Clinical Neurology and Neurosurgery 155 (2017) 63–69

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Full Length Article

Cavernous sinus syndrome: A prospective study of 73 cases at a tertiary care centre in Northern India

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ARTICLE INFO

Article history:
Received 9 May 2016
Received in revised form
22 December 2016
Accepted 20 February 2017
Available online 22 February 2017

Keywords:
Cavernous sinus
Aspergillus
Mucormycosis
Painful ophthalmoplegia
Tolosa hunt syndrome
Pituitary adenoma

ABSTRACT

Objectives: To study the clinical and etiological profile of patients with cavernous sinus syndrome (CSS) and identify factors which could determine the etiology and influence the outcome of these patients.
Patients and methods: This prospective observational study included 73 consecutive patients satisfying the criteria of CSS (i.e. involvement of any 2 of the 3rd, 4th, 5th and 6th cranial nerves or any one of them with radiological evidence of cavernous sinus involvement). All these patients were subjected to detailed haematological, biochemical and radiological investigations and diagnosed and treated as per guidelines. The clinical and investigational data was recorded and analysed meticulously.
Results: A definitive etiological diagnosis of CSS could be achieved in 86% of patients. Tumours, fungal infections and Tolosa Hunt syndrome (THS) were most common causes. On univariate analysis, diabetes, severe vision loss (visual acuity of <3/60 in at least one eye), and presence of nasal discharge showed a significantly positive association with a fungal CSS. Evidence of paranasal sinusitis, bone erosion and ICA (internal carotid artery) involvement on Gadolinium enhanced MRI (magnetic resonance imaging) of brain were significantly associated with a fungal CSS ($p = 0.0001$), whereas involvement of orbital apex had a negative association with a neoplastic etiology ($p = 0.014$). On multiple logistic regression, orbital apex involvement on MRI was associated with diagnosis of THS ($p = 0.019$, OR: 18.7; 95% CI: 1.6–217.4) while MRI evidence of paranasal sinusitis ($p = 0.014$, OR: 45; 95% CI: 2.1–94.3) and bone erosion (($p = 0.019$, OR: 12.5; 95% CI: 1.5–103) correlated with diagnosis of fungal CSS. 65.2% of patients (fungal CSS- 70%) had a good prognosis at six months follow up.
Conclusion: Most patients with CSS can be diagnosed accurately and managed properly with good outcomes.

1. Introduction

The term cavernous sinus syndrome (CSS) denotes any disease process affecting the cavernous sinus (CS), a small but complex structure containing several important structures within its walls namely internal carotid artery, ocular motor nerves, trigeminal nerves, and sympathetic fibers. The close proximity of CS to paranasal sinuses and other important structures of brain makes it susceptible to several unique disease processes such as fungal infections (which commonly spread from adjoining paranasal sinuses), malignancies (e.g. nasopharyngeal carcinomas), internal carotid artery disorders (e.g. aneurysm) and many others [1]. CSS is associated with considerable: a) morbidity due to involvement of structures associated with several vital functions (vision, mastication), and b) mortality mainly due to serious nature of underlying disease entities such as malignancies or fungal infections [2].

A unique aspect of CSS is difficulty in finding out the exact underlying etiology. This is partly due to diverse nature of disease processes affecting CS and partly due to the fact that this region is often not amenable to biopsy. Thus, more often than not, treatment is empirical [2].

Very few authors have tried to delineate epidemiological and etiological profile of CSS. Most of our knowledge about CSS is based on retrospective data from developed countries and these results may not be applicable to developing countries such as India where infections are supposed to account for a major chunk of CSS [3–5]. Thus we conducted this study to analyze the clinical and etiological profile of patients with CSS in North Indian population.

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http://dx.doi.org/10.1016/j.clineuro.2017.02.017
0303-8467/

2. Aims and objectives

a) To study the clinical, investigational and etiological profile of CSS.
b) To determine clinical and radiological parameters which can predict etiology of CSS.

3. Patients and methods

The current prospective observational study was carried out from January 2014 to July 2015 (1½ years) at a tertiary care centre and teaching hospital in Northern India. Patients of either sex attending neurology outpatient department (OPD) or getting admitted in emergency and neurology wards were included in the study. The study was approved by institutional ethics committee and written informed consent was obtained from all the participants before inclusion in the study. CSS was defined as involvement of two or more of the third, fourth, fifth (V1, V2), or sixth cranial nerves, or involvement of only one of them in combination with a neuroimaging-confirmed lesion in the CS. The inclusion and exclusion criteria for the study are given below:

Inclusion criteria:

1. Diagnosis of CSS
2. Patients willing to give written informed consent and ready for follow up

Exclusion criteria: Lack of informed consent and/or not willing for follow up

Detailed history and examination were carried out in all the patients as per a predetermined protocol. All the patients underwent necessary investigations. Wherever we were not able to ascertain the etiology of CSS, patients were labelled as CSS of undetermined etiology. Diagnosis of THS was made according to ICHD-II criteria [6]. All patients underwent standard treatment according to the etiology and were followed up at three monthly intervals for a minimum of six months (Figs. 1–3).

4. Statistical analysis

Statistical analysis was done by using SPSS version 22. Quantitative data was expressed in mean (± SD) and or median. Qualitative/categorical data was expressed in frequency/percentage. Chi square/Fisher's exact test was applied to determine association of clinical and radiological symptoms/signs with etiology as well as outcome of CSS. Finally, multivariate logistic regression was used to identify factors which could predict etiology of CSS. Two tailed P value of <0.05 was taken as significant.

5. Results

5.1. Demographic variables

Current study included 73 patients (males- 47; females- 26) of CSS with a mean (±SD) age of 44.45 ± 14.7 years (range 11–70 years).

5.2. Clinical profile of CSS

18 (24.7%) patients had acute (onset of symptoms to presentation ≤1 week), 20 (27.4%) had subacute (onset of symptoms to presentation: 8 days to 1 month) while 35 (47.9%) patients had a chronic presentation (onset of symptoms to presentation: >1 month). 12 (16.4%) patients has bilateral CSS. Commonest symptoms were headache (97.2%) followed by binocular diplopia (90.4%), ptosis (68.4%) and facial numbness (56.2%). All the demographic and clinical data is summarized in Table 1.

Table 1
Clinical and demographic profile of patients with cavernous sinus syndrome.

Variable	Value (n = 73)
Age in years	44.45 ± 14.7 (Range 11–70)
Men: women	47:26
Symptoms	
Acute presentation	18 (24.7%)
Subacute presentation	20 (27.4%)
Chronic presentation	35 (47.9%)
Bilateral involvement	12 (16.4%)
Headache [unilateral in 50 (70.4%); Bilateral in 21(29.6%)]	71 (97.2%)
Diplopia	66 (90.4%)
Ptosis [Bilateral in 4 (8%)]	50 (68.4%)
Proptosis [bilateral in 6 (26.1%)]	23 (31.5%)
Facial numbness (unilateral in all)	41 (56.2%)
Visual loss [bilateral in one (8.3%)]	12 (16.5%)
Fever	9 (12.3%)
Nasal blockage	5 (6.8%)
Facial deviation (unilateral in 6)	7 (9.5%)
Hearing loss	2 (2.7%)
Altered sensorium	5 (6.8%)
Limb weakness	7 (9.6%)
Seizures	2 (2.7%)
Signs	
6th cranial nerve	60 (82.1%)
3rd cranial nerve [Bilateral in 7/57 (12.2%); Pupils spared in 25/57 (43.8%)]	57 (78.1%)
4th cranial nerve	50 (68.4%)
Trigeminal nerve	
Ophthalmic division	34 (46.5%)
Maxillary division	22 (30.1%)
Mandibular division	6 (8.2%)
Ophthalmic + Maxillary divisions	22 (30.1%)
All three divisions	6 (8.2%)
7th cranial nerve (Bilateral in one)	11 (15%)
Lower cranial nerves (9th to 12th)	3 (4.1%)
Optic nerve	17 (23.2%)
Severe visual loss	8 (10.9%)
Horner's syndrome (Unilateral in all)	4 (5.4%)

Table 2
Common etiologies of cavernous sinus syndrome.

Etiology	Number of patients (%age) (n = 73)
Neoplastic involvement (Metastases-5; pituitary macroadenoma-5; nasopharyngeal carcinoma-3; meningiomas-2; Leukaemia/lymphoma/myeloma-one each; Esthenioblastoma/Schwannoma/Chordoma- 1 each	21 (28.8%)
Fungal infections (Aspergillosis-8; Mucromycosis-4; Probable fungal −6)	18 (24.6%)
Tolosa Hunt syndrome	17 (23.2%)
Vascular causes	5 (6.8%)
Others (Hypertrophic pachymeningitis-3; septic cavernous sinus thrombosis-2; Wegener's granulomatosus/Neurosarcoidosis/tuberculosis- 1 each; Diabetic ophthalmoplegia-2; Unclassified-2)	12 (16.4%)

5.3. Etiologic diagnosis of CSS (Table 2)

In present study (n = 73), neoplastic involvement (n = 21; 28.8%) was the commonest cause of CSS, followed by fungal infections (n = 18; 24.6%), THS (n = 17; 23.2%) and vascular etiologies (n = 5; 6.8%). Other etiologies (Table 2) were seen in 12 (16.4%) patients. Distribution of various neoplasms is also shown in Table 2. The diagnosis of metastatic carcinoma was confirmed