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A case of primary peripheral T-cell type Non-Hodgkin lymphoma originating in the iris – clinicopathological findings

Primarni periferni T-ćelijski limfom dužice – kliničkopatološke karakteristike

Biljana Mihaljević*, Aleksandra Sretenović*, Ljubomir Jaković*, Maja Peruničić Jovanović*, Dragana Kovačević†, Dejan Rašić†, Zoran Latković†

Clinical Center of Serbia, *Institute of Hematology, †Institute of Ophthalmology, **Belgrade, Serbia**

Abstract

Background. The ocular adnexal region is the primary localization of extranodal lymphoma in 5% to 15% of all Non-Hodgkin lymphoma. Intraocular lymphoma of T-cell origin is extremely rare and such sites of infiltration have been rarely observed in clinical examination. **Case report.** We presented a 56-year-old man with iris infiltration by primary intraocular peripheral T-cell lymphoma. The patient was in clinical stage I BE and the treatment was initiated according to cyclophosphamide, hydroxydaunorubicin, oncovin, prednisone (CHOP) regimen. When the second course of the therapy was scheduled, the patient developed central nervous system lymphoma infiltration. Although De Angelis regimen was used, 3 months after the diagnosis was established, lethal outcome ensued due to disease progression. **Conclusion.** According to our experience we can conclude that further therapeutical approach to patients with primary intraocular T-cell lymphoma requires modification of conventional treatment regimens. The lower median survival in these patients suggests that the disease may be of more aggressive course.

Key words:
lymphoma, non-hodgkin; iris diseases; diagnosis; neoplasm staging; histological techniques; therapeutics; treatment outcome.

Apstrakt

Uvod. Okularni adneksi su primarna lokalizacija ekstranodalnih limfoma kod 5–15% svih *non*-Hodgkin limfoma. Intraokularni limfom T-ćelijskog porekla je redak i u dosadašnjoj kliničkoj praksi nije zabeleženo mnogo ovakvih slučajeva. **Prikaz bolesnika.** Prikazali smo bolesnika, starog 56 godina, sa infiltracijom dužice primarnim perifernim T-ćelijskim limfomom. Bolesnik je inicijalno bio u I BE kliničkom stadijumu i započeto je lečenje prema ciklofosfamid, hidroksidaunorubicin, onkovin, prednizon (CHOP) terapijskom protokolu. U terminu kada je zakazan drugi terapijski ciklus potvrđena je infiltracija centralnog nervnog sistema. Iako je lečenje nastavljeno prema De Angelis protokolu, došlo je do progresije bolesti i smrtnog ishoda tri meseca nakon postavljanja dijagnoze. **Zaključak.** Na osnovu našeg iskustva možemo da zaključimo da konvencionalni terapijski pristup u lečenju bolesnika sa primarnim intraokularnim T-ćelijskim limfomom zahteva modifikaciju. Niža stopa preživljavanja ovih bolesnika ukazuje na to da bolest može imati agresivniji tok.

Ključne reči:
limfom, nehodžkinov; dužica, bolesti; dijagnoza; neoplazme, određivanje stadijuma; histološke tehnike; lečenje; lečenje, ishod.

Introduction

Neoplasmas may affect the eye orbit as a direct result of metastatic neoplastic infiltration, compression, or circulating antibodies involving paraneoplastic retinal degeneration [1]. Non-Hodgkin lymphoma (NHL) constitute one half of all orbital malignancies and ocular adnexa are the primary extranodal lymphoma localization in 5%–15% of all extranodal NHL [2]. Marginal zone B-cell lymphoma of mucosa associated lymphoid tissue (MALT) is the most common lymphoma category arising in these anatomical structures [3]. Intraocular lymphoma of T-cell origin is extremely rare and these sites of infiltration have rarely been observed on clinical examination.

Lymphomas derived from mature (post-thymic) T-cells and natural killer (NK) cells, referred to as peripheral T-cell lymphomas (PTCL), encompass less than 15% of all NHL [4]. Peripheral T-cell lymphoma, Not Otherwise Specified (PTCL NOS) is the most common and most heterogenous category of PTCL. Presentation is usually nodal but any site can be affected and extranodal involvement is common. The median age of patients is 70 years, and almost 65% have ad-

Correspondence to: Biljana Mihaljević, Clinical Center of Serbia, Institute of Hematology, Koste Todorovića 2, 11 000 Belgrade, Serbia. Phone: +381 11 30 65 112. E-mail: bimih@eunet.rs

vanced, clinical stage IV of the disease [4, 5]. The most commonly used treatment is chemotherapy, the cyclophosphamide, hydroxydaunorubicin, oncovin, prednisone (CHOP) regimen or its variations [6].

We studied clinical and histopathological findings of a patient with a very rare iris infiltration by primary intraocular PTCL NOS.

Case report

A 56-year-old man was admitted at the Institute of Hematology, Clinical Center of Serbia, with diagnosis of PTCL, unspecified type, localized in the iris. The diagnosis was made at the Institute of Ophthalmology in May 2008. The clinical features included hyperemic right eye with white membrane in the front segment. On presentation, physical and laboratory findings were normal without B symptoms (systemic symptoms of fiver, night sweats and weight loss). Virusological and bacterial findings, hemostasis of the chest, X-ray, abdominal ultrasound and bone marrow biopsy were normal. Computerized tomography (CT) scan of the brain and paranasal cavities was without pathological findings.

A biopsy of the right eye was performed. Bioptic samples were analysed according to standard histopathological (hematoxylin-eosin, Giemsa and Gordon Sweet) and immunohistochemical (Dako LSAB 2 HRP) procedures.

Histopathological evaluation of the iris tissue specimen showed diffuse tumor infiltration, composed predominantly of the medium-sized lymphoid cells, and rare single large lymphoid cells with vesicular nuclei, central prominent nucleoli and scant basophilic cytoplasm (Figure 1 A, B). Immunohistochemical studies revealed that tumors cells were LCA+, TdT-, CD20-, CD3+, CD5+weak, CD43+, CD45RO+ and CD30- (Figure 1 C–E). Ki-67 was positive in 60% of the tumor cells (Figure 1 F). There was also an inflammatory polymorphus background with clustered CD20+ small lymphocytes, rare eosinophils, plasma cells and epitheloid histiocytes. The morphologic appearance together with the immunophenotype of the tumor were diagnostic for PTCL.

The patients clinical stage was I BE and chemotherapy (CHOP regimen) was started in June 2008. A month later, at the time for the second cycle of the CHOP regimen, the patient was admitted at our Institute in a generally very poor condition, with a fever (38.4 °C) and neurological symptoms: disorientation and left side hemiparesis. Pathological laboratory findings were mild anemia hemoglobin (Hb) 117 g/L, erythrocyte sedimentation rate (ESR) 28 mm/h, elevated lactic dehydrogenase (LDH) 620 U/L and elevated C-reactive protein (CRP) 9,09 mg/L normal range: 0–3 mg/L. Abdominal ultrasound showed mild hepatomegaly (166 mm). Nuclear magnetic resonance (NMR) of the brain revealed multifocal cortical lesions, lesions of the basal ganglias, predominantly periventricular. Although secondary therapy for central nervous system (CNS) lymphoma localization (De Angelis regimen) was started, the disease had progressed and the patient died 3 months after the diagnosis was established.

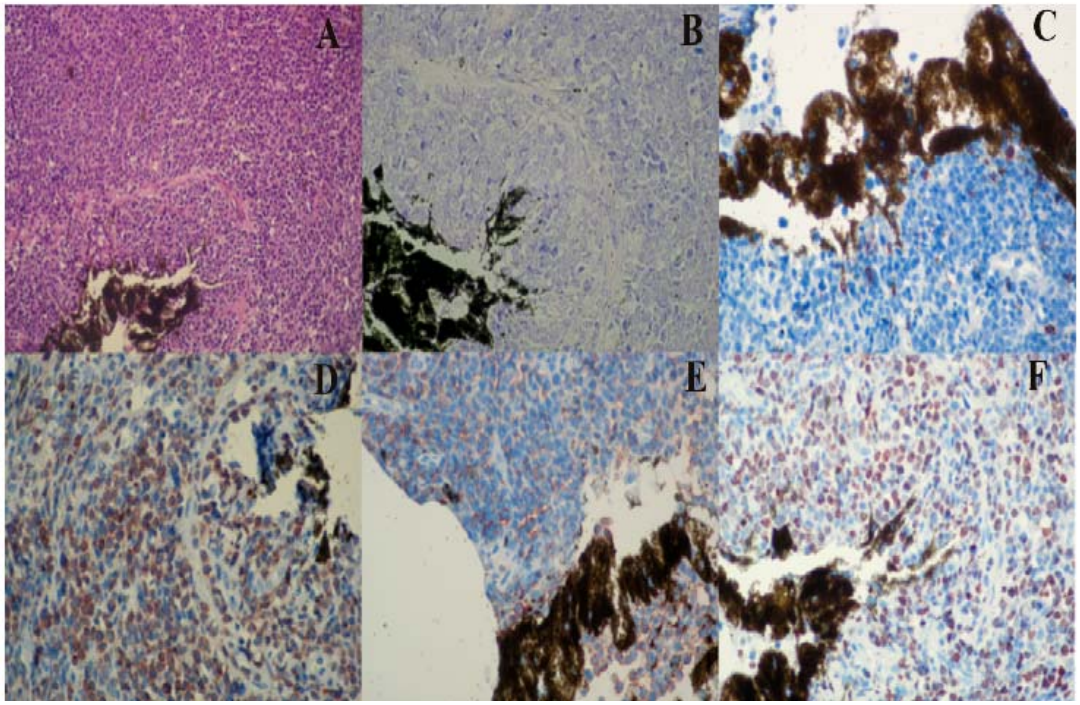

Figure 1 – (A) Iris tissue samples: diffuse tumor infiltration, composed predominantly of the medium-sized lymphoid cells, and rare single large lymphoid cells with vesicular nuclei, central prominent nucleoli and scant basophilic cytoplasm (peripheral T-cell lymphoma; hematoxylin and eosin, ×200); (B) Diffuse tumor infiltration (peripheral T-cell lymphoma; Giemsa, ×400); (C) The tumor cells negative for CD20 (peripheral T-cell lymphoma, ×400); (D) The tumor cells positive for CD3 (peripheral T-cell lymphoma, ×400); (E) The tumor cells positive for CD45RO (peripheral T-cell lymphoma, ×400); (F) The tumor cells positive for Ki67 (peripheral T-cell lymphoma, ×400)

Discussion

Non Hodgkin lymphoma affects ocular tissues either as a primary tumor or as a secondary metastasis from systemic NHL [1]. Intraocular lymphoma is generally of the B-cell type, similar to NHL elsewhere in the body, whereas T-cell type lymphoma is quite rare. The intraocular involvement can be divided into 2 general types [7]. The first is vitreoretinal lymphoma, the most common form, associated with CNS lymphoma, which is usually of the B-cell type. The second is uveal lymphoma, which is associated with visceral or nodal involvement. Between 56% and 85% of patients who initially present with primary intraocular lymphoma alone will develop cerebral lesions [8].

The appropriate diagnosis of ocular NHL can be made on identification of malignant cells in the eye by biopsy, but neuroimaging techniques are fundamental for differential diagnosis, staging and evaluation of therapeutic response. The clinical picture depends on the anatomical sites involved. Usually, there is a slowly growing, painless mass that displaces rather than infiltrates the normal structures, causing an eyelid lump, ptosis or proptosis [9–11]. In our patient, NHL simulated uveitis, and there are some papers describing this as a first NHL sign [12–16]. Some reported cases have been presented as hypopyon uveitis, neovascular glaucoma, diffuse iris thickening or as a lymphomatous lesion [17–19]. Our patient was staged as CSIE with primary iris infiltration, but all published papers of iris lymphoma describe association with systemic NHL, and in one case with primary CNS involvement [15, 18, 19].

Although our patient had no neurological symptoms or signs on presentation, confirmed with normal brain and paranasal cavity CT scan, we speculated whether the iris was the only initial localization because of the very rapid progress to CNS. Lymphoma brain infiltration was confirmed with NMR imaging technique month after the patient started therapy. The routes of infiltration to these specific sites have already been a topic of research [20]. The lymphoma cells enter the brain preferentially through the choroids plexus and cranial nerves. Once within the brain, the cells spread and migrate along the optic nerve sheath into the eyes where they continue to migrate along the choroids, ciliary body, iris, and into the anterior chamber of the eye. The orbit is also infiltrated by the lymphoma cells. However, this occurs independently of the brain-optic nerve-intraocular route.

The therapeutic strategies for this specific localization is controversial due to the fact that the primary lymphoma in the iris, especially of T-cell type, is extremely rare [6, 21]. Orbital lymphomas of MALT type show a better prognosis compared to other lymphoma subtypes arising in the ocular adnexa. Surgical resection, radiotherapy, and alkylating agent-based chemotherapy are the standard approaches for MALT orbital lymphomas [3]. The clinical course of PTCL lymphomas is aggressive, with frequent relapses and poor overall outcomes, using conventional management, with a 5-year overall survival 20%–30% [6]. Many alternate strategies have been assembled based on retrospective data, small case series, single institute experience and phase II studies [21]. Unfortunately, chemotherapy was not sufficient therapeutic approach in our patient, we speculated whether local and CNS prophylactic radiotherapy would have been a better choice. Radiotherapy could normalize the intraocular pressure followed by a reduction in neovascularization of the iris [22].

Conclusion

Presenting our experience with an unusual ocular site of PTCL, we conclude that further therapeutical approach require modification of conventional treatment regimens. The lower median survival in these patients suggests that the disease may be prone to a more aggressive course requiring CNS prophylaxis.

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