Section of Laryngology

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The Orbit in Relation to Rhinology

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Cavernous Sinus Thrombosis Revisited

My purpose is to discuss the problem of cavernous sinus thrombosis, from the standpoint of diagnosis, differential diagnosis, treatment and also the history of the disease entity. The problem of cavernous sinus thrombosis spans about one and one-half centuries, as the disease was first recognized as a pathologic entity in 1821. I have reviewed the history of the development of the disease and the various methods of treatment that have been utilized over the years, and as these facts are well recorded, I will not dwell upon them again. It is interesting to note, however, that the progress of medicine over the past century is to some small extent emulated in the approach to this disease entity. Late in the nineteenth century the disease was recognized as a catastrophic phenomenon from which virtually no patient could be expected to survive. In an attempt to find something that might be done to alter the morbid course of the disease, surgery was recommended and attempted. The results, of course, were no less fatal, but probably considerably more dramatic. Subsequently, with the development of the sulpher drugs in the 1930s, the first cures were reported. In the 1940s and 1950s, with the development of the antibiotic era, even more cures were reported. By 1960 the disease had become uncommon and the combination of the rarity of the disease with the even more uncommon cure culminated in what we now refer to as 'a reportable case'.

Thus, in 1960, I had the opportunity to review a case which had been treated by my father and his colleague, Dr Marshall Louis, which was subsequently published in the *Journal of the American Medical Association*. While case reports are not viewed as one of the most scholarly forms of medical writing, this particular report served as an initial inspiration which drew me out of the field of general surgery into the field of otolaryngology. It further served as an inspiration to use the tool of medical writing as a means of study, as I believe it is well recognized that the author of a medical paper always gets more out of it than the reader.

I mention these facts, as one might easily wonder why an individual would maintain an interest in cavernous sinus thrombosis over a period of 17 years when everyone knows that it is no longer a real clinical problem. I might counter with the comment that 25 years ago it was thought that the field of otolaryngology might cease to exist because antibiotics controlled infections and our specialty was based on the treatment of infections and their sequelæ. Today, obviously, infections are still with us, although we have thoughtfully added cancer and æsthetic surgery to our armamentarium on the off-chance that the ultimate antibiotic is forthcoming. My message today is that cavernous sinus thrombosis is still a problem. It is not a common problem, it does not have the universal mortality it once had, the mortality and morbidity can even be brought to reasonably acceptable levels; but still, if unrecognized, if unexpected, or if ignored, the onset of the disease is no less rapid, the progress no less catastrophic, and the outcome no less tragic.

As a means of emphasizing these points, I can recall the only case of cavernous sinus thrombosis in which I was ever consulted primarily as an expert witness. This involved a nationally known athlete who was beset with an upper respiratory tract infection and presumed sinusitis. The progression of his disease process and the symptoms which occurred, which seemed out of proportion to the physical findings, made the patient somewhat suspect as a malingerer in the eyes of the physicians and trainers who were involved in his care. His special status as an athlete, the concern

that he might miss scheduled competition, and the previously conceived diagnosis of a simple upper respiratory infection, all resulted in repeated trips to an emergency room by the athlete with failure on the part of his physicians to recognize the seriousness of his infection, the early signs of meningismus, and the ultimate danger of complications. The resultant case of cavernous sinus thrombosis was treated and the patient survived, although with permanent bilateral and total blindness. This type of case does not have to occur very often to engender a considerable respect for this disease process.

The diagnosis of this disease is based entirely upon the objective findings which are directly attributable to the pathologic anatomy of the disease process. The cavernous sinuses are bilateral in their occurrence and are connected by the posterior and anterior communicating sinuses. They are basically venous sinuses which receive the venous drainage from the face, principally the middle third of the face and periorbital and nasal areas. The sinuses are interlaced with septa which create a somewhat sieve-like effect, rendering lodgement of bacterial emboli or thrombi more probable, in much the same manner as cardiac valvular disease increases the risk of endocarditis. In short, the cavernous sinuses are a set-up for thrombophlebitis once a phlebitis or mycotic embolus is introduced.

Coursing through the cavernous sinuses on each side are the internal carotid artery and the third, fourth and sixth cranial nerves. Also, the upper two divisions of the fifth cranial nerve may be found just adjacent to the inner wall of the sinus.

The disease process may occur in one of three ways. Most common, in all probability, is the development of an abscess, cellulitis, or other infected source which leads to phlebitis of the veins draining the central portion of the face toward the cavernous sinus. Propagation of phlebitis and/or thrombophlebitis along these veins to the cavernous sinus results in a thrombophlebitis of the cavernous sinus which, due to the intercommunicating sinuses, rapidly becomes bilateral. The infectious process in a vascular space leads to severe toxæmia. The direct relationship between the cavernous sinus and the dura results in meningismus if not frank meningitis. The infectious process directly circling the internal carotid artery results in severe, profound retro-orbital pain, paresis of the third, fourth and sixth motor nerves and paræsthesia of the upper two divisions of the trigeminal nerve. Accompanying these findings are the ones that would be expected with complete occlusion of venous blood flow from the middle third of the face and the periorbital area: chemosis, proptosis, venous engorgement, occasional loss of vision depending upon the involvement of the orbital apex, and variable retinal signs depending again upon involvement of the orbital apex. As the disease becomes bilateral, so also do symptoms, accompanied by advancing and severe signs of toxæmia, meningitis, and several complications. The complications include multiple brain abscesses or systemic abscesses on the basis of intravascular propagation, pituitary gland dysfunction, cerebral œdema, and a usually rapid fatal course.

A second method of pathogenesis of the disease process is that of mycotic embolism. Here, usually through trauma, an abscess or infection in the middle third of the face may be damaged or injured in such a way as to cause a mycotic embolus which may lodge in the cavernous sinus and initiate a thrombophlebitis resulting in the same chain of events as listed above.

A third mechanism for pathogenesis would be a phlebothrombosis occurring primarily in the cavernous sinus or one of the veins directly associated with that structure. The so-called aseptic cavernous sinus thrombosis occurs in this manner, not infrequently after intracranial surgery or other manipulation during which a thrombus is created, with direct continuity to the cavernous sinus. The signs and symptoms of this disease process are far more subtle and include all of those listed above with the exception of signs of toxæmia or meningitis or primary infection. The basic difference is that of phlebothrombosis and thrombophlebitis. More on this later.

The treatment of this disease process should be characterized by two common denominators. These are aggressiveness and promptness. Nothing so alarms me as to see a patient in consultation who has been admitted to the hospital with an initial diagnosis of 'rule out cavernous sinus thrombosis', and who has not been placed on intensive antibiotic therapy, but rather is still, after many hours or several days, in the process of being 'worked up'. In my opinion, if a knowledgeable physician considers the possibility of cavernous sinus thrombosis seriously enough to record it as a possible diagnosis, he is obliged to take the initiative and treat the patient aggressively, if not for cavernous sinus thrombosis, at least to prevent it.

We know that the disease was universally fatal over the first century of its existance, or rather of its recognition. Of the cases recorded in the literature up to 1963, the mortality rate stood at 80%. Those that survived had a 75% chance of having residual and permanent neurologic deficit. Today, the results have improved vastly (Table 1). This is manifested in the reported cases from 1965 to the present; and in the fact that fewer cases are being reported, which implies either that fewer cases are being seen or that a cure is not so uncommon. Still, these results have been achieved by early recognition, aggressive therapy and, perhaps most im-

Table 1

Cavernous sinus thrombosis: prognosis

	No. of cases	*Time*	*Mortality*	*Morbidity*
Yarington (1961)	878	1821–1960	80%	75%
Clune (*see* Malik *et al.* 1970)	36	1963	28%	50%
Gupta (Malik *et al.* 1970)	7	1970	28.6%	—
Yarington (1977, this report)	28	1977	13.6%	22.7%

portant, preventing the problem in the first place. In my opinion, therefore, if the diagnosis is entertained, appropriate treatment should be underway while differential diagnostic possibilities are being considered.

The disease is usually caused by streptococcus, staphylococcus, or pneumococci. Anaerobic bacteria are not infrequently involved and certainly are an important consideration, the longer the process continues. In the debilitated patient or the patient who has been taking antibiotics, or in the hospital infection, the problem of penicillin-resistant staphylococci must be seriously considered; in fact, it is so common that the use of antibiotics primarily designed to combat this problem is recommended. Therefore, the primary choice of antibiotics should include a penicillin and/or a synthetic penicillin capable of combating penicillinase-producing staphylococci. These medications are usually administered intravenously in the highest recommended dosage. Chloramphenicol is the drug of choice in the initial treatment of possible anaerobic infection frequently seen in this disease process. The risk of complications from this medication is probably far less than the risk of inadequate treatment when the disease is suspected.

Considerable controversy exists concerning the efficacy of anticoagulant therapy in cavernous sinus thrombosis. With a full-blown infection, occlusion of the cavernous sinus, and bilateral involvement, anticoagulation is thought by some to be dangerous from the standpoint of intracranial bleeding, bleeding complications about the orbit, and propagation of infection throughout the body. On the other hand, there is apparently some evidence that heparin contributes to recannulization and dissolution of the thrombus. Certainly in the patient who is in obvious danger of or is developing the disease, anticoagulation would be of prophylactic or therapeutic value. In 1961 and 1963, I could find no statistical evidence that anticoagulation affected the outcome. Today I must say, however, that it is more often used than not: in the early and/or prophylactic stages of the disease it is to be recommended; while in the full-blown established disease there seems little to lose and much to gain by its use.

Ancillary forms of treatment, such as hypothermia for severe pyrexia, the control of pain, or the control of primary infections, are all self-evident and I will not enlarge upon them.

Other forms of therapy, such as the use of streptokinase or fibrinolytic enzymes, should be considered. Intravenous streptokinase has been used with success; low molecular weight dextran has been recommended for the prevention or treatment of thrombophlebitis in the past; and doubtless in the future many enzymatic agents will be available for consideration in the treatment of thrombophlebitis. I can only recommend consultation with an experienced vascular surgeon and consideration of currently used drugs which have been demonstrated by experience and use to be effective in similar instances.

In the differential diagnosis of cavernous sinus thrombosis certain other specific entities should be considered. Perhaps the most important aspect of differential diagnosis is the presence of severe toxæmia. Obviously an intravascular bacterial infection producing phlebitis and thrombosis will produce the severe, and, indeed, rapidly fatal infection previously described. Therefore, the absence of these findings should suggest either the absence of a cavernous sinus thrombosis or an aseptic form of this disease.

Aseptic cavernous sinus thrombosis is usually secondary to some mechanical or iatrogenic phenomenon which should be suggested by appropriate diagnostic studies or by history. The critical absence of life-threatening infection allows time for definitive diagnostic studies. Primary among these is orbital venography. Boniuk (1972) has pointed out the ocular manifestations of ophthalmic vein thrombosis, aseptic cavernous sinus thrombosis, and endocrine exophthalmos and myopathy. The former two diagnoses are not infrequently associated with mechanical obstructive pathology such as tumour or aneurysm, and carotid arteriography and jugular venography are frequently helpful.

In the debilitated patient suffering from chronic disease, or the patient on long-term chemotherapy or with an altered immune response, an unusual response to disease may be seen. Where the physical findings suggest cavernous sinus thrombosis in a patient who manifests signs of infection, but who is just 'not sick enough', an altered response or an unusual disease should be considered. My procedure would be to initiate treatment appropriate for cavernous sinus thrombosis, but to consider such things as mucormycosis. X-ray studies of the sinuses, aspiration with smear and culture, or biopsy are appropriate studies.

Another diagnosis which must be considered is pseudotumour of the orbit. This is usually diagnosed following a workup for orbital tumour and cavernous sinus thrombosis is ruled out by lack of toxæmia and by results of appropriate angiographic studies.

Of the inflammatory lesions which pose a diagnostic dilemma, orbital cellulitis is the most serious and acute ethmoiditis the most common. Each has the potential danger of producing a cavernous sinus thrombosis and therefore requires vigorous prophylactic treatment.

The diagnosis of orbital cellulitis is characterized by unilateral involvement, proptosis, chemosis, lid œdema, and limitation of movement due to œdema and congestion. The patient lacks the cranial nerve involvement (III, IV, V, VI), bilateral progression, and central nervous system signs of infection seen in cavernous sinus thrombosis. The treatment of both conditions, however, should be the same, and the clinical course and development of symptoms and signs rapidly clarifies the diagnosis.

Acute ethmoiditis in the child is usually more self evident in that extraocular motility is infrequently affected, and X-ray findings and history are usually helpful. Prompt response to appropriate therapy is the usual course.

Finally, a word about the management of the primary source of infection. Frequently, in abscesses or superficial infections of the nose or midface, inappropriate treatment or trauma is the initial precipitating event. Dental and sinus pathology are also frequently seen. Once the patient has responded to treatment and is 'on the mend', this primary pathology should not be forgotten. Definitive drainage or other appropriate measures should be instituted while the patient is still under appropriate antibiotic therapy.

In summary, cavernous sinus thrombosis is still with us. Patients now survive the disease more often than not, and therapy and diagnosis are reasonably clear cut. An increasing array of antibiotic-resistant bacteria have been balanced by an increasing army of antibiotics. The controversy over anticoagulation has not changed since reviewed by Parsons (1967). Ancillary measures remain more of value in diagnosis than in therapy. It is a disease primarily diagnosed by physical signs and symptoms, which requires prompt treatment. In our modern age of computerization and laboratory-based medical care, cavernous sinus thrombosis demands the diagnostic skill of the clinician, whose prompt ministrations should usually yield a favourable result.

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Lesions of Common Interest to the Ophthalmologist and the Rhinologist
Mr John Wright
(*Moorfields Eye Hospital, City Road, London EC1V 2PD*)

A Rhinologist's Thoughts on Thrombotic and Space-occupying Lesions of the Orbit
Mr R C Hughes
(*Royal Hospital, Wolverhampton*)