

Cavernous Sinus Syndrome as the Presentation of Systemic Non-Hodgkin's Lymphoma

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Abstract

Background: Cavernous sinus (CS) involvement has rarely been reported in malignant lymphoma. CS syndrome is uncommon as an initial presentation of non-Hodgkin's extra nodal lymphomas.

Case report: A 57-year-old man presented with a one-month history of headache, ocular pain and diplopia. Neurological examination revealed incomplete palsy of the left III and right VI nerves, and sensory loss of the first division of the left trigeminal nerve. Initial Magnetic Resonance Imaging (MRI) suggested left CS thrombosis. Despite optimal anticoagulation therapy, he developed right oculomotor nerve palsy, with ptosis and mydriasis of the left eye and bilateral sensory loss of the first and second division of the trigeminal nerves. MRI demonstrated a homogenous tissue lesion occupying the CS with moderate gadolinium enhancement. A body scan showed hepatosplenomegaly with hepatic and splenic nodules. The patient underwent percutaneous transhepatic biopsy and the lesion was histologically diagnosed as non-Hodgkin's lymphoma, diffuse large B-cell type. Tumor cells were positive for CD20, CD79a and Ki67. Following four cycles of intravenous and intrathecal chemotherapy, the right oculomotor nerve palsy was completely resolved. There was partial improvement of enhancing lesion noted on follow-up MRI.

Conclusion: CS syndrome is a rare presentation of malignant non-Hodgkin lymphoma. The diagnosis rests largely on imaging and biopsy results. It is associated with poor prognosis and Aggressive combined modality treatment appears to improve survival.

Keywords: Non-Hodgkin lymphoma; Cavernous sinus; MRI; Diplopia

Introduction

Central nervous system involvement by non-Hodgkin lymphoma (NHL) can occur as a late manifestation of systemic NHL and may include mainly mass lesions and meningeal infiltration [1]. Nasosinus localization of NHL is exceptional and represents only 0.17% [2]. Bilateral cavernous sinus (CS) syndrome is rarely the initial manifestation in immunocompetent adults with systemic NHL. We report here a new case of isolated and inaugural CS manifestation of systemic NHL.

Case Report

A 57-year-old man presented with a one-month history of headache, ocular pain associated with nausea and diplopia. There was no history of fever, weight loss, or nocturnal sweating. Ophthalmological examination revealed incomplete palsy of the left III and right VI nerves, and sensory loss of the first division of the left trigeminal nerve. Fundoscopy was normal. Complete blood count, urinalysis and other routine laboratory tests including blood biochemistry hormonal tests were within normal limits. Viral serologic testing including human immunodeficiency virus (HIV), varicella-zoster virus (VZV) and syphilis serology were negative. Initial Magnetic Resonance Imaging (MRI) showed bulging CS appearing isointense on T1 (a) and T2 FLAIR (b) weighted images with homogenous enhancement and irregular filling defects after gadolinium (c) suggesting an acute thrombus (Figures 1a-1c). Despite optimal anticoagulation therapy for ten days, the patient developed right oculomotor nerve palsy, with ptosis and mydriasis of the left eye and bilateral sensory loss of the first and second division of the trigeminal nerves. Inflammatory as well as tumoral lesion was suspected. There was no lymphadenopathy in the cervical, supraclavicular or axillary areas nor extra-neurological symptoms. Lumbar puncture (LP) showed normal protein level in the cerebrospinal fluid (CSF) with a normal cell count. PCR of CSF did not find viral or bacterial genome. A cytology test is performed to look for malignant cells were negative. Immunological tests, conversion enzyme as well as tumor markers were

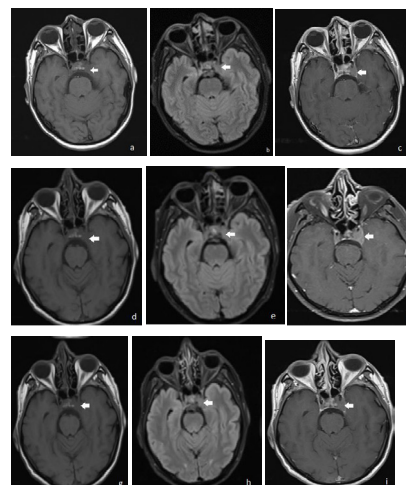


Figure 1: First brain MRI (one month after onset) (a/b/c): axial sequences: Bulging CS appearing isointense on T1 (a) and T2 FLAIR (b) weighted images with homogenous enhancement and irregular filling defects after gadolinium (c) suggesting an acute thrombus. Second brain MRI (two months after onset) (d/e/f): axial sequences: Expansion of the CS lesion Third brain MRI (six months after onset) (g/h/i): axial sequences: Slight improvement of the enhancing lesion (i).

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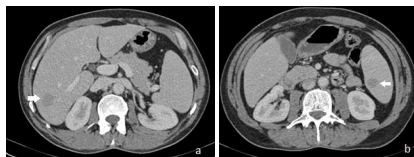


Figure 2: Hepatosplenomegaly with hepatic (a) and splenic (b) nodules on the axial body scan sequences.

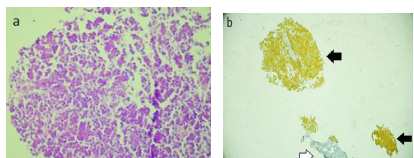


Figure 3: Photomicrograph of the hepatic biopsy demonstrating non-Hodgkin's lymphoma of the diffuse large B-cell type, which has uniform, round-to-oval nuclei with vesicular chromatin and one or multiple conspicuous nucleoli (H & E) (a). These tumor cells are positive for CD20, CD79a and Ki67 (b) Black arrow: tumor tissue; white arrow: normal tissue

normal. A second MRI (two months from onset) demonstrated an expansion of the CS lesion. The masse appeared isointense to the cortex on -T1- and T2-weighted images and FLAIR sequence, and enhanced homogeneously after gadolinium. The CS infiltration did not extend into the contiguous regions (Figures 1d-1i). No improvement was seen after adjunction of corticotherapy.

With all these features and progressive involvement, to rule out nasopharyngeal growth which was suspected on MRI, the patient was planned for nasal endoscopy. On the endoscopy, growth was observed in right side of nasopharynx near to fossa of Rosenmuller but the biopsy was negative. A second laboratory studies showed elevated liver enzymes (AST: 413 IU/L; ALT: 459 IU/L), C-reactive protein level was increased (79.3 mg/l) and there was a marked elevation in the level of lactate dehydrogenase (LDH) (646 IU/L) suggesting the presence of tumor lysis syndrome. A body scan was performed showing hepatosplenomegaly with hepatic and splenic nodules (Figures 2a and 2b). The patient underwent percutaneous transhepatic biopsy and the lesion was histologically diagnosed as NHL, diffuse large B-cell type. Tumor cells were positive for CD20, CD79a and Ki67 (Figures 3a and

References	Age/ Gender	Inaugural symptoms	Clinical signs	Histology	Treatment	Outcome
[15]	44/M	Left Ptosis and complete ophthalmoplegia	Incomplete left pupil constriction, sensory disturbance in the left V1 with diminished corneal sensation	Undifferentiated ML	-	Death within 23 days from the onset
[16]	61/M	Vertical diplopia, right ptosis and blurred vision	Right partial III palsy with pupillary dilatation, complete VI palsy and sensory impairment in the right V1	ML	RT	Relief of pain, visual acuity remained at finger counting and complete ophthalmoplegia
[17]	43/NA	NA	NA	Diffuse hitiocytic	NA	NA
[18]	6 patients	NA	NA	ML	NA	NA
[10]	57/F	Diplopia with right ptosis and periorbital pain	3-mm exophthalmos on the right eye, right partial III and VI palsies and decreased right facial sensation in the V1 and V2	Hitiocytic ML	RT	Death within 11 months from the onset
[19]	46/M	Diplopia, paraesthesia and pain in the right orbital region	Paralysis of the right VI nerve and reduced visual acuity at 5/10	Lymphosarcoma	CT/ RT	*Complete remission *Death 7 months after the onset from marrow aplasia
	70/F	Diplopia, right ptosis and pain in the right orbit	Paralysis in the right III and loss of sensation in the area supplied by the right V	Lymphosarcoma	RT	Death 13 months after the onset
[20]	45/NA	NA	NA	ML	NA	NA
[21]	40/M	Diplopia with right orbital pain	Complete right VI palsy	Large cell immunoblastic	RT	Died 3 and ½ months after the onset
[22]	4/F	Sudden squinting in both eyes and headache	Bilateral abducens and right trochlear palsy	Small, noncleaved NHL	CT	*Ptosis regressed and limited Eye movements improved
						*Death 12 days after beginning CT
[23]	77/M	Diplopia on left gaze	Left mild limitation of extraocular muscle movement in all directions, sensory disturbance in the left V1 and V2	DLBL	Gamma Knif	*Local tumor control *Death from sepsis 31 months after the onset
[12]	59/F	Diplopia and right facial hypesthesia	Right VI palsy and sensory disturbance affecting all three divisions of the right V	DSBL	RT	Partial improvement
[9]	78/M	Painful ophthalmoplegia	Left III palsy, bilateral VI palsy and sensory disturbance affecting left V1,2,3	ML	-	Rapidly fatal
[24]	71/M	Diplopia	Left partial III palsy without involvement of the pupil	DLBL	NA	NA
	89/F	Diplopia and left ptosis	Left complete III palsy without involvement of the pupil	DLBL	CT	Partial improvement
Present case	57/M	Diplopia with ocular pain	Incomplete left III and right VI palsy, and sensory loss of the left V1	DLBL	CT	Partial improvement

Table 1: CS involvement in NHL.

3b). The patient was referred to medical oncology department for a staging work-up, including bone marrow biopsy, which was negative. It was classified as stage IV according the Ann Arbor classification [3].

The patient received chemotherapy consisting of four cycles of R-CHOP (Rituximab, cyclophosphamide, Hydroxydaunomycin, oncovin, and prednisone) and intrathecal administration of methotrexate and hydrocortisone. Following four cycles of intravenous and intrathecal chemotherapy, the right oculomotor nerve palsy was completely resolved. There was partial improvement of enhancing lesion noted on follow-up MRI (six months from onset) (Figure 1i). The patient is currently under regular follow-up monthly in the medical oncology department.

Discussion

The manifestations of NHL are numerous, the most common being painless and progressive enlargement of the cervical or other groups of lymph nodes [4]. Approximately 10% to 34% of all NHL arise from extranodal sites [5].

Of these, nasal or paranasal lymphomas account 0.17% of all malignant extranodal lymphomas. They occur either as a metastasis from systemic lymphoma or invasion from a nasal or pharyngeal primary lymphoma [2].

The onset and course of NHL are variable and rapid dissemination is common in patients with neurologic involvement [4]. In rare cases, involvement of the CS can be the inaugural sign of lymphoma and neurologic signs may appear rapidly as in our patient. Presentation of lymphoma with CS involvement are no specific and may present with painful ophthalmoplegia, chemosis, proptosis, Horner's syndrome and sensory deficits in the first or second division of the trigeminal nerve [6].

Few case series of CS involvement in NHL are reported in the literature. The clinical characteristics of these cases are summarized in Table 1.

The spread of tumor to leptomeningeal the most common pathogenesis of CS involvement by NHL. Leptomeningeal spread manifests by the presence of lymphoma cells involving the meningeal membranes and CSF. Hematogenous spread is less common, but lymphoma can form nodular deposits by infiltration from the subarachnoid space through the Virchow-Robin spaces [7].

Radiologic examination is very important in the diagnosis of patients with CS lymphoma. On MRI the lymphoma enlarges the CS without compressing the intracavernous ICA. It is usually isohypointense on both T1 and T2-weighted images and enhances homogeneously [6]. Bilateral CS involvements by NHL constitute a diagnostic challenge, particularly when appearing at the presentation of the disease. In fact, a wide range of disorders can affect the CS including neoplastic, vascular, infectious, and inflammatory lesions. Imaging can often provide a diagnosis, which helps determine the need and approach for treatment [6].

For example, MRI scans of CS thrombosis, complicating especially infectious invasion of the sinuses, can be used to help diagnose. It shows a lack of enhancement inside the CS and increased enhancement along the lateral border of the CS [8].

Inflammatory lesions such as Wegener granulomatosis, sarcoidosis and Tolosa hunt syndrome have to be considered [9]. On MRI, the CS is usually iso or hypointense on T1-weighted imaging and enhances homogeneously. Hypointensity on T2-weighted imaging may be seen with chronic inflammation representing fibrous tissue [6].

Further complementary examinations play a crucial role in diagnosis and management of conditions affecting the CS. In NHL's CS involvement, biopsy of associated locations usually confirms the diagnosis as in the literature and herein reported case. When CS involvement is solitary, surgical biopsy of this location is mandatory [10,11].

NHL treatment include aggressive chemotherapy and radiotherapy as the clinical characteristics are rapid growth and poor prognosis [12].

Literature suggests that the best treatment outcomes are obtained with the R-CHOP regimen, given at three-week intervals [13]. Intrathecal methotrexate and hydrocortisone reduces CNS recurrence and improves survival in aggressive NHL [14]. In our case, the right oculomotor nerve palsy and enhancing lesion noted on follow-up MRI were improved over the course of chemotherapy [15-24].

Conclusion

NHL should be considered in the differential diagnosis of CSS and a work-up of other foci of involvement is mandatory. The diagnosis rests largely on imaging and biopsy results. Aggressive combined modality treatment appears to improve survival.

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