Hypopituitarism associated with cavernous sinus thrombosis

Report of a case

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Reports of pituitary insufficiency following intracranial sepsis are rare. Wetherbee and Turner (1963) described a patient with a bacterial meningitis who responded well to antibiotics, but who developed hypopituitarism five years later. In his original illness, this patient had shown erosion of the posterior clinoid processes and decalcification of the sella, which had returned to normal.

Weisman (1944) described a boy with a cavernous sinus thrombosis, probably secondary to an empyema of the lung, who died 24 days after the start of his illness and was found to have pituitary necrosis probably due to infarction.

Bouche, Guiot, Carrez, Cotin, and Comoy (1964) gave an account of four patients, all of whom had long histories of headache, who developed the clinical signs of cavernous sinus thrombosis with decalcification of the sella. Bouche and his colleagues drained the sphenoidal sinus in all these patients and obtained pus. In one woman they found an osteomyelitis of the sphenoid, and on removing the roof of the sella found that the pituitary had been destroyed and the sella was full of pus.

CASE REPORT

In March 1965, the patient, a housewife and part-time barmaid of 57 years, was admitted to hospital with a four-day history of increasing drowsiness, headache (both occipital and behind the left eye), fever, vomiting, and diplopia on looking to the left. Before this she had enjoyed good health apart from a liability to bronchitis. She did not often have headaches. Ten years previously she had had a hysterectomy. She had adopted two children but had none of her own.

On admission her temperature was 101°F and she was drowsy and disorientated. She was tender over the left frontal sinus and the left conjunctiva was injected. There were purulent spots around the mouth. Her pupils were unequal, the left being larger than the right, but both reacted to light. She had some proptosis of the left eye and on this side there was ptosis with limitation

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FIG. 1. March 1965. Lateral film of sella. There is extensive erosion of the floor of the sella and of the dorsum (small arrows). The sphenoidal sinuses (S.S.) are partially opaque due to thickening of the mucosa.

of upward, inward and outward movement of the eyeball. Both optic disc margins were blurred.

A clinical diagnosis of cavernous sinus thrombosis was made.

Her white cell count was 20,000/cu.mm with a neutrophil leucocytosis and her erythrocyte sedimentation rate was 54 mm/hr. Her cerebrospinal fluid contained 13 white cells, 10 of which were polymorphs. The electroencephalogram showed diffuse slow wave activity in both fronto-temporal regions. Radiographs of the skull showed erosion of the floor of the sella turcica with thickening of the mucosa in the sphenoidal sinus, probably due to chronic infection (Fig. 1). A swab from the spots around the mouth grew a penicillin-sensitive *Staph. aureus*.

She was treated with penicillin 10,000 u. intrathecally twice daily for three days and crystalline penicillin 1 mega unit intramuscularly four-hourly for two weeks, together with streptomycin 0.5 g intramuscularly twice daily for the same period.

FIG. 2. March, 1967. Lateral film of sella. The floor and dorsum have now fully reformed but there is residual irregularity and sclerosis. The sphenoidal sinuses are clear.

After a week her temperature had settled but she was still complaining of a severe occipital headache and her optic discs were still blurred. Bilateral carotid arteriograms at this time were normal.

Her recovery was slow but she was discharged home seven weeks after admission with an ophthalmoplegia and a moderate ptosis on the left, the radiological appearances of the sella being unchanged. Pituitary function tests were performed but, although urinary ketosteroids were at the lower limit of normality, nothing abnormal was otherwise found.

Six months later she began to complain of lethargy and a year later in May 1966 she was re-admitted with unequivocal myxoedema. She had cold intolerance, constipation, and a dry skin, and her ankle jerks showed delayed return. The protein-bound iodine was $1.6 \mu\text{g}/\text{ml}$ and the serum cholesterol $850 \text{ mg}\%$. Her electrocardiogram was typical of myxoedema. Her thyroid uptake tests showed a low radio iodine uptake which was markedly increased by T.S.H. Her electrolytes were normal but her glucose tolerance curve was flat. Her urinary ketosteroids were low (17 ketosteroids (17-KS) average 2 mg in 24 hr , and 17 hydroxy corticoids (17-OHCS) $6 \text{ mg}/24 \text{ hr}$) but her plasma cortisol was normal ($15.3 \text{ mg}/100 \text{ ml}$).

The adrenal gland responded well to stimulation with ACTH, the 17-KS excretion rising to $12 \text{ mg}/24 \text{ hr}$, and 17-OHCS rising to 60 mg in 24 hr . A metapirone test suggested inadequate pituitary reserve, in that after she had been given metapirone 0.75 g four-hourly for two days her 17-KS excretion was 4.3 mg in 24 hr and 17 OHCS 20 mg in 24 hr (Liddle, Estep, Kendall, Williams, and Townes, 1959).

The clinical response to this test was impressive. When she was given ACTH she looked more alert, had a better colour, and took off three cardigans. During the meta-

pirone test she replaced the cardigans and looked very miserable.

Treatment was begun with ACTH and triiodothyronine with considerable improvement. She is now maintained on cortisone 15 mg daily and thyroxin 0.1 mg daily, is feeling well, and is no longer clinically hypothyroid. Serial radiographs of the skull have shown that the sella has re-calcified. The sinuses are now clear (Fig. 2).

DISCUSSION

Classically, thrombosis of the cavernous sinus follows an infection on the face, the spread being via the deep facial vein to the pterygoid plexus which is connected by an emissary vein to the cavernous sinus. This would be a plausible explanation in this patient were it not for the decalcification of the sella which was apparent in the first x-ray examination of the skull which was undertaken four days after the beginning of her illness. It is difficult to attribute this to osteomyelitis spreading from an infection of the cavernous sinus of a few days duration, for osteomyelitis usually takes several weeks to become radiologically obvious.

Another possibility is that the patient had a long-standing sphenoidal sinusitis leading to osteomyelitis of the sella. There might then have been an acute exacerbation of this sinusitis infecting the cavernous sinus by direct spread (Fig. 3). The radiological appearances are in keeping with a diagnosis of chronic sphenoidal sinusitis and silent sphenoidal sinusitis is by no means unknown. The alternative suggestion of a symptomless osteomyelitis of the sella is less convincing.

It is of interest that in the case reported by Wetherbee and Turner (1963), the changes in the

FIG. 3. Coronal section through pituitary fossa and sella turcica (ST) illustrating relation of cavernous sinus (CS) to hypophysis (H) and the sphenoidal sinus (SS) (ICA—internal carotid artery).

sella were also found four days after the start of the illness. We feel that whatever the mechanism here, this patient is unique in having sphenoidal sinusitis, osteomyelitis of the sella (with radiological as well as clinical recovery), cavernous sinus thrombosis, and subsequent frank clinical, as well as biochemical, hypopituitarism.

SUMMARY

A woman aged 57 developed a cavernous sinus thrombosis from which she made a good recovery, although a year later she developed hypopituitarism. During her original illness, changes were found, on radiography, in the sella turcica and these later resolved.

The problem discussed here is whether the bone of the sella was attacked by pus above it, lying in the cavernous sinus and bathing the hypophysis, or whether the infection spread from a chronic infection of the sphenoidal sinus *via* an osteomyelitis of the

sphenoid to the cavernous sinus. In either case, pituitary insufficiency might be due to infarction from thrombophlebitis, or from direct infection.

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