness, subretinal patches, with corresponding hyperfluorescence.

Investigations are aimed at finding the occult primary malignancy, which may be challenging including biochemical analysis of the serum, chest and abdominal CT or Positron emission tomography (PET) imaging, MRI of the brain, bone marrow aspiration, and even biopsy and histopathological analysis of lymph nodes.

Although the etiology of this syndrome remains unknown, a number of researchers have suggested there is a humoral factor in the development of this entity. Miles et al (6) reported the detection of a specific serum-bound protein in patients with BDUMP. This protein has been found to cause in vitro melanocytic proliferation and was thus named cultured melanocyte elongation and proliferation factor (CMEP factor).

Treatment options for ocular involvement include management of the underlying malignant neoplasm, corticosteroids, surgery, external beam radiotherapy and monolonal antibodies(2,4,5). Some authors (7) suggest that plasmapheresis may stabilize vision in patients with BDUMP, but it requires a healthy patient. The poor general condition of our patient didn't allow such treatment.

## CONCLUSION

Given that the diagnosis of BDUMP can precede detection of the underlying systemic malignancy, consideration of this entity during clinical examination may lead to an earlier diagnosis of malignancy so that systemic therapy may be successfully instituted and vice versa be alert in patients with a history of previous cancer.

**Consent** :

Written informed consent was obtained from the patient for publication of this Case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal. This report adhered to the tenets of the Declaration of Helsinki.

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