EUROPEAN OPHTHALMIC PATHOLOGY SOCIETY

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51-years old male patient with unilateral sudden visual loss due to cellular vitreous infiltration

Clinical History

The 51-year-old patient was presented for the first time in March 2020 by our dermatologists due to bilateral blepharitis and complete madarosis. There was additional focal ulceration and hyperkeratosis on the right lower eyelid. Visual acuity was OD 1.0, OS 0.8 with best correction. At that time, our patient was treated as an inpatient for 5 eczematous skin lesions that had been noticed 9 months earlier and had been treated with topical and systemic cortisone, respectively. The face was also affected for about 1 year, and the eyelids for 3 months. Alopecia was present since 2016. We recommended antibiotic and immunomodulatory treatment with ofloxacin ointment and azithromycin eye drops. Dermatologic workup revealed the diagnosis of cutaneous T-cell lymphoma with rearrangement of T-cell receptors ß and ɣ.

In September 2021, a year and a half later, we saw him again. This time, he complained of amaurosis fugax lasting 2-3 hours OU 2 weeks before. Visual acuity was OU 0.63. Fundus examination revealed mild vitreous infiltrates in the left eye with bilateral optic disc hyperemia and exudation on fluorescein angiography. There was no evidence of choroidal infiltrates on ICG angiography. Systemically, meanwhile, lymphoma stage deteriorated to T3NxB0M1 (IVB) with skin nodules >1cm (T3), lymph node involvement (not histologically confirmed, therefore Nx), lack of evidence of tumor cells in the blood (B0), pulmonary involvement and suspicious cerebral and vitreal infiltration (M1). Because a switch of chemotherapy (previously 4/2020 bexarotene, 3/2021 gemcitabine, 5/2021 mogamulizumab) to i.v. methotrexate was planned, no ocular treatment was recommended. A neurological examination for amaurosis fugax did not reveal any other pathological changes.

In December 2021, 3 months later, our patient noticed a subacute visual deterioration of the left eye to hand movement perception. This time, we saw significant vitreal and retinal infiltrates, thus therapeutic and diagnostic vitrectomy was performed. Fortunately, visual acuity increased to 0.63.

No neoplastic T lymphocytes were detected in the blood and CSF.

Ocular Pathology

Macroscopy: 95 ml slightly turbid vitrectomy fluid

Light microscopy: Vitreous material with numerous, small to large, atypical, polymorphic lymphocytic cells with large, irregular, partly nucleoli-containing nuclei and numerous apoptoses. Most cells were CD3 positive while only single cells stained positively with antibodies against CD20 and CD30. More than 30% of the cells were MIB1-positive.

Molecular genetics:

As in the March 2020 skin biopsy, a monoclonal TCR-Vɣ rearrangement was detected. However, in contrast to the skin sample, no monoclonal TCR-Vß rearrangement was present.

Diagnosis

Intraocular metastasis of a primary cutaneous T-cell lymphoma of Mycosis fungoides Subtype

Discussion

Our patient had an advanced stage of primary cutaneous peripheral T-cell lymphoma (PCPTCL) of the mycosis fungoides subtype. The vitreous involvement represented its metastasis. Intraocular T-cell lymphoma is very rare and occurs mainly in the advanced stage of the disease, as was the case in our patient. Neoplastic T-cell infiltration of the vitreous can also occur in other subtypes as adult T-cell lymphoma/leukemia (ATL) [1,2]. A review of intraocular involvement in peripheral T-cell lymphoma (PTCL) was published by Levy-Clarke in 2008, with an analysis of a total of 29 cases from the literature, 8 of which had mycosis fungoides. The age of the patients ranged from 24-83 years with a median of 57 years. The gender distribution was even. The time interval to manifestation of PTCL was 76 months (range 4-360 months) [2].

The most common ophthalmologic involvement of PCPTCL is periocular "blepharoconjunctivitis". In addition, cicatricial ectropion, madarosis, secondary meibomitis, and chalazia may also occur [3]. "Blepharoconjunctivitis", madarosis, discrete cicatricial ectropion, and chalazion were also

present in our patient at the time of initial diagnosis. In the course of disease, the eyelids were irradiated in addition to the initial therapy with retinoids.

As already mentioned above, intraocular involvement of PTCL is comparatively rare and manifests as retinal infiltrates and hemorrhages, anterior "uveitis" in 45%, vitritis" in 66%, and optic infiltration in some cases. CNS involvement was relatively common and was noted in 30% of cases [2]. In our patient, retinal infiltrates, vitreous involvement, and probably optic infiltration were present with clinical optic disc hyperemia and exudation on fluorescein angiography. Cerebral involvement was suspected from imaging but histology only revealed T-lymphocytes without TCR rearrangement. Insufficient material might have been the cause of failed monoclonality detection, including the discrepancy between the TCR rearrangement of the skin biopsy and the vitreous material in our case. Since the TCR rearrangement Vɣ of skin and vitreous material were identical, vitreous metastasis of the preexisting PCPTCL was very likely in our case.

Cases with simultaneous intraocular and cerebral PTCL without skin involvement have been reported, analogous to intraocular B-cell lymphoma [3]. Levy-Clarke et al. found in their case series that metastatic intraocular T-cell lymphoma is clinically rather similar to primary intraocular B-cell lymphoma with infiltrates of the vitreous and retina and/or infiltrates between retinal pigment epithelium and Bruch's membrane [2]. Therefore, the surprising histopathologic finding of a T-cell lymphoma seems to be possible -albeit rare- if intraocular B-cell lymphoma is suspected.

Not only intraocular, but also in general, T-cell lymphomas are less frequent. Primary cutaneous peripheral T-cell lymphoma (PCPTCL) accounts for 10-15% of non-Hodgkin lymphomas. Patients are usually older than 45 years of age [4]. In contrast to patients with intraocular involvement, men are more commonly affected than women (2:1-1.5:1) [5]. The incidence of the most common form, mycosis fungoides was 0.55/100000 in the USA over 10 years ago [6], and that of PCPTCL in general was approximately 1/100000 [7]. Between 1973 and 2008, there has been a 300% increase in mycosis fungoides, possibly due to a change in diagnostic criteria, increasing population age, and other unknown factors [6]. The increase of other lymphomas is estimated to be 25% for the same period [8, 9]. The most common PCPTCL subtypes are: Mycosis fungoides (60% of all PCPTCL), the leukemic variant Sézary syndrome (5% of all PCPTCL), primary cutaneous CD30+ lymphoproliferation (25% of all PCPTCL: primary cutaneous anaplastic large cell lymphoma and lymphomatoid papulosis) [10]. Sézary syndrome is defined by the triad of erythroderma, generalized lymphadenopathy, and the detection of malignant T cells in the blood in the form of Sézary cells [11]. Despite the unfavorable course of our patient there was no evidence of Sézary cells or malignant T lymphocytes in the blood.

Progression of mycosis fungoides from the plaque stage to a tumor stage or erythroderma (affecting 80% of the skin area), as in our patient, occurs in 30% of cases [8]. The estimated median survival time of patients with clinical stage IVB as it was in our case is 1.4 years, while that of patients with stage IA hardly differs from that of the rest of the population [12]. In this respect, early diagnosis is important. However, the average duration between symptoms and diagnosis in early stage I, when the lesions are indistinguishable from eczema, is 3-6 years [13]. This is aggravated by the clinically variable appearance, rarely with even clinically inconspicuous skin [14].

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