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THE INTERESTING CASE

Paraneoplastic Vitelliform Retinopathy Secondary to Metastatic Melanoma.

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BACKGROUND

Traditionally, the paraneoplastic retinopathies have been classified into two entities: CAR (carcinoma-associated retinopathy) and MAR (melanoma-associated retinopathy). Recently, a vitelliform retinopathy has been described in both metastatic cancer and melanoma patients: in 2001, Borkowksy reported the first patient as a case of MAR with unusual retinal features [1]. Since then, only 20 cases have been reported [2-5]. This auto-immune disorder is caused by circulating autoantibodies, cross-reacting with the neuroretina and retinal pigment epithelium (RPE) [2].

HISTORY and SIGNS

A 41-year-old lady, with pelvic lymph node metastases from an unknown melanoma was screened for her primary tumour. On ophthalmic examination, Snellen visual acuity (VA) was found to be 0.5 OU. She reported no blurred vision, nyctalopia or metamorphopsia. Ishihara colour vision and pupil light reflexes were normal. The anterior segment presented no signs of inflammation, and intraocular pressure was 18 and 16 mmHg respectively in the RE and LE. Fundus examination revealed in both eyes multiple retinal detachments with a vitelliform sedimentation level, bullous in the macular area and subtle in the peripapillary regions (Figure 1 A-B). On Infrared Reflectance (IR), the number of retinal detachments appeared higher with the edges of the lesions clearly delineated (Figure 2, A-B). On blue light autofluorescence (AF), the pseudovitelliform deposits within the larger lesions showed a dense hyperautofluorescence (Figure 2, C-D). On fluorescein angiography (FA), the subretinal fluid provoked a slight masking effect in the LE in the early and late

phases (Figure 2, E-F), while on indocyanine green angiography (ICG-A) a clear masking effect was caused by the lesions in all phases OU (Figure 2, G-H).

Single line acquisition of SD-OCT across the fovea revealed OU a diffuse hyperreflective thickening of the external retina at the level of ellipsoidal zone and interdigitation layer, and a large subretinal fluid detachment with irregular hyperreflective deposits at the surface of the RPE layer. Subfoveal choroidal thickness of 417 µm (RE) and 427 µm (LE) was measured manually on an enhanced depth imaging (EDI) single line. Multifocal ERG recorded a reduction of amplitudes in the central 10-15° OU. The differential diagnoses included MAR, choroidal metastases, central serous chorioretinopathy, Best's disease and paraneoplastic vitelliform retinopathy. A specific serum analysis was performed and revealed antibodies against a 45kDa retinal protein, probably the Pigment Epithelium-Derived Factor (PEDF).

THERAPY and OUTCOME

Patient underwent surgical excision of the inguinal metastatic lymph nodes. The postoperative evolution of both the visual function and fundus examination was stable. The indication of an immuno-regulatory treatment, such as steroids, plasmapheresis or monoclonal antibodies was considered. We decided for observation due the potential risk of an antagonistic effect against the patient's own cancer antibodies with possibly deleterious consequences [6]. Six months later, VA had improved to 0.8 OU and on OCT both maculae were partially reapplied (Figure 3, E-F).

DISCUSSION

We present a rare case of pseudovitelliform retinopathy, extensively documented with multi-modal imaging and presenting antibodies against a 45KDa retinal protein probably the Pigment Epithelium-Derived Factor (PEDF). We speculate that a reduction in the tumour load might have played a significant role in the positive evolution of both visual function and retinal detachments.

Multimodal imaging allowed us to narrow rapidly the differential diagnosis, as well as to precisely document periodic longitudinal evolution. Fundus examination revealed areas of retinal detachments, but a higher number of lesions were identified on IR and ICGA suggesting an important role in RPE dysfunction. Spaide et al. suggested that the thickening observed on SD-OCT in the external retinal layers is probably due to RPE dysfunction secondary to the important accumulation of hyperreflective pseudovitelliform material in the subretinal space [7].This partially explains the hyperreflectivity shown on OCT in our case when referring to the subretinal fluid accumulation. The thickened hyperreflective layer just adjacent to the inferior external retina suggests both an elongation of the outer segment of the photoreceptor and accumulation of inflammatory microglial cells possibly migrating from the neuroretinal tissue.

Excessive production of cross-reacting antibodies against retinal structures has been found in most of the reported cases of PVR [1-4]. However, despite a similar retinal phenotype for the 20 reported cases, a variety of antibodies have been reported, suggesting specificity in the molecular mimicry of the primary tumour. Our case exhibited antibodies against a 45 KDa retinal antigen, possibly the Pigment

Epithelium-Derived Factor (PEDF). There is no evidence based treatment for the management of CAR and MAR, the most frequent paraneoplastic disorders. Reduction of the tumour mass may have a beneficial effect on the ocular signs, due to a reduced level of autoantibodies synthesis [8]. Following tumour debulking surgery, the pseudovitelliform deposits and retinal detachments regressed, and VA improved to 0.8 OU. Unfortunately, the autoantibodies serum levels have not been measured since the metastases excision. However, the favourable clinical evolution seems to support the positive role of tumour load reduction as a first line treatment in such cases. To our knowledge, this is the first case of Paraneoplastic Vitelliform Retinopathy showing antibodies activity against a 45 kDa RPE protein.

CONCLUSION

Bilateral multiple vitelliform retinal detachments can be associated with metastatic disease. Serum retinal or RPE auto-antibodies support the diagnosis. Reducing the tumour load might stabilize this rare paraneoplastic retinopathy.

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FIGURE LEGENDS:

Figure 1. Bilateral Wide Field Fundus imaging at the initial visit (A-B) showing retinal detachments and pseudovitelliform deposits [RE is on the left, LE is on the right]. Six months later (C-D) the macular lesions were significantly less prominent.

Figure 2.

Bilateral baseline multimodal imaging at presentation (Heidelberg Engineering, Heidelberg, Germany). A-B. IR showing a higher number of retinal detachments as compared to the colour images. C-D. The pseudovitelliform deposits are hyperautofluorescent on AF. E-F. A slight masking effect on FA is present in the LE. G-H. Evident masking effect by all lesions on ICG-A.

Figure 3. .

OCT scans through macular region of the RE and LE at presentation (A-D) and after six months' follow up (E-F) (Heidelberg Engineering, Heidelberg, Germany). A-D. Initial examination revealed subretinal fluid (arrowheads), thickening of the external layers (arrow) and an inhomogeneous pseudovitelliform sedimentation (asterisk). E-F. The neuroretinal detachments have significantly regressed after tumour load reduction.

Figure 1

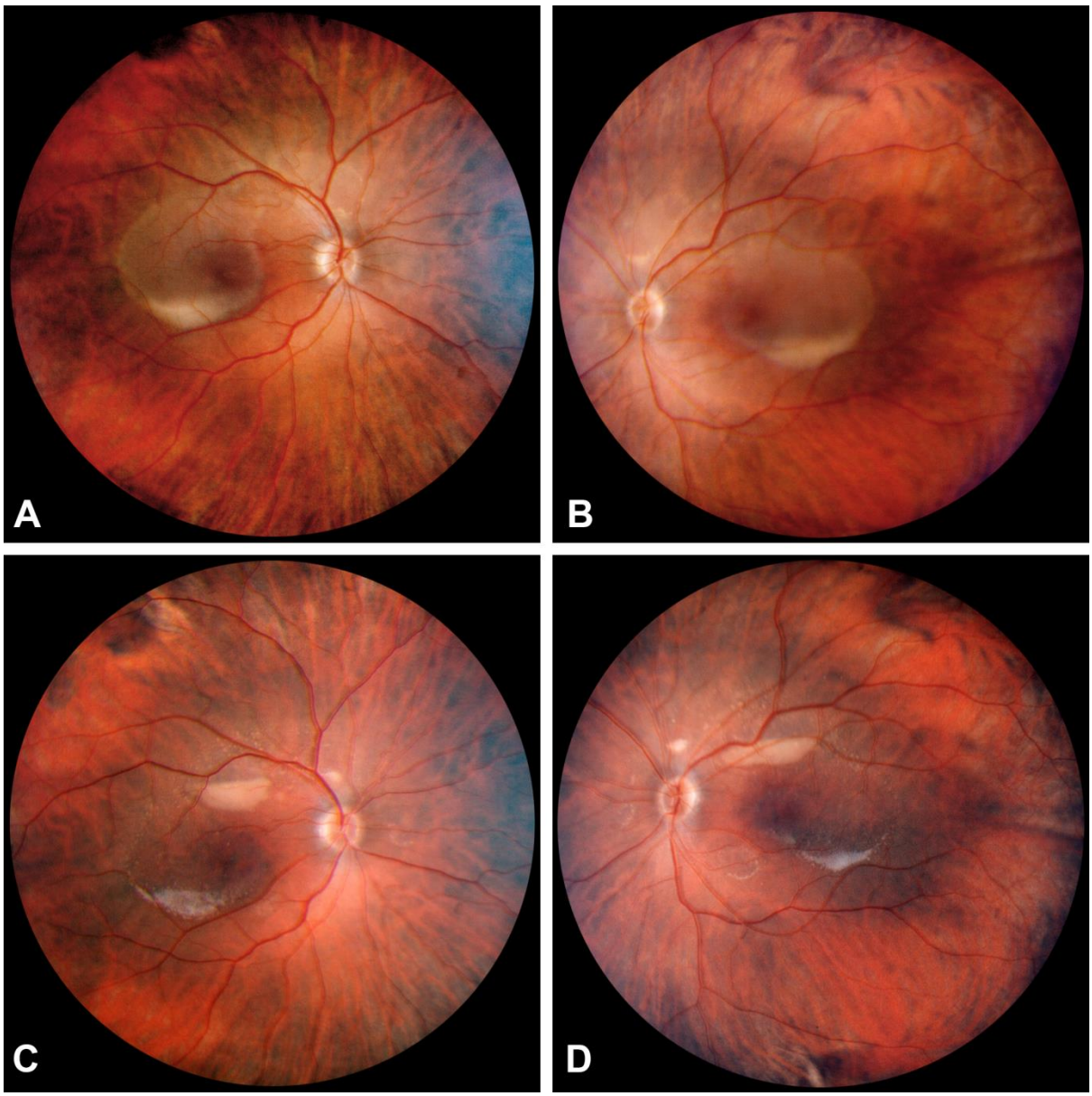

Figure 2

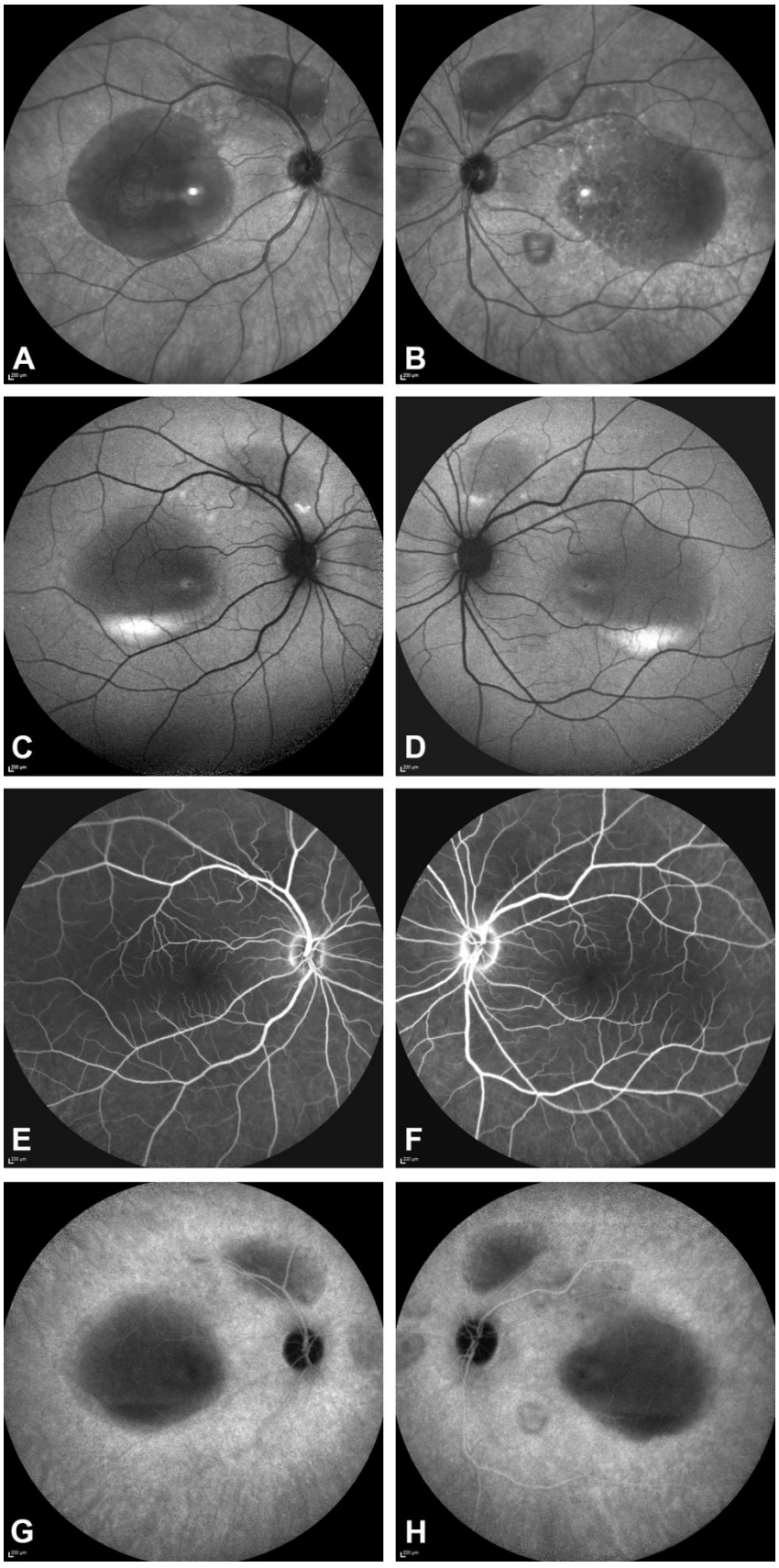

Figure 3