Cancer Associated Retinopathy in Non-Hodgkin's Lymphoma

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Abstract: Cancer-associated retinopathy (CAR) is an uncommon paraneoplastic retinopathy usually associated with small cell lung carcinoma. To our knowledge, there is no previous report in the English literature of CAR syndrome occurring in lymphoma patients. We describe a rare case of CAR syndrome in a 62-year-old male with non-Hodgkin's lymphoma (NHL) treated with four doses of intravenous immunoglobulin.

Keywords: CAR, Retinopathy, Lymphoma.

INTRODUCTION

Paraneoplastic neurologic syndromes are a group of neurologic disorders caused by mechanisms other than metastases. Metabolic deficit, infections and the side effects of chemotherapy are all possible causes of these disorders. One such syndrome in this group is the paraneoplastic visual syndrome comprising cancer-associated retinopathy (CAR), melanoma-associated retinopathy (MAR), and paraneoplastic optic neuropathy [1]. The CAR syndrome is uncommon and usually associated with small cell lung carcinoma [2, 3]. We report, to our knowledge, the first case in the English literature of CAR syndrome occurring in a patient with non-Hodgkin's lymphoma and treated with intravenous immunoglobulin.

CASE REPORT

A 62-year-old male was diagnosed with stage IV, B-cell follicular non-Hodgkin's lymphoma, and he was treated with six cycles of rituximab and conventional chemotherapy (R-CHOP). Five weeks after the last cycle, he presented with progressive decrease of vision in both eyes, flickering lights and night blindness, over a two weeks period. Laboratory tests showed a low hemoglobin level (10.2 g/dL), elevated total serum protein (11.8 g/dL), lactate dehydrogenase (305 IU/L) and creatinine level (2.3 mg/dL). Serum IgG level was increased to 8760 mg/dL (nl. 564-1765). On examination, corrected visual acuity was 20/80 and 20/100 in the right and left eye, respectively. The pupils were equal in size and reactive to light and near accommodation, extra-ocular movements were full without nystagmus, and color vision by the Ishihara method was diminished bilaterally. Intraocular pressure was within the normal limits in both eyes. Fundus examination revealed pallor of the optic disks while visual field examination showed profound field constriction. Magnetic resonance imaging of the head and orbits showed no signs of metastases or other abnormalities.

We initially performed visual evoked potentials, which were diffusely abnormal, but not diagnostic. A multi-focal electroretinogram (ERG) revealed dysfunction of both rods and cones characteristic of diffuse photoreceptor degeneration, which is supporting the diagnosis of CAR syndrome. Western blot analysis of the patient's serum showed a positive antibody reaction with 23-kDa component coinciding with the molecular mass of human recoverin.

The patient was started on oral prednisone 60 mg daily. However, three weeks later he still complained of decreased vision in both eyes. Intravenous immunoglobulin (400 mg/kg/day) was given for four doses. Following the second dose, the patient showed signs of improvement. Four weeks after finishing the full treatment, visual acuity improved to 20/40 in both eyes, with no relapse during 8 months follow up period.

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DISCUSSION

Ocular involvement in NHL lymphoma is rare and can be classified clinically into two major groups: 1- primary ocular NHL and 2- systemic NHL with secondary metastatic ocular involvement [4]. Primary ocular NHL usually presents as chronic vitritis that dose not respond to topical steroid treatment [4, 5]; Such primary ocular NHL is generally associated with central nervous system involvement by NHL later in the course of the disease [6].

The second group, which occurs more frequently, consists of ocular involvement in systemic NHL, as a result of metastatic spread of the lymphoma to the choroid or the anterior chamber [7, 8]. In addition, there are occasional reports of optic nerve neuropathy or infiltration by lymphoma [9-11]. Finally, and very rarely, there may be a lymphoma stimulated uveitis in the absence of metastases [12].

To our knowledge, there has been only one previous report (in the French literature) of CAR syndrome in lymphoma patients. Matus *et al*. described two NHL patients with symptoms of CAR, which was confirmed by the presence of anti-reoverin antibodies. Both cases were treated by corticosteroids with only minimal response [13].

Patients with CAR develop symptoms related to dysfunction of both cones (photosensitivity, abnormal visual acuity, color vision abnormalities, central scotomata) and/or rods (nyctalopia or night blindness, prolonged dark adaptation, peripheral or ring-like scotomata), and the ERG is extremely helpful in the diagnosis of CAR syndrome [14, 15]. Fifteen different antigens have been described in association with CAR. However, the only characteristic paraneoplastic marker is the presence of antibodies against recoverin [16, 17] and the a-enolase [18]. Recoverin is a retina-specific calcium binding protein that is expressed in photoreceptors and retinal bipolar cells [19]. The discovery of anti-recoverin antibodies in CAR patients' serum led to the hypothesis that the retinal degeneration that occurs in this syndrome is caused by the recoverin-specific antibodies reacting with the retinal tissue [20, 21]. Interestingly, a group of patients with anti-recoverin antibodies has been identified without any malignancy; these patients presented similar progressive visual loss, retinal degeneration and ERG changes as did CAR patients [22].

Since CAR syndrome is a rare condition, no specific treatment has been shown to be effective, and the visual prognosis is usually poor [23]. Treating the underlining malignancy has not been shown to result in better visual outcomes [24] and immuno-suppression with oral or intravenous corticosteroid exhibits only a transient or undetectable response [13, 25]. Furthermore, plasmapheresis has not been effective [22]. Finally, intravenous immunoglobulin (IVIG) therapy has also been employed with various results; improvement of visual acuity and fields was noted in one patient, improvement of visual fields only in a second patient, and no effect in the third [26, 27]. However, our patient showed significant improvement after four cycles of treatment with IVIG.

Conclusion: CAR may occur in NHL as well as the more common small cell cancer and other malignancies. Intravenous immunoglobulin may be an effective option for treating these patients, especially if started early enough before permanent retinal damage occurs. The results of present case represent the potential use of IVIG in this condition.

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