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Case Report

Tolosa-Hunt Syndrome Masquerading Burkitt's Lymphoma

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Abstract

Tolosa-Hunt syndrome is characterized by painful opthalmoplegia of idiopathic nature in the absence of any obvious etiology. Numerous pathological conditions may produce Tolosa-Hunt like clinical features, so its diagnosis is of exclusion. This condition is extremely responsive to steroid therapy. Burkitt lymphoma is a very aggressive disease. Though very rare, it may present with Tolosa-Hunt like features. If suspected, early diagnosis and treatment is warranted. Here we are presenting a rare case of Burkitt lymphoma in old age patient which was mimicking Tolosa-Hunt syndrome. The neurological findings were explained by a lymphomatous infiltration of the cavernous sinus. As part of this report, the diagnostic criteria for Tolosa-Hunt syndrome and Burkitt's lymphoma is reviewed, and updated recommendations are presented.

Keywords: Tolosa-Hunt Syndrome; Burkitt Lymphoma; Painful Opthalmoplegia

Introduction

Tolosa-Hunt syndrome is a constellation of symptoms characterized by painful opthalmoplegia due to granulomatous inflammation within cavernous sinus in the absence of other causes of painful opthalmoplegia including infective, aneurysms, tumors, etc. [1]. It is a rare entity with an annual incidence approaching one case per million population with no gender differences in incidence [2]. It is exquisitely sensitive to steroid therapy [3].

Burkitt lymphoma is an uncommon and an aggressive type of non-Hodgkin's lymphoma, most commonly affecting children.[4] Clinically, adult patients commonly present with abdominal disease and leptomeningeal, testicular and inguinal nodal involvement is very rare. Being a very aggressive disease, it necessitates quick evaluation and prompt initiation of treatment (chemotherapy).

Case Summary

A 66-year-old gentleman initially presented to Neurology department of JIPMER with recent onset, worsening left frontal and temporal headache, blurred vision and ipsilateral diplopia. He is a known diabetic on oral hypoglycemic and had undergone left iliofemoral bypass for peripheral vascular disease two years back. Examination revealed of the mild ptosis of the left eye with restricted lateral and medial recti activity. The pupil was dilated (4 mm) and was sluggishly reactive, which was suggestive of paresis of left III and VI cranial nerves. Contralateral eye was normal. Neurological examinations revealed loss of sensation in left V1 (ophthalmic) and V2 (maxillary) territory also. There were no meningeal signs, and other CNS examinations showed no abnormal finding.

MRI of the brain showed mildly enhancing soft tissue lesion extending from the left orbital apex into the left cavernous sinus with no other intracranial abnormal finding (Figure 1). CSF examinations were acellular with no significant finding including the tubercular profile. Based on above findings, a presumptive diagnosis of Tolosa-Hunt syndrome was made, and intravenous methylprednisolone was started. He achieved a

partial symptomatic response. Meanwhile, on 10th admission day he was found to have right lower limb edema and inguinoscrotal swelling. Given the clinical scenario and past peripheral vascular disease history, a provisional diagnosis of deep vein thrombosis (DVT) was considered which was proved on a duplex scan. His prophylactic dose of Enoxaparin (LMWH) was converted to the therapeutic dose. Whole body CECT revealed soft tissue lesion brain similar to MR, right axillary, bilateral inguinal, pelvic and retroperitoneal lymph adenopathy and irregular heterogeneous soft tissue mass in right inguinoscrotal region encasing ipsilateral femoral vessel with uninvolved testis. In view of malignancy, he was transferred to surgical oncology department. Inguinal lymph node biopsy showed medium size atypical lymphoid cells admixed with the prominence of foamy macrophages and starry sky appearance. On immunohistochemistry tumor cells were positive for leucocyte common antigen (LCA) and CD 20 and negative for CD 5, Tdt, CD 10, c-Myc. Ki 67 labeling index was 99% (Figure 2). The histopathological findings were suggestive of Burkitt's lymphoma. The patient expired within three days of diagnosis before any definitive treatment could be started.

Figure 1: MR images showing enhancing lesion (arrow) in from orbital apex to cavernous sinus.

Figure 2: Histopathology shows tumor composed of (a) Sheets of monomorphic medium sized lymphoid cells (H&EX40): (b) Cells show round nuclei with fine dispersed chromatin, basophilic cytoplasm admixed with macrophages gives starry sky appearance (H&EX400): (c) Tumor cells show strong immunohistochemistry positivity for leucocyte common antigen (LCA) as well as (d) CD20 (H&EX400): (e) Negative for Tdt (f) Ki-67 shows nuclear positivity in 99% of cells.

Discussion

Tolosa-Hunt syndrome was first reported by Tolosa in 1954 and then by Hunt in 1961 [1]. Tolosa-Hunt syndrome nomenclature was given by Smith and Taxdal in 1966 [1]. Currently it has been described by International Headache Society as: Unilateral orbital pain associated with paresis of one or more of the IIIrd, IVth and/or VIth cranial nerves caused by an idiopathic granulomatous inflammation in the cavernous sinus, superior orbital fissure or orbit [5]. Various MRI features - presence of a lesion within the anterior cavernous sinus, local increase in size of the cavernous sinus, bulging of the dural contour of the cavernous sinus etc. has been described by Schuknecht., *et al*. with great reproducibility in their series of 15 patients [6]. Diagnosis is made after excluding other causes of painful opthalmoplegia including inflammatory, vascular, traumatic or neoplastic causes. The steroid has remained the mainstay and extremely effective treatment since the first description by Hunt., *et al*. 45 years back [3].

Burkitt lymphoma was first reported by Denis Burkitt in 1958 in children [7]. Burkitt Lymphoma is a pediatric disease, and adult presentation is rare [4]. It is commoner in males. Clinically it has three types of presentations – Endemic (African), Nonendemic and Immunodeficiency related. Most of the nonendemic cases present with massive abdominal mass, B symptoms and tumor lysis syndrome. Bone marrow and Leptomeningeal involvement may be up to 70% and 40% respectively [8]. Evaluation is done with CT thorax, abdomen, and pelvis; bone marrow study, renal and liver function test. On microscopy, Burkitt lymphoma cells show typical Starry Sky appearance due to the presence of atypical noncleaved lymphoid cells admixed with tangible body macrophages. KI-67 is typically high (99% or greater). Immunophenotypically these cells express B-cell markers - CD19, CD20, sIgM, CD10, and BCL6 but not BCL2 [9]. Prompt diagnosis and earliest initiation of treatment is the cornerstone of management.

Based on initial clinical and MR features in the absence of symptomatology of other systemic disease, our patient was marked as Tolosa-hunt syndrome. Probably cavernous sinus lesion was leptomeningeal metastases. But in the absence of typical abdominal presentation and prominence of CNS symptoms diagnosis of Burkitt's was masqueraded. Response to steroid further strengthened the diagnosis. But we should remember that steroid not only brings symptomatic improvement in Tolosa-Hunt syndrome but also in various other neoplastic and lymphoproliferative lesions thus resulting in delayed diagnosis [5]. Though cavernous lesion was not biopsy proven, in the presence of Burkitt's lymphoma the lesion had a high likelihood of being a metastasis. So this uncommon presentation of Burkitt's lymphoma resulted in late diagnosis and was confused initially with Tolosa-Hunt syndrome.

Conclusion

Tolosa-Hunt syndrome may be an unusual presentation of Burkitt's lymphoma. So if any suspicion this deadly disease should be excluded. Though uncommon, Burkitt's lymphoma may present with inguinal lymph node enlargement. Tolosa-Hunt syndrome is a diagnosis of exclusion and should remain. High-grade lymphoma should be treated promptly.

Disclosure

No funding or financial support was received from any commercial organization.

Written consent from patient's relatives obtained for publication of disease and treatment related information.

Conflict of Interest

We declare that there is no conflict of interest regarding the publication of this paper.

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