Orbital fine-needle aspiration biopsy in patients with cavernous sinus syndrome

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The authors report their experience with five patients presenting with cavernous sinus syndrome who, on computerized tomography (CT) studies, were shown to have a lesion simultaneously involving the cavernous sinus and a portion of the orbit. All patients underwent an orbital fine-needle aspiration biopsy (FNAB). A specific cytological diagnosis was made in three of the five patients. To obtain pathological diagnosis in the case of cavernous sinus tumors, invasive diagnostic procedures are sometimes necessary. Extension of lesions from the cavernous sinus into adjacent areas should be carefully looked for on CT scans. In the specific subset of patients with cavernous sinus tumors and simultaneous orbital involvement, orbital FNAB may provide a simple alternative to more invasive procedures. The limitations of the procedure are discussed.

KEY WORDS • cavernous sinus syndrome • orbital tumor • computerized tomography • fine-needle aspiration biopsy

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imultaneous ipsilateral paralysis or paresis of the third, fourth, and sixth cranial nerves, and occasionally of the oculosympathetic nerves and first or second division of the trigeminal nerve constitutes the cavernous sinus syndrome. It is not possible to clearly distinguish an isolated cavernous sinus lesion from one involving the superior orbital fissure. Anterior extension may lead to optic nerve involvement, and extension posteriorly from the cavernous sinus may also compromise the mandibular division of the trigeminal nerve. Venous congestion may lead to proptosis and lid edema. With or without pain, the ophthalmoplegia of the cavernous sinus syndrome is nonspecific, occurring with a variety of types of lesions. The possible etiology of this syndrome includes neoplasms, both primary and metastatic, carotid artery aneurysms, infectious and inflammatory processes, arteriovenous fistulas, and dural sinus fistulas. Radiological studies frequently help in characterizing the lesion. Computerized tomography (CT) scanning has become the most helpful method of studying lesions in the cavernous sinus. Nevertheless, a number of neoplasms and inflammatory processes remain indistinguishable by radiological assessment. For some lesions, medical or radiation therapy rather than surgical excision may be the preferred mode of treatment, but lack of a pathological diagnosis may preclude selection of the most appropriate treatment regimen. However, open biopsy of cavernous sinus lesions subjects the patient to the risks of general anesthesia and intracranial surgery.

Due to the contiguity of the cavernous sinus to the superior orbital fissure, tumors may involve both the cavernous sinus and the orbit. High-resolution CT scanning permits good delineation of masses and readily demonstrates orbital involvement if it is present. In spite of the absence of orbital pain or exophthalmos and even in the absence of optic nerve involvement, high-resolution CT scanning may demonstrate involvement of the posterior orbit.

In an attempt to reach a specific pathological diagnosis, orbital fine-needle aspiration biopsies (FNAB’s) were performed by one of us (T.L.S.) on five patients who presented with cavernous sinus syndrome and who had CT evidence of simultaneous tumor involvement in the cavernous sinus and the orbit. The technique has been utilized for orbital tumors but has not been specifically described in patients with the cavernous sinus syndrome.

Biopsy Technique

Orbital FNAB’s were performed as outpatient procedures. The patient was seated in an examination chair with a headrest. No anesthetic agent was administered. A No. 22 disposable needle 4 cm in length was attached to a 20-ml syringe, which in turn was attached to a pistol-type syringe holder. As described elsewhere the
equipment permits the surgeon to obtain strong aspiration pressure with one hand. Approach for biopsy of the tumor is based on the tumor's location as seen on axial and coronal CT scans. Ultrasound or CT guidance may be used, but is not necessary for biopsy of lesions outside the muscle cone. Once the needle is within the mass, aspiration is applied while the needle tip position is gently changed and angled. The needle is removed only after suction pressure has been released. The cytological specimen is fixed in 95% alcohol. If material is present for cell block, it is fixed in 4% formaldehyde. As has been stressed elsewhere, experienced physicians and technicians are required to perform the biopsy and immediately prepare it for cytological examination.

**Case Report**

A summary of our cases is presented in Table 1.

**Case 1**

This 55-year-old woman presented with a 2-year history of progressive horizontal diplopia and occasional deep right orbital pain. Her visual acuity was 6/6 (20/20) in each eye. Color vision was intact and symmetrical in both eyes. There was an evident abduction deficit on the right. Mild ptosis and miosis of the right upper lid were seen (Fig. 1) and pharmacological testing was compatible with a postganglionic right Horner's syndrome. No proptosis was present. There was hypesthesia in the distribution of all three divisions of the trigeminal nerve. Visual fields were normal bilaterally. Funduscopy was normal bilaterally, and the remainder of the neurological examination was also normal.

A CT scan demonstrated an enhancing lesion in the right cavernous sinus extending medially into the posterior orbit (Fig. 2). An orbital FNAB was performed. Cytological study showed well differentiated neoplastic
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epithelial cells, compatible with adenocarcinoma (Fig. 3). No primary site could be found on systemic metastatic work-up and otolaryngological evaluation. Focal external radiation to the right cavernous sinus and orbit led to resolution of diplopia. The patient remained asymptomatic for 1 year after treatment and then developed symptoms of diplopia. A follow-up CT scan demonstrated tumor persisting in the same location. Reevaluation at regular intervals has failed to reveal any other sites of involvement and the primary source of the adenocarcinoma remains unknown. Two years after presentation the patient is well except for diplopia due to her cavernous sinus-related cranial neuropathies.

Case 2

This 64-year-old woman experienced the sudden onset of oblique diplopia, a partial ptosis of the left upper lid, and decreased visual acuity in the left eye. She had a history of breast carcinoma and underwent a partial mastectomy 3 years earlier, which was followed by radiation therapy. There was a history of systemic hypertension, well controlled by medications. She was recently found to have diabetes mellitus.

Visual acuity was 6/6 (20/20) in the right eye and limited to hand motions in the left eye. The left globe was displaced downward and there was a partial ptosis of the left upper lid. Exophthalmometry measurements were 17 mm on the right and 20 mm on the left. Motility of the right eye was normal, while the left eye was immobile except for minimal abduction. The left pupil was unreactive and there was an inverse afferent pupillary defect on the left. Corneal and facial sensations were intact. Funduscopic examination showed pallid disc elevation in the left eye. Visual field testing was normal in the right eye. The left visual field was constricted with a large central scotoma. A CT scan documented an enhancing tissue-density mass in the left cavernous sinus, middle cranial fossa, and orbital apex.

A left orbital FNAB was performed. The specimen was sufficient to permit both cytological and histological evaluation. Findings were consistent with adenocarcinoma metastasis from the breast (Fig. 4). The patient...
was given external port radiation and tamoxifen. The left exophthalmos decreased. A right proximal humerus metastasis was found and was also treated with radiation therapy. The patient died 11 months later of metastatic breast carcinoma.

Case 3

This 59-year-old woman had been aware of proptosis of the left eye and of left facial pain for 4 months. She was seen in consultation for evaluation of a 2-week history of decreased visual acuity in the left eye. Her history was significant for adenocarcinoma of the breast 4 years earlier which had been treated with a right mastectomy followed by a 1-year course of chemotherapy. She had recently experienced weight loss.

On examination her visual acuity was 6/6 (20/20) in the right eye and limited to finger counting at 1 m in the left eye. There was 6-mm proptosis of the left eye. Extraocular muscle movements were full on the right, and on the left there was only a minimal abduction and adduction deficit. The pupils were of equal size, but the left pupil reacted sluggishly to light and exhibited an afferent defect. Left facial sensation was diminished in all three divisions. The left optic disc was pallid. The visual field of the right eye was normal, but only a small peripheral island of vision was present in the left eye. A CT scan showed an enhancing tissue-density mass involving the cavernous sinus, the anterior temporal fossa, and the lateral and posterior sections of the orbit on the left side.

An FNAB of the left orbit was performed. Cytological examination showed neoplastic epithelial cells consistent with adenocarcinoma. A systemic evaluation revealed the presence of metastatic disease in the left ischium and acetabulum as well. The patient was treated with external radiation. She regained full peripheral vision in the left eye, but a dense central scotoma persisted and visual acuity remained limited to finger counting. The left facial pain resolved, and the left proptosis decreased from 6 to 2 mm. Two years later the patient reported that she was in good health and that no further evidence of cancer was present on her most recent medical examination. She was receiving no treatment of any kind for her cancer. Central visual acuity remains poor on the left but her peripheral field is subjectively unchanged since termination of her radiation therapy.

Case 4

This 57-year-old woman presented with a 10-month history of right periorbital pain with progressive diplopia and ptosis of the right eye. Her medical history was unremarkable. At the onset of her visual symptoms she was evaluated elsewhere. Extensive workup, including skull x-ray films with attention to the superior orbital fissure and basal foramina, CT scanning, angiography, lumbar puncture studies, and ear, nose and throat examination, resulted in negative findings. The presumptive diagnosis of Tolosa-Hunt syndrome was made. A course of systemic steroids was started, with transient improvement in proptosis and lateral rectus function on the right. As steroids were tapered from 60 to 20 mg, the patient’s symptoms recurred and now she also noted some decrease in visual acuity. She was referred to us for further evaluation.

Visual acuity was limited to finger counting in the right eye and 6/6 (20/20) in the left eye. There was a 3-mm proptosis of the right upper lid, and a 3-mm exophthalmos on the right. Right eye ductions were absent except for intorsion and minimal abduction. Ductions of the left eye were full. Right facial sensation in the ophthalmic and maxillary divisions was decreased. Right optic disc pallor was present. The left visual field was normal, while on the right a large inferotemporal and cecocentral scotoma was demonstrated. A CT scan demonstrated an enhancing tissue-density lesion in the right orbital apex, cavernous sinus, and region posterior to the dorsum sellae.

A right orbital FNAB was performed. The specimen revealed lymphocytes suggestive of either benign lymphoid hyperplasia or possibly lymphoma. The patient was referred for further medical evaluation for possible lymphoma, and radiation therapy to the cavernous sinus was begun. Oral prednisone was also continued. Following radiation therapy, there was a decrease in right eye proptosis but no improvement in motility or visual acuity. Two weeks after completion of radiation therapy the patient died suddenly. An autopsy revealed the presence of a massive pulmonary embolus which was presumed to be related to a recent fall and bone fracture. A right intracavernous tumor was also found encasing the oculomotor nerve; this was interpreted as a histiocytic malignant lymphoma.

Case 5

This 71-year-old man was referred to us for evaluation of a right ophthalmplegia. One year previously he had sought treatment for vague symptoms believed to be sinusitis. At that time he was found to be anemic and a work-up was instituted elsewhere for occult malignancy. The work-up, including bronchoscopy, was negative. Three months later he developed pain on the right side of the forehead, decreased visual acuity in the right eye, and right-sided proptosis. He was admitted to another hospital and underwent further evaluation including barium enema, an upper gastrointestinal series, intravenous pyelogram, and further blood tests, all of which were negative. Shortly after his discharge from the hospital he developed herpes zoster in the distribution of the second division of the right trigeminal nerve. After resolution of the infection there was still obvious residual proptosis. The patient was also noted to have undergone personality changes and memory loss, and was found to be disoriented. He was thought to have poor vision in the right eye.

At the time of our initial examination, the patient’s
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TABLE 1
Summary of patients with cavernous sinus syndrome with orbital FNAB diagnosis*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs)</th>
<th>Sex</th>
<th>Signs &amp; Symptoms</th>
<th>Orbital FNAB Diagnosis</th>
<th>Treatment</th>
<th>Course</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>55, F</td>
<td></td>
<td>diplopia, facial numbness</td>
<td>malignant epithelial cells</td>
<td>external radiation</td>
<td>improvement, then recurrence of diplopia, which persists 2 yrs after presentation</td>
</tr>
<tr>
<td>2</td>
<td>64, F</td>
<td></td>
<td>diplopia, ptosis, decreased vision, history of breast cancer</td>
<td>malignant cells consistent with breast cancer (cytology &amp; cell block)</td>
<td>external radiation, tamoxifen</td>
<td>died of metastatic breast cancer 11 mos after presentation</td>
</tr>
<tr>
<td>3</td>
<td>59, F</td>
<td></td>
<td>ptosis, proptosis, decreased vision, facial pain, history of breast cancer</td>
<td>malignant cells consistent with breast cancer</td>
<td>external radiation</td>
<td>resolution of proptosis, return of peripheral visual field with remaining right central scotoma 2 yrs after presentation</td>
</tr>
<tr>
<td>4</td>
<td>57, F</td>
<td></td>
<td>diplopia, ptosis, periorbital pain</td>
<td>atypical lymphocytes (? lymphoma vs benign lymphoid hyperplasia)</td>
<td>external radiation, steroids</td>
<td>sudden death due to pulmonary embolus 2 mos after presentation; autopsy finding of intracavernous malignant lymphoma</td>
</tr>
<tr>
<td>5</td>
<td>71, M</td>
<td></td>
<td>diplopia, proptosis, decreased vision, headache</td>
<td>one group of dysplastic cells but insufficient for diagnosis after multiple biopsy attempts</td>
<td>none</td>
<td>patient refused further work-up; died 11 mos after presentation; no autopsy performed</td>
</tr>
</tbody>
</table>

* FNAB = fine-needle aspiration biopsy.

vision was limited to hand motions at 6 in. on the right and 6/12 (20/40) in the left eye. A 7-mm proptosis was measured on the right. The right pupil was fixed, while the left reacted normally to direct and near stimuli. Except for minimal torsion, there was a complete right ophthalmoplegia and complete right upper-lid ptosis. A right facial paresis was also evident. Facial sensation was decreased in all three divisions of the trigeminal nerve. Ocular motility and facial sensation were normal on the left. Fundus examination was normal on the left and unobtainable on the right because of the presence of a dense cataract.

A CT scan demonstrated the presence of tumor in the posterior orbital apex. A right orbital FNAB was attempted at that time without yielding any pathological specimen. A subsequent CT scan 1 month later showed increase in the size of the lesion as well as extension into the intertemporal fossa. Another FNAB was attempted, this time under direct CT monitoring. The needle was visualized within the lesion, and three separate aspirations were obtained. The lesion was of firm consistency and could not be readily aspirated. The cytological specimen consisted of fibrin and peripheral blood cells. One group of dysplastic cells was seen, but the specimen was thought to be insufficient for diagnosis. The patient refused more invasive biopsies or intervention and asked to be sent home. In spite of encouragement from his family he refused to undergo further tests or hospitalization. He died at home, and no autopsy was done.

Discussion

The use of FNAB for orbital disease has been described and popularized by Kennerdell, et al.7,8 Orbital FNAB is particularly useful in cases of epithelial tumors. We suggest that the use of this technique may have a particular indication in certain patients with cavernous sinus lesions. The advent of high-resolution CT scanning has made neuroradiological definition of intracavernous lesions quite possible. It is, nevertheless, true that even after complete medical and neuroradiological evaluation, including cerebral arteriography, there remain diagnostic dilemmas relating to neoplastic or inflammatory processes.

We suggest that on high-resolution CT coronal and axial views attention be given to possible orbital involvement by tumor. Such involvement is more likely to be found with proptosis and visual loss associated with optic nerve compression, but should be looked for even in the absence of any clinical signs or symptoms of orbital involvement. Hasso, et al.,9 reviewed CT findings in patients with cavernous sinus lesions. They divided the tumors into a benign and a malignant group. There were 59 patients with malignant lesions. Only two of the 59 patients had tumor limited strictly to the cavernous sinus. In the other 57 there was extension into adjacent structures such as the nasopharynx, orbits, sphenoid bone, paranasal sinuses, and posterior cranial fossa. Even without proptosis, and in the absence of visual loss or visual field defects, orbital involvement may be present. This was true in our Case 1. Surgical exploration of the cavernous sinus may be hazardous, and the outpatient use of orbital FNAB may yield a pathological diagnosis without the risk of general anesthesia, and without the morbidity associated with open surgical biopsy of the deep orbit or cavernous sinus.

The potential complications of orbital FNAB are the same as those associated with retrobulbar injections, such as retrobulbar anesthetic administration used with
cataract extraction. Complications of orbital FNAB in 50 patients reported by Kennerdell, et al., included six cases of orbital hemorrhages; these were described as mild and resolved spontaneously. Of the five patients reported in this paper, one patient (Case 5) had retrobulbar hemorrhage which resolved spontaneously and without sequelae. When performed by an experienced physician who is familiar with orbital anatomy, using the technique described (see Methods), the procedure is quite safe.

Several points can be made about our cases. In spite of a thorough work-up, no primary tumor focus was found in Case 1; the orbital FNAB provided a diagnosis that otherwise could not have been made without a more invasive surgical approach. In Cases 2 and 3, findings on FNAB were compatible with history of adenocarcinoma of the breast. The orbital FNAB was nevertheless a relatively noninvasive, low-risk procedure that helped rule out other inflammatory or malignant processes.

Multiple primary cancers do occur. Cahen estimated that 5% to 10% of patients surviving their first cancer may develop a second cancer elsewhere. Newell and Krementz found that women with initial breast carcinoma had statistically significant (greater than 5%) increases in incidence of second cancers. An additional point to be made in Case 3 is that FNAB, although primarily allowing cytological sampling, may occasionally yield a histological specimen, thereby making evaluation of the cell type even more accurate.

Case 4 demonstrates the usefulness but also the limitation of the orbital FNAB. The cytological specimen provided a means of narrowing the diagnostic possibilities to benign lymphoid hyperplasia versus lymphoma. The difficulty in distinguishing between these two entities has been described elsewhere. The biopsy in Case 4 did not permit a definite diagnosis but provided a guide-line for further medical evaluation. The autopsy findings confirmed definitely that a lymphoid process (in this case lymphoma) was present in the cavernous sinus and posterior orbit. Interestingly, the patient had cavernous sinus involvement as the presenting symptom of her lymphoma, similar to one of six patients reported by Kori and Mitsumoto, all of whom had histologically proven lymphoma involving the cavernous sinus. We agree with those authors that recognition is important for this potentially treatable disease.

Case 5 points out an obvious limitation of the procedure. In spite of multiple attempts at aspiration, no adequate specimen could be obtained because of the firm tumor mass. This problem has been described in lesions with a predominantly fibrous matrix where cohesion is strong and cellularity diminished. Failure to obtain an adequate specimen by FNAB does not preclude a repeat attempt or open biopsy, if deemed necessary for diagnosis.

In summary, we recommend that all patients with cavernous sinus syndrome have, as part of their neuroradiological evaluation, high-resolution axial and coronal CT scanning of their cavernous sinus as well as of their orbit, even in the absence of signs or symptoms of orbital involvement. Orbital FNAB is a relatively low-risk procedure, particularly when considering the alternative of open surgical biopsy of the deep orbit or cavernous sinus. In the specific subset of patients who have radiologically demonstrated cavernous sinus lesions with simultaneous involvement of the orbit, we recommend that orbital FNAB be considered for solid tumors if the pathological diagnosis is in question.

References