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The Ishikawa Classification of Cavernous Sinus Lesions by Clinico-anatomical Findings

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Purpose: The Jefferson classification has been used to localize cavernous sinus lesions. However, this classification occasionally showed dissociation between identified localization and clinical findings. We investigated the clinical applicability of the newly proposed Ishikawa classification based on serial topographic sections of human cavernous sinus and the clinical findings.

Methods: In the Ishikawa classification, the cavernous sinus is divided into three portions, that is, anterior, middle, and posterior, demarcated by the location of the intracranial orifice of the optic canal and the entry of the maxillary nerve into the cavernous sinus. A total of 162 patients with cavernous sinus lesions were classified using both the Jefferson and the Ishikawa classifications and the clinical applicability of these two classifications was studied. Characteristics of the localization of lesions were also examined in each etiological type.

Results: By the Jefferson classification, 11% of the 162 patients had the anterior type of lesion, 12% the middle, 8% the posterior type, and 69% the unclassifiable type. However, by the Ishikawa classification, 35% had the anterior type, 10% the middle type, 22% the posterior type, 5% the whole type, and 28% the unclassifiable type of lesion. Furthermore, the Ishikawa classification revealed that the etiology of the anterior type was mainly inflammation, and that the etiology of the posterior and whole types was tumors.

Conclusion: The Ishikawa classification is clinically useful to identify and classify the localization of cavernous sinus lesions. **Jpn J Ophthalmol 2001;45:420–424** © 2001 Japanese Ophthalmological Society

Key Words: Anatomy, cavernous sinus, classification, clinico-anatomical findings.

Introduction

The cavernous sinus contains ocular motor nerves: the oculomotor, trochlear, and abducens nerves, the ophthalmic and maxillary branches of the trigeminal nerve, and the oculosympathetic nerve. Therefore, the ophthalmologist has a great interest in the cavernous sinus.

In 1938, Jefferson[1] proposed a term, "cavernous sinus syndrome," in a study on aneurysms of the internal carotid artery in the cavernous sinus. As shown in Table 1, he classified the cavernous sinus syndrome into three types based mainly on trigeminal nerve involvement. However, many problems arose with the clinical use of the Jefferson classification because of a lack of clinico-anatomical evidence. In 1996, Ishikawa[2] proposed a new classification based on the localization of cavernous sinus lesions determined by the investigation of serial topographical sections of human cavernous sinus and clinical findings. Corresponding to the three portions of the cavernous sinus separated by the locations of the intracranial orifice of the optic canal and the entry of the maxillary nerve into the cavernous sinus, he classified cavernous sinus lesions into four types: anterior, middle, posterior, and whole.

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Table 1. Jefferson Classification for Cavernous Sinus Syndrome

Anterior cavernous syndrome:
First division of trigeminus affected, other two divisions spared. Paralysis of superior division of oculomotor nerve, or all nerves supplying mobility of eyeball.
Middle cavernous syndrome:
First and second divisions of trigeminus affected, third spared. Paralysis of one nerve, usually of all nerves, supplying muscles of eye.
Posterior cavernous syndrome:
Whole trigeminus affected with ocular palsys, sometimes only abducens. Motor root of trigeminus affected, but may escape.

We investigated the clinical application of the Ishikawa classification to our patients and cavernous sinus lesions.

Materials and Methods

Classification of Localization of Cavernous Sinus Lesions

Figure 1 shows the topographical anatomy of the cavernous sinus by the Ishikawa classification.[2] The anterior portion is located from the orbital apex to 3.5 mm posterior, that is, the intracranial orifice of the optic canal; the middle portion is located from 3.5 mm behind the orbital apex to 10 mm posterior, that is, the site of the entry of the maxillary nerve into the cavernous sinus; and the posterior portion is located from 10 mm behind the orbital apex to the posterior wall.

Figure 2 shows neurological involvement for each portion in the Ishikawa classification. The optic nerve is easily involved in a lesion of the anterior portion, because it runs close to the supero-medial wall of the cavernous sinus. Therefore, optic nerve involvement is classified as the anterior type, regardless of ocular motor nerve or ophthalmic nerve involvement. The oculomotor nerve separates into the superior and inferior branches in the anterior portion of the cavernous sinus. Thus, when either the superior or the inferior branch is separately involved, the lesion is classified as the anterior type. However, in this classification, lesions are not classified as the anterior type when both superior and inferior branches are involved regardless of symptomatic differences between them.

When ophthalmic nerve involvement is combined with ocular motor nerve involvement, the lesion is classified as the middle type.

The oculosympathetic nerve runs in parallel with the abducens nerve for a short distance in the posterior portion of the cavernous sinus. When maxillary nerve involvement occurs, the lesion is classified as the posterior type, regardless of ocular motor nerve or ophthalmic nerve involvement. Furthermore, when both abducens nerve palsy and Horner's syndrome are present, the lesion is classified as the posterior type.

When both optic nerve and maxillary nerve involvement is observed in addition to ocular motor nerve and ophthalmic nerve involvement, the lesion is considered to extend over the entire cavernous sinus and it is classified as the whole type.

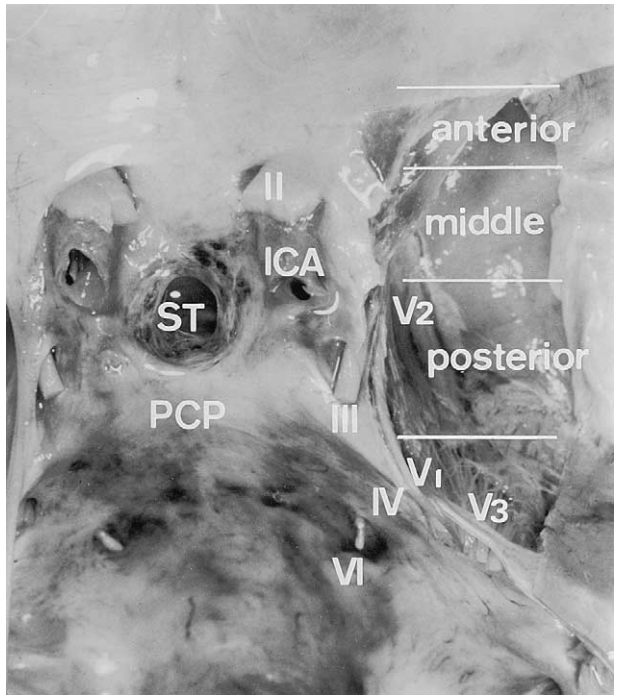

Figure 1. Skull base in vicinity of cavernous sinus. Lateral wall of cavernous sinus has been removed. Three portions, that is, anterior, middle, and posterior, divided by location of intracranial orifice of optic canal and entry of maxillary nerve into cavernous sinus, are indicated. II: optic nerve, III: oculomotor nerve, IV: trochlear nerve, V_1: ophthalmic nerve, V_2: maxillary nerve, V_3 mandibular nerve, VI: abducens nerve, ICA: internal carotid artery, ST: sella turcica, PCP: posterior clinoid process.

Clinical Diagnosis of Patients with Cavernous Sinus Lesion

The subjects were 162 patients with the cavernous sinus syndrome examined in Nihon University Hospital during a period of 16 years from 1981 to 1996. Table 2 shows their etiologies.

Inflammation was regarded as Tolosa-Hunt syndrome. A tumor extending from an adjacent lesion

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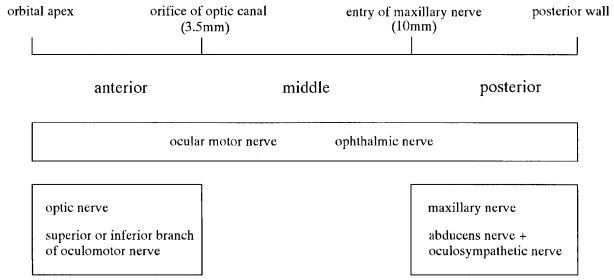

Figure 2. Ishikawa classification for cavernous sinus lesions. When optic neuropathy or isolated palsy of superior or inferior branch of oculomotor nerve is present, lesion is classified as anterior type, regardless of other ocular motor nerve or ophthalmic nerve involvement. If ocular motor nerve and ophthalmic nerve involvement are present concurrently, lesion is classified as middle type. When maxillary nerve involvement or abducens nerve involvement with Horner's syndrome is present, lesion is classified as posterior type, regardless of ocular motor nerve or ophthalmic nerve involvement.

was considered in the pituitary gland or the paranasal sinus. Except for patients with inflammation, it was confirmed neuroradiologically that their lesions were located in the cavernous sinus.

These 162 patients were classified using both the Jefferson and Ishikawa classifications and the applicability of these two classifications was studied. Furthermore, characteristics of the localization of lesions were also examined in each etiology by the Ishikawa classification.

Results

Table 3 shows the results of our study of the classifications with respect to the localization of lesions. Most of the cases (69%) were unclassifiable by the Jefferson classification. However, the unclassifiable types were reduced to 28% when the Ishikawa classification was applied. The difference between these two classifications was statistically significant (χ-square test, $P < .01$).

The results of the localization of lesions in each etiology using the Ishikawa classification is shown in the lower part of Table 3. It was interesting that the anterior type accounted for 55% of cases with inflammation. In cases with tumors, the posterior type was relatively common and the whole type was observed more than any other etiology. Definitive characteristics could not be obtained for other etiologies because of the small number of patients. Because 69% of the total cases were unclassifiable, etiologic characteristics depending on the localization of lesions could not be considered in the Jefferson classification.

Table 2. Etiologies of Subjects

Etiology	No. of Cases
Inflammation	58
Tumor	56
Metastatic	15
Primary and extension from adjacent region	41
Carotid-cavernous fistula	22
Internal carotid-cavernous fistula	8
Dural arterio-venous malformation	14
Paranasal sinusitis	17
Intracavernous carotid aneurysm	9

Discussion

The structure of the cavernous sinus has been studied from various aspects, but all of these studies

Table 3. Comparison Between Jefferson Classification and Ishikawa Classification of Present Subjects

	Inflammation	Tumor	Carotid-cavernous fistula	Paranasal sinusitis	Intracavernous carotid aneurysm	Total*
Jefferson classification						
Anterior	9	7	0	1	1	18 (11)
Middle	5	12	2	0	0	19 (12)
Posterior	6	6	1	1	0	14 (8)
Unclassifiable	38	31	19	15	8	111 (69)
Total	58	56	22	17	9	162
Ishikawa classification						
Anterior	32	10	3	7	4	56 (35)
Middle	7	4	4	1	0	16 (10)
Posterior	12	15	4	3	2	36 (22)
Whole	1	8	0	0	0	9 (5)
Unclassifiable	6	19	11	6	3	45 (28)
Total	58	56	22	17	9	162

*Values in parentheses are percentages.

have been performed depending on macroscopic findings[3–6] alone. Miyazaki[7] examined the topographical structure of the cavernous sinus using frozen sections, but did not study the structure quantitatively. Ishikawa[2] analyzed the structures of the cavernous sinus stereotaxically in 30-μm serial sections of human cavernous sinus. As a result, he divided the cavernous sinus into three portions.

It has been considered that the cavernous sinus lesion was first reported by Adams[8] in 1869. He observed a patient who developed oculomotor, trochlear, trigeminal, and abducens nerve involvement with an intracavernous carotid aneurysm the size of a walnut on autopsy. In 1922, Foix[9] proposed the term "external wall syndrome of the cavernous sinus" and Jefferson[1] advocated the term "cavernous sinus syndrome" in 1938. Various syndromes similar to the cavernous sinus syndrome have been reported, including the orbital apex syndrome, superior orbital fissure syndrome, orbital floor syndrome, and petrous sphenoid syndrome. However, it is difficult to differentiate among these syndromes clearly, because they overlap each other.

Jefferson classified the cavernous sinus syndrome into three types; the anterior, middle, and posterior cavernous sinus syndrome based on trigeminal nerve involvement. However, when we applied the Jefferson classification to our patients, 69% of the total cases were unclassifiable. Therefore, this classification seems to have low specificity. In comparison with the Jefferson classification, unclassifiable cases accounted for only 28% in the Ishikawa classification. One reason for this difference in unclassifiable cases is that optic nerve involvement is considered in the Ishikawa classification. Foix[9] proposed that optic nerve involvement should be included in the definition of cavernous sinus syndrome. Godtfredsen[10] classified the cavernous sinus syndrome into the anterior type with optic neuropathy and the posterior type without optic neuropathy. However, van Overbeeke et al[11] opposed the inclusion of optic nerve involvement in the definition of cavernous sinus syndrome. The optic nerve is not located in the cavernous sinus; however, it passes close to the anterior portion of the cavernous sinus. As 40 of our 162 patients had optic neuropathy concomitantly with ocular motor nerve and trigeminal nerve involvement, we consider that optic neuropathy should be included in the definition of cavernous sinus lesions. Miller[12] proposed the concept of the spheno-cavernous syndrome in consideration of both opinions.

Another factor is the consideration of superior and inferior branch involvement of the oculomotor nerve. The oculomotor nerve separates into superior and inferior branches in the anterior portion of the cavernous sinus at 4.5 mm from the orbital apex. As the ratio of nerve fibers between the superior and inferior branches is 1:3.213 and the superior branch has fewer nerve fibers, it is suggested that the superior branch is more vulnerable than the inferior branch.[13] The Jefferson classification mentioned only paralysis of the superior branch of the oculomotor nerve. However, because isolated paralysis of the inferior branch was also observed in our patients, we believe it should be included in the definition of anterior cavernous sinus lesion.

Many of the unclassifiable cases under the Jefferson classification could be classified into the posterior type in the Ishikawa classification because of maxillary nerve involvement. For example, patients with isolated maxillary nerve involvement or with both maxillary and mandibular nerve involvement are unclassifiable in the Jefferson classification. However, they were classified as the posterior type in the Ishikawa classification. As the mandibular nerve does not extend into the cavernous sinus, it cannot be involved in a lesion localized within the cavernous sinus. When the lesion extends lateroinferiorly, the mandibular nerve may be involved. However, only 14 of our 162 patients had involvement of the mandibular nerve. In the Jefferson classification, the posterior type needs to have total trigeminal nerve involvement including the mandibular nerve, so it is expected that few patients will meet this criterion. Actually, only 8% of all our patients were classified as the posterior type by the Jefferson classification.

The oculosympathetic nerve leaves the internal carotid artery just before this artery bends anteriorly and then joins with the abducens nerve in the posterior portion of the cavernous sinus. At this point, only the abducens nerve runs in the medial part of the cavernous sinus away from its lateral wall. Therefore, in a posterior cavernous sinus lesion, disturbance of the oculosympathetic nerve and the abducens nerve may occur concurrently. These symptoms have been actually found in patients with intracavernous carotid aneurysms,[14] paranasal sinusitis,[15,16] and metastatic tumor.[17] Abad et al[18] reported that a combination of abducens nerve palsy and Horner's syndrome was a specific symptom of intracavernous carotid aneurysm. It seems to be one reason for the decrease in unclassifiable cases under the Ishikawa classification that a combination of abducens nerve palsy and Horner's syndrome is considered as the posterior type of lesion.

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Regarding the localization of lesions in each etiology using the Ishikawa classification, many patients with inflammatory disorders are included in the anterior type. Paranasal sinusitis has been suggested as a cause of the Tolosa-Hunt syndrome.[19] It is assumed that inflammation is likely to occur more often in the anterior portion of the cavernous sinus adjacent to the ethmoid sinus, which is the most frequent lesion site in paranasal sinusitis. On the other hand, the posterior type was prominent in patients with tumors, and the whole type was also more frequent in tumors than in any other etiology. Pituitary tumors and paranasal sinus tumors originating mainly in the sphenoid sinus are common and it is suggested that these tumors are likely to invade and extend throughout the entire cavernous sinus. No definitive tendency could be found in other etiologies, because of the small number of patients. These results indicate that some etiologies, such as inflammation and tumor, may be diagnosed by their characteristic clinical symptoms. Additionally, these results may provide important information for surgical approaches to tumors, paranasal sinusitis, and intracavernous carotid aneurysms. Because carotid-cavernous fistula is not a space-occupying lesion, the localization of its lesion cannot be determined. However, the Ishikawa classification enables us to determine which portion of the cavernous sinus is involved most severely.

It was concluded that the Ishikawa classification based on the analysis of serial topographical sections is clinically useful for identifying and classifying the localization of cavernous sinus lesions.

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