Original Article

Which Classification of Cavernous Sinus Syndrome is Better - Ishikawa or Jefferson? A Prospective Study of 73 Patients

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INTRODUCTION

The term cavernous sinus syndrome (CSS) is used to denote any disease process which affects the CS.[1-4] Determination of exact etiology of CSS is often difficult due to the lack of amenability to tissue diagnosis. Thus, treatment is often empirical and based on clinical presentation and radiological findings. Thus, if the classification of CSS into different types can throw light on underlying etiology, it might help in further management.

CSS was first classified by Jefferson[5] into three types based on the extent of involvement of trigeminal nerve [Table 1]. Since then, this classification has been the gold standard and given in most textbooks of neurology. In 1996, Ishikawa[6] emphasized the lack of clinico-anatomical correlation in Jefferson’s classification and proposed a new classification of CSS [Table 1].[7] Subsequently, a Japanese study found that majority of patients who remained unclassified by Jefferson classification can be classified using Ishikawa scheme. Furthermore, when classified according to Ishikawa’s scheme, anterior CS lesions were often due to inflammatory etiologies, whereas middle and posterior CS lesions were due to malignancies, suggesting that this classification system may play a role in determining etiology of CSS.[7] However, etiological profile of CSS is likely to be different in developing countries (e.g., India) where infections constitute a major chunk. There is no data regarding the utility of these two classification schemes from developing world. Thus, we planned this study to compare utility of these two systems of classification in CSS.

Aims and objectives

To compare the utility of Jefferson versus Ishikawa classification in the evaluation of CSS.

PATIENTS AND METHODS

This prospective observational study was conducted from January 2014 to July 2015, on 73 patients of CSS at a Tertiary Care

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The whole trigeminus affected with ocular palsy, sometimes only 2. Among the ten patients, in which, First and second divisions of trigeminus affected, third spared.

Involving both optic nerve and maxillary nerve in addition to ocular

Unclassifiable

Whole cavernous syndrome

Posterior cavernous syndrome (from 10 mm behind the orbital apex to 10 mm posterior, that is, at the site of the entry of the maxillary nerve)

Posterior cavernous syndrome (from 10 mm behind the orbital apex to the posterior wall)

Whole cavernous syndrome

Statistical analysis

Statistical analysis was performed using SPSS version 22 (IBM Corp. Released 2013. IBM Statistics for windows, Version 22.0. Armonk, NY: IBM Corp). Quantitative data were expressed in mean and or median. Qualitative or categorical data were expressed in frequency or percentage. Chi-square or Fisher’s exact test was applied to compare the discrete variables. \( P < 0.05 \) was considered statistically significant.

RESULTS

Demographic, clinical, and etiological profile of cavernous sinus syndrome

The data regarding demographic and clinical profile are given in Table 2. The exact etiology of CSS was obtained in 63/73 (86.3%) patients of CSS. The detailed etiological profile is also given in Table 2. Among the ten patients, in which, we could not establish exact etiology, six had probable fungal CSS; two had probable diabetes-related ophthalmoplegia, and two remain unclassified.

Jefferson versus Ishikawa classification of cavernous sinus syndrome

All the patients were classified by Ishikawa and Jefferson schemes [Table 3]. The number of patients which could be classified using Ishikawa classification \( (n = 69; 95.5\%) \) was much higher than Jefferson classification \( (n = 34; 46.6\%) \). Using Jefferson classification, CSS could be classified as anterior, middle, and posterior in 12 (16.4%), 16 (21.9%), and 6 (8.2%) patients, respectively. Patients with middle CSS were significantly \( (P = 0.045) \) more likely to have fungal CSS. As per Ishikawa classification, 27 patients each (37%) had anterior and posterior CSS [Figure 1] whereas 12 (16.4%) had middle

| Table 1: Jefferson’s and Ishikawa classification of cavernous sinus lesions |
| --- |
| **Jefferson classification** |
| Anterior cavernous syndrome |
| Middle cavernous syndrome |
| Posterior cavernous syndrome |
| **Ishikawa classification** |
| Anterior cavernous syndrome (from the orbital apex to 3.5 mm posterior, i.e., the intracranial orifice of the optic canal) |
| Middle cavernous syndrome (from 3.5 mm behind the orbital apex to 10 mm posterior, that is, at the site of the entry of the maxillary nerve) |
| Posterior cavernous syndrome (from 10 mm behind the orbital apex to the posterior wall) |
| Whole cavernous syndrome |
| Unclassifiable |

First division of trigeminus affected, other two divisions spared. Paralysis of superior division of oculomotor nerve, or all nerves supplying mobility of eyeball

First and second divisions of trigeminus affected, third spared. Paralysis of one nerve, usually of all nerves, supplying muscles of eye

The whole trigeminus affected with ocular palsy, sometimes only abducens. Motor root of trigeminus affected but may escape

Optic neuropathy or isolated palsy of superior or inferior branch of oculomotor nerve, regardless of other oculomotor nerves or ophthalmic nerve involvement

Concurrent oculomotor nerve and ophthalmic nerve involvement

Involving the maxillary nerve or abducens nerve with Horner’s syndrome

Involving both optic nerve and maxillary nerve in addition to oculomotor nerves and ophthalmic nerve involvement
### Table 2: Clinical and demographic profile of patients with cavernous sinus syndrome

| Variable                        | Value (n=73) |
|---------------------------------|--------------|
| Age (years)                     | 44.45±14.7   |
| Men                             | 47           |
| Common symptoms (%)             |              |
| Headache                        | 97.2         |
| Diplopia                        | 90.4         |
| Ptosis (bilateral in 4)         | 68.4         |
| Proptosis (bilateral in 6)      | 31.5         |
| Facial numbness                 | 56.2         |
| Visual loss                     | 16.5         |
| Uncommon symptoms (%)           |              |
| Fever                           | 12.3         |
| Facial deviation (unilateral in 6) | 9.5   |
| Altered sensornium              | 6.8          |
| Limb weakness                   | 9.6          |
| Hearing loss                    | 2.7          |
| Seizures                        | 2.7          |
| Signs (%)                       |              |
| Sixth cranial nerve             | 82.1         |
| Third cranial nerve (bilateral in 12.2%; pupils spared in 43.8%) | 78.1 |
| Fourth cranial nerve            | 68.4         |
| Trigeminal nerve                | 46.5         |
| First division (100%); second division (64.7%); third division (17.6%) | |
| Seventh cranial nerve (bilateral in one) | 15 |
| Lower cranial nerves (9th-12th) | 4.1  |
| Optic nerve                     | 23.2         |
| Severe visual loss              | 10.9         |
| Horner’s syndrome (unilateral in all) | 5.4  |
| Etiological profile (%)         | 86.3         |
| Definitive diagnosis            |              |

CSS and 3 (4.1%) had whole CSS. Patients with anterior CSS were significantly more likely (P = 0.005) to have vascular etiology. Overall, inflammatory causes accounted for maximum number of anterior CSS while tumors accounted for maximum cases of posterior CSS, although the difference was not statistically significant.

### DISCUSSION

Ishikawa was the first author who studied CS structure by stereotaxically analyzing 30 µm serial CS sections. Based on his observations, Ishikawa proposed his classification for CS lesions.

In the current study, 35 (48.9%) additional patients could be classified using Ishikawa scheme similar to that reported by Yoshihara et al.[7] The reason for this is the presence of some inherent deficiencies in Jefferson classification. Jefferson classification is heavily biased toward trigeminal nerve and ignores other structures contained within CS such as optic nerve, oculosympathetic fibers, inferior division of the 3rd cranial nerve and maxillary nerve either alone or in combination with mandibular nerve. This may lead to an increase in number of unclassifiable cases in Jefferson scheme. For instance optic nerve was involved in 17 (23.2%) patients in this study. After leaving the internal carotid artery, oculosympathetic fibers join 6th cranial nerve in the posterior CS for a short distance. Lesions here may affect 6th nerve and sympathetic fibers alone. Although such lesions will remain unclassifiable as per Jefferson scheme, these will be classified as posterior CSS in Ishikawa scheme. In the current study, we had one patient secondary to carotid aneurysm. Similarly, while patients with isolated maxillary nerve involvement or both maxillary and mandibular nerve involvement would fall into posterior CSS in Ishikawa classification, these will remain unclassified as per Jefferson scheme. Similar results have been reported by other authors.[7-9]

In the present study, CSS could be classified as anterior, middle, and posterior in 12 (17.8%), 16 (21.9%), and 6 (8.2%) patients, respectively, as per the Jefferson classification and 27 (37%), 27 (37%), and 12 (16.4%) as per Ishikawa classification.

### Table 3: Jefferson versus Ishikawa classification in cavernous sinus syndrome

| Type of CSS   | Tolosa-Hunt syndrome, n=17 (%) | Fungal CSS, n=18 (%) | Neoplastic CSS, n=21 (%) | Vascular CSS, n=5 (%) | Other causes of CSS, n=12 (%) | Overall (%) |
|---------------|--------------------------------|----------------------|--------------------------|-----------------------|-------------------------------|-------------|
| Ishikawa classification of CSS |                                 |                      |                          |                       |                               |             |
| Anterior CSS  | 8 (47.1)                       | 5 (27.8)             | 6 (28.6)                 | 5 (100)               | 3 (25)                        | 27 (37)     |
| Middle CSS    | 3 (17.6)                       | 3 (16.7)             | 3 (14.3)                 | 0                     | 3 (25)                        | 12 (16.4)   |
| Posterior CSS | 6 (35.3)                       | 8 (44.4)             | 9 (42.9)                 | 0                     | 4 (33.3)                      | 27 (37)     |
| Whole CSS     | 0                              | 2 (11.1)             | 1 (4.8)                  | 0                     | 0                             | 3 (4.1)     |
| Unclassified | 0                              | 0                    | 2 (9.5)                  | 0                     | 2 (16.7)                      | 4 (5.5)     |
| Jefferson classification of CSS |                                 |                      |                          |                       |                               |             |
| Anterior CSS  | 3 (17.6)                       | 3 (16.7)             | 3 (14.3)                 | 0                     | 3 (25)                        | 12 (16.4)   |
| Middle CSS    | 2 (11.8)                       | 7 (38.9)             | 4 (19)                   | 0                     | 3 (25)                        | 16 (21.9)   |
| Posterior CSS | 1 (5.8)                        | 2 (11.1)             | 3 (14.3)                 | 0                     | 0                             | 6 (8.2)     |
| Unclassified | 11 (64.7)                      | 6 (33.3)             | 11 (52.4)                | 5 (100)               | 6 (50)                        | 39 (53.4)   |

On comparison, it was found that presence of middle CSS on Jefferson scheme is significantly (P=0.045) more likely to have fungal CSS. In addition, patients with anterior CSS on Ishikawa classification are significantly more likely (P=0.005) to have vascular CSS. CSS: Cavernous sinus syndrome.
Yoshihara et al. showed anterior CS involvement to be the most common (35%) followed by posterior (22%) and middle (10%) as per Ishikawa classification. The difference between above series and ours is likely related to the different etiological profile of CSS in these series.

Using Jefferson classification, middle CSS was significantly associated with the presence of fungal infections \( (P = 0.045) \). Using Ishikawa classification, all the patients with vascular etiology have anterior CSS. Overall, inflammatory causes were the most common cause for anterior CSS, while tumors accounted for maximum cases of posterior CSS, although the difference was not statistically significant. The explanation for these observations is straightforward. Anterior CS is likely to be affected by inflammatory pathologies more often due to its close proximity to ethmoid sinus (most common site of paranasal sinusitis), while posterior CS is likely to be affected by tumors especially pituitary adenomas due to anatomical reasons. Our findings are similar to Yoshihara et al. who reported inflammation to dominate in anterior CSS and tumors to dominate in posterior CSS.

CONCLUSION

Our study further emphasizes that many more patients with CSS can be classified using Ishikawa scheme as compared to Jefferson scheme. However, when it comes to etiological profile of CSS, Ishikawa classification did not score over Jefferson scheme. In fact, Jefferson scheme gave a better idea to etiology as middle CSS in this scheme had a significantly higher chances of fungal CSS.

Main limitation of our study was small sample size. That may be the main reason why some of our results did not reach statistically significance. Future studies with more patients may help to understand the utility of these two classification systems better.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES
1. van Overbeeke JJ, Jansen JJ, Tulleken CA. The cavernous sinus syndrome. An anatomical and clinical study. Clin Neurol Neurosurg 1988;90:311-9.
2. Keane JR. Cavernous sinus syndrome. Analysis of 151 cases. Arch Neurol 1996;53:967-71.
3. Fernández S, Godino O, Martínez-Yélamos S, Mesa E, Arruga J, Ramón JM, et al. Cavernous sinus syndrome: A series of 126 patients. Medicine (Baltimore) 2007;86:278-81.
4. Parkinson D. Lateral sellar compartment O.T. (cavernous sinus): History, anatomy, terminology. Anat Rec 1998;251:486-90.
5. Jefferson G. On the saccular aneurysms of the internal carotid artery in the cavernous sinus. Br J Surg 1938;26:267-302.
6. Ishikawa H. Clinical anatomy of the cavernous sinus. Shinkei Ganka (Neuroophthalmol Jpn) 1996;13:357-63.
7. Yoshihara M, Saito N, Kashima Y, Ishikawa H. The Ishikawa classification of cavernous sinus lesions by clinico-anatomical findings. Jpn J Ophthalmol 2001;45:420-4.
8. Foix MC. Syndrome of the wall of cavernous sinus. Rev Neurol 1922;38:827-32.
9. Godtfredsen E. Studies on the cavernous sinus syndrome 1. Incidence, aetiology and differential diagnosis of infranuclear ophthalmoplegias. Acta Neurol Scand 1964;40:69-75.