Communications

Ischaemic ocular necrosis from carotid-cavernous fistula

Pathology of stagnant anoxic "inflammation" in orbital and ocular tissues

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Acute carotid-cavernous fistulae reduce arterial pressure in the ophthalmic artery and cause marked elevation of pressure in the orbital veins (Sanders and Hoyt, 1969). Together the effects of vascular dilatation, oedema, and slowing of orbital circulation impair clearance of cellular metabolites and lead to a stagnant type of anoxia that differs clinically and pathologically from the ischaemic effects caused by arterial insufficiency alone. These stagnant anoxic changes may be aggravated rather than cured by neurosurgical procedures designed to "trap" the fistula by arterial ligations and embolization (Walker and Allègre, 1956; Stern, Brown, and Alksne, 1967).

This report concerns the clinical course and histopathological findings in three unusual cases in which the haemodynamic effects of acute carotid-cavernous fistula led to stagnant anoxic changes in portions of the orbit and eye. These changes appear to have been intensified rather than decreased by the consecutive superimposition of the anoxic effects of treatment.

Hypoxia due to slowing or stagnation of blood flow to the eye and orbit may result in a severe reduction in the clearance of metabolites and blockade of enzyme synthesis with associated loss of function. Irreversible local tissue damage occurs when this type of hypoxia is prolonged or unusually severe and passes the critical point for vulnerable portions of the involved tissue (Robbins, 1967). When stagnant anoxia results from obstruction to venous outflow, or greatly increased venous pressure, a complex degradative process may ensure. The combined effects of anoxia due to stagnation of blood flow and tissue swelling due to vascular congestion and extravasation of fluid produce a form of tissue breakdown which differs from the hypoxic, anaemic, and histotoxic forms of anoxia in which the tissue destruction is almost solely due to ischaemia. The congestive and haemorrhagic components in these forms of anoxia are often absent. The following cases illustrate the devastating combined effects of consecutive stagnant and hypoxic anoxia on ocular and orbital tissues.

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Case reports

Case 1, a 42-year-old woman, developed severe left-sided retro-orbital and frontal headache which was continuous and not relieved by aspirin. There was no associated lid swelling or proptosis. Three days later she noted double vision when looking to the left. On the fourth day the lids of the left eye became swollen and during the next few days vision in her left eye began to fail. On the eleventh day she could see only vague forms with the left eye; the left globe was proptosed and the conjunctiva was chemotic. She also became aware of a pulsating swishing sound in her left ear.

Examination

When she entered to the University Hospital in Iowa City 13 days after the onset of disease, the left eye was blind and immobile, and protruded 13 mm. more than the right eye. The lids were swollen and tense with chemotic conjunctiva obscuring the globe (Fig. 1). The orbital tissues were intensely congested and firm. A loud pulse-synchronous bruit was heard over the left orbit and temple. The view of the ocular fundus was obscured by haemorrhage in the vitreous.

FIG. 1 Case 1. *Pre-operative appearance. Congested chemotic conjunctiva protrudes through the palpebral aperture. The lids are swollen and tense*

Carotid angiograms showed a large intracavernous internal carotid aneurysm with a carotid-cavernous fistula causing marked dilatation of the orbital veins.

Operation

Treatment consisted of craniotomy with clipping of the internal carotid artery proximal to the posterior communicating artery, embolization of the cavernous segment of the internal carotid artery with muscle, and ligation of the left internal and external carotid arteries in the neck.

Course

After surgery the patient had a complete right hemiplegia and was aphasic. The proptosis of the left eye receded and the oedema of the lids diminished, but at the same time the conjunctiva and lid margins became necrotic and began to slough. The cornea became oedematous and opaque, and then necrotic, and finally both the cornea and the surrounding sclera were transformed into a white purulent mass (Fig. 2, opposite).

Second operation

On the 10th day after the craniotomy, the anterior half of the globe was excised and the posterior half which contained the abscess was eviscerated. The necrotic portions of the lids were excised and the remaining skin was sutured together.

FIG. 2 Case 1. A week after trapping and intracarotid embolization procedure for carotid-cavernous fistula. The black crust is all that remains of the inferior conjunctiva. The lid margins are necrotic with sloughing of cilia. There is confluent necrosis of the cornea, sclera, and other structures of the anterior segment of the eye

Result

The patient made a slow but satisfactory recovery with eventual clearing of the hemiplegia and aphasia and healing of the tissues of the left orbit.

Case 2, a 39-year-old man, suffered multiple fractures including a basal skull fracture when he was struck by an automobile. He was transported in an unconscious state to the University of Iowa Hospital.

Examination

The initial examination showed brisk pupillary reactions to light, normal-appearing ocular fundi, and conjugate doll's-head movements. There were also multiple fractures of the legs and arms. Chemosis of the conjunctiva of the right eye was noted on the following day. On the 3rd day this swelling was more pronounced and reflex movements of the right globe were restricted in all directions. The next day the right pupil was slightly larger than the left but still reacted briskly to light. On the 7th day after the injury the patient was still unconscious and the right pupil was dilated (4 mm.) and failed to react directly or consensually to light. He now had moderate proptosis with marked erythematous swelling of the lids and conjunctiva. There was stromal and epithelial oedema of the cornea, and vitreous haemorrhage obscuring the view of the right ocular fundus. A loud pulse-synchronous bruit was now audible over the right eye. The patient's condition remained critical, the ocular signs intensified, and by the 12th day the swelling was so great that the lids could hardly be separated (Fig. 3A,B). The conjunctiva showed areas of pallid necrosis particularly at the limbus (Fig. 4A). The corneal opacity became greater and spread centrally until the cornea was almost white.

Angiographic studies demonstrated an internal carotid-cavernous sinus fistula supplied by the right internal carotid artery and branches of the right external carotid artery.

Operation

23 days after the injury the right internal carotid artery was clipped above the cavernous sinus, muscle emboli were introduced into the intracavernous segment of the carotid artery, and the internal and external carotid arteries were ligated in the neck.

Course

In the days that followed the orbital and palpebral tenseness and congestion slowly diminished (Fig. 3C,D). Although well protected from exposure, the cornea became necrotic and finally perforated (Fig. 4B,C,D), with sloughing of its central portions.

FIG. 3 Case 2. Acute palpebral and orbital oedema from traumatic carotid-cavernous fistula. (A and B). Two stages of swelling with cyanotic appearance and stagnant changes in orbital and ocular tissues. (C and D). Reduction in palpebral swelling and congestion after a trapping procedure with intra-cavernous embolization of the internal carotid artery

Second operation

The eye was enucleated on the 38th day after the injury.

Termination

The patient never regained consciousness and died 4 months later.

Case 3, a 75-year-old woman, who had always been in good health except for intermittent periods of hypertension, awakened in the night with a loud pulse-synchronous "hissing" sound in her head and a dull steady pain behind the right eye. By morning she felt tenseness in the right orbit. The right eye was immobile, proptosed, injected, and swollen, and the visual acuity was much diminished.

Examination

2 days later she was admitted to the University of California Hospital where the visual acuity was found to be 20/200 with a depressed field of vision in the affected eye and 20/400 in the left—a consequence of amblyopia ex anopsia from strabismus in childhood. The right eye was severely chemotic with congested conjunctival vessels; it protruded 5 mm. more than the left eye. The right cornea was clear but the pupil was mid-dilated and reacted only sluggishly to direct and consensual light stimulation. The right fundus was obscured by blood cells in the vitreous space. The media of the left eye were clear and the fundus showed evidence of long-standing hypertensive vascular changes. The pain continued unabated, the conjunctival chemosis increased, and the blood pressure was recorded as 210/110 in the right arm.

FIG. 4 Case 2. (A) Pre-operative changes in conjunctiva and cornea showing patchy necrosis extending to the limbus (arrow). (B) After trapping procedure and intracavernous carotid embolization. The lid oedema and erythema are greatly reduced but the cornea is completely opacified and the conjunctiva is sloughing. (C and D) Progressive necrosis, perforation, and sloughing of the cornea 7 and 9 days after operation

Treatment

She was given reserpine and intravenous dextran, and the blood pressure dropped to 130/100.

Course

Within several hours she lost all vision in the right eye.

Carotid angiograms showed a carotid-cavernous fistula supplied solely by the right internal carotid artery. On the 5th day of her illness an unsuccessful attempt was made to occlude the cavernous sinus by electrothrombosis, using a copper wire inserted through the superior ophthalmic vein.

Operation

8 days later a craniotomy was performed and an attempt was made to thrombose the right cavernous sinus directly, but this procedure also failed.

Termination

She died 2 days later without regaining consciousness.

Necropsy

There was massive infarction of the right cerebral hemisphere and a radiologically unsuspected carotid aneurysm which had distended the cavernous sinus and ruptured to cause the fistula. The aneurysm and the carotid artery were occluded by the intracranial surgical procedure and electrothrombosis of the cavernous sinus.

Histological findings and their significance

The fragments of tissue from the anterior half of the globe in Case 1 together with the eviscerated contents of the posterior segment exhibited severe structural breakdown with almost complete coagulative necrosis of all cellular and connective-tissue elements. Haemorrhagic areas interspersed with collections of acute and chronic inflammatory cells were observed, but there was no evidence of secondary infection. These changes were present to a lesser degree in the enucleated eye in Case 2, where the most severe histological abnormalities involved its anterior portions. The microscopic appearance was dominated by coagulative necrosis of the conjunctiva, episclera, sclera, and peripheral cornea associated with a fibrinopurulent exudate. This corresponded to the clinical appearance depicted in Fig. 4B, C, D. The central cornea was absent with adherence of the markedly necrotic anteriorly displaced iris to the posterior aspect of the peripheral corneal remnants. There was no histological evidence of secondary infection, but the potential for this complication in the devitalized exposed tissue in this situation is great. The anterior segment structures appeared relatively avascular in contrast with the dilated, congested, posterior choroidal vessels.

Earlier, less severe, and more instructive manifestations of anoxia were seen in the histological material in Case 3, in which both eyes together with their orbital contents were obtained at autopsy. In this specimen radio-opaque contrast medium had been injected into the right internal carotid artery during *post mortem* radiological studies of the carotid cavernous fistula. The material entered the vessels of the eye and orbit, where it could

FIG. 5 Section through a temporal leaf of the iris in Case 3, showing focal necrosis of midstroma, sphincter, and pigmented epithelium. The subcapsular epithelium of the lens subjacent to the sphincter is also destroyed. Haematoxylin and eosin. $\times 8$

be detected at gross examination as opaque white matter, and microscopically by its amorphous basophilic appearance. Unlike the findings in the first two cases, the cornea, conjunctiva, and episclera in Case 3 showed only minimal histological evidence of ischaemia manifested primarily by episcleral round-cell infiltration. There was focal necrosis of the sphincter and midstroma of the iris (Fig. 5). With one important exception, the histological appearance of the iris is strikingly similar to that observed in patients with acute angle-closure glaucoma, where compression of the iris root against the posterior surface of the peripheral cornea and trabecular meshwork results in vascular strangulation and subsequent ischaemic necrosis of the sphincter and midstroma. In Case 3, however, the anterior chamber angle was open without evidence of peripheral iris compression.

The anterior subcapsular epithelial cells of the lens in Case 3 immediately subjacent to the zone of necrotic iris exhibited degeneration, migration, and clumping. Similar changes have been observed in the lens epithelium after an acute attack of glaucoma (*Glaukomflecken*). It is possible that ischaemia serves as the common pathogenetic mechanism in both instances but admittedly these changes are non-specific and may occur after a variety of insults to the lens epithelium.

The posterior segment of the eye showed dilatation and congestion of the choroidal and retinal vessels without necrosis. The small vitreous haemorrhage observed clinically was not apparent in the specimen.

Acute segmental degeneration was observed in the anterior portion of the right optic nerve of Case 3 (Fig. 6). This degeneration differed from that observed in Schnabel's cavernous degeneration in several respects. Cavernous degeneration usually occurs in association with glaucoma and affects the optic nerve just behind the lamina cribrosa. It is characterized by the presence of hyaluronic acid, presumed to be derived from the vitreous, which partially replaces the degenerated optic nerve fibres. Macrophages are not seen. In contrast, the zone affected in Case 3 lay further back in the nerve (occupying a 3-mm. zone starting 7 mm. behind the sclera) and did not contain hyaluronic acid (AMP

FIG. 6 Cross-section of optic nerve in Case 3, showing acute segmental degeneration of nerve bundles on right. Haematoxylin and eosin. $\times 8$

stains were negative), and macrophages were present. These are the histological components of an early infarct, and are apparently related to focal anoxia rather than the effects of increased intraocular pressure.

Ocular immobility was a clinical feature in all three cases. Histological examination of the muscles of the affected eyes in Cases 2 and 3 showed diffuse infiltration with chronic inflammatory cells without evidence of ischaemic necrosis. Scattered collections of round cells were noted throughout the orbit, particularly in areas containing orbital fat. Presumably, the ophthalmoplegia recorded clinically in all three cases was in part mechanical (swelling) and in part due to metabolic impairment of the neuromuscular apparatus. The term necrosis suggests that evolutionary morphological changes have occurred within affected cells. They do not occur suddenly. Ultrastructural and biochemical studies (Majno and Palade, 1961) have shown that cells lose function and die biochemically before they exhibit light-microscope evidence of morphological change. Ultrastructural studies were not performed in the foregoing cases, but light-microscope examination suggests that a spectrum of degradative changes has occurred. Tissues rendered anatomically more vulnerable by their limited vascular supply appear to show earlier and more severe morphological consequences of ischaemia than do such tissues as the extraocular muscles.

Conclusions

The catastrophic ocular complications of carotid-cavernous fistulae described in this report, while extraordinary in degree, underscore our continuing inability to manage effectively the acute, severe orbital effects of this disease. These effects include reduction in arterial pressure from the arteriovenous shunt and elevation of venous and capillary pressure with resulting vascular congestion, tissue oedema, and stagnant anoxia. Intra-orbital oedema and congestion were extreme, and moderate to severe hypoxic signs were evident clinically in most of the orbital and ocular tissues before surgical intervention. Carotid ligation and trapping procedures in Cases 1 and 2, while lowering orbital venous pressure, also lowered critically the ophthalmic perfusion pressure in the tense retro-orbital space, and thus superimposed anoxic anoxia on stagnant anoxia. Pharmacological depression of blood pressure from 220/160 to 130/100 by reserpine in the elderly hypertensive patient in Case 3 may have been the deciding factor responsible for infarction of the optic nerve, a histological finding which has not been documented previously in cases of carotid-cavernous fistula. Intracranial obliteration of this fistula (by electrothrombosis of venous channels entering the orbit from the cavernous sinus) would not have been attempted if the irreversible nature of her blindness had been recognized.

Until a satisfactory surgical procedure is devised for closure of the arteriovenous fistula in the cavernous sinus, and for restoration of normal pressure and flow in the ophthalmic artery, the severe functional and organic changes exemplified in this report will continue to be a potential ocular and orbital hazard of these fistulae.

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