Orbital Hemangiopericytoma

Review of the Literature and Report of Four Cases*

DAVID N. BROWN, M.D., COLIN S. MCCARTY, M.D., AND EDWARD H. SOULE, M.D.
Sections of Neurologic Surgery and Surgical Pathology,
Mayo Clinic and Mayo Foundation, Rochester, Minnesota

Stout and Murray,21 in 1942, first described the hemangiopericytoma and demonstrated by tissue cultures17,21 that the cell of origin was the capillary pericyte of Zimmermann. As described by Zimmermann,22 the pericyte is a specific type of cell related closely to smooth-muscle cells but having no contractile fibers. Included in the initial report of Stout and Murray was a case of hemangiopericytoma arising intra-orbitally and extending into the orbit, and in a subsequent report by Stout20 2 more cases of orbital hemangiopericytoma were added to the literature, one starting in the ethmoid sinus and invading the orbit and the other beginning in the subcutaneous tissue over the middle of the infraorbital ridge. In the latter case, a single surgical procedure was performed; in the other multiple operations were done. In 1955, Goodman8 and Fox5 almost simultaneously reported the first hemangiopericytoma that was primary in the orbit; these patients also underwent multiple surgical procedures. Since then only 3 more orbital hemangiopericytomas have been reported,9,10,19 1 of them occurring in a child.10 All of these tumors were treated surgically by anterior orbitotomy, and 2 of them promptly recurred. MacCarty and Brown,13 in a report on 40 children with orbital tumors that were removed by the transcranial approach, did not list any hemangiopericytomas.

The following case reports involve hemangiopericytomas arising in the orbit and removed transcranially. Two of these patients had previously undergone operation by the anterior approach.

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Report of Cases

Case 1. A 63-year-old man was first seen in February 1960, at the age of 60, with a history of unilateral exophthalmos for 26 years. In 1954, a diagnosis of orbital tumor had been made elsewhere; the patient had refused operation but had received radiation therapy resulting in some recession of the protruding eye but never to normalcy. The proptosis began to increase in January 1959. In 1960 visual acuity was 20/70 on the left and 20/20 on the right. Hertel exophthalmometric measurements were O.D. 16 mm. and O.S. 25 mm. There was grade 1 paresis of ocular rotation in the left eye. The fundi were normal. Shistz tension was 14.6 in each eye. Visual field was normal in the left eye but there was a scotoma in the right eye. Roentgenograms of the skull taken elsewhere showed enlargement of the left orbit, and a left carotid angiogram revealed a highly vascular spherical tumor behind the globe. The patient was unwilling to accept the risk of visual loss in the affected eye that could possibly arise secondary to operation and was therefore given a course of radiation therapy, which had no effect.

The patient returned to the Mayo Clinic in April 1963, at age 63, because of further increase in proptosis, pain in and around the eye, and gradual loss of vision to complete blindness in the left eye.

Examination revealed a pulsating exophthalmos; a blind left eye with normal visual acuity on the right; grade 2 limitation of ocular movements on the left; Hertel exophthalmometric measurements of O.D. 18 mm. and O.S. 32 mm.; Shistz tension of O.D. 10.2 mm. and O.S. 15.9; negative funduscopic findings; and unchanged visual field of the right eye. Laboratory investigation was noncontributory.

A left carotid angiogram revealed a vascular tumor in the left orbit with feeding vessels from the internal carotid system and from an enlarged ophthalmic artery (Fig. 1).

Left frontal craniotomy and left blepharorhaphy were performed. The roof and the lateral wall of the orbit were very thin. The tumor, which appeared in the superior lateral aspect of the globe, was entered by many large vascular channels, and it measured 4.5×3×3 cm. The mass was removed totally (Fig. 2).
Postoperative course was uneventful, and the patient was dismissed 6 days after operation. The visual acuity in the left eye improved to 20/200 and 20/70 with a pinhole, remaining 20/20 in the right eye. Fundi were normal, although the left disk might have been a little lighter in color. Hertel measurements were O.D. 17 mm. and O.S. 26 mm., and rotations had returned to normal. The visual field of the left eye exhibited a temporal and central scotoma to the 2-mm. white bead at 1 meter and was full to the 10-mm. bead at 1 meter; the visual field of the right eye was unchanged.

Case 2. A 36-year-old woman had come to the ophthalmologic section in March 1947, at the age of 21, with the complaint of painless swelling of the left upper eyelid for 18 months. At that time, examination revealed that the globe was pushed downward, and a rather irregular, freely movable mass, measuring about 1×2 cm., with a wormy feeling to palpation, was present in the upper temporal portion of the orbit just beneath the orbital rim. Exophthalmometric readings were O.D. 19 mm. and O.S. 21 mm., and fundi were normal, as were the visual fields.

Subtotal removal through an anterior orbitotomy was performed by an ophthalmic surgeon. The tumor extended deeply into the muscle cone, and the posterior limits of the tumor could not be defined. The mass measured 2×3×4 cm.

The pathologic diagnosis at that time was malignant hemangioendothelioma, and a postoperative course of radiation therapy was administered.

The patient returned in May 1959, because of recurrence of the mass in the left upper lid.

A large mass was palpable, being movable anteriorly but fixed deeply. Palpebral fissures measured O.D. 9 mm. and O.S. 6 mm.; Hertel exophthalmometric readings were O.D. 16 mm. and O.S. 17 mm.; and extraocular movements were normal. There was change in the left eye indicative of early cataract, but fundi and visual fields were normal. Orbital roentgenograms were negative. It was felt that nothing more should be done at that time.

The previous pathologic diagnosis was amended to cellular hemangioma.

The patient returned again in April 1961, because of marked progression of the swelling of the left lid. The mass was now approximately 15×12 mm.; the left globe was 5 mm. lower than the right; palpebral fissures measured O.D. 10 mm. and O.S. 2 mm.; and Hertel exophthalmometric measurements were O.D. 17 mm. and O.S. 25 mm. Radon seeds were inserted, but the swelling again worsened in the fall of 1961.

The patient returned to the ophthalmologic section in February 1962, because of further swelling, but Hertel measurements were unchanged. There was an increase in the denseness of the posterior subcapsular cataract of the left eye. It was felt that further radiation therapy

![Fig. 1. Visualization by angiography of intraorbital hemangiopericytoma by means of the subtraction read-out technic.](image1)

![Fig. 2. Tumor in superior lateral aspect of globe, 4.5×3×3 cm., was entered by many large vascular channels.](image2)
would be of no help. Laboratory investigation was noncontributory. Films of the skull showed a large soft-tissue mass in the left orbit, containing radon seeds. No definite bony destruction of the orbital roof was present. A left carotid angiogram was negative.

Left frontal craniotomy and left blepharorhaphy were performed; after removal of the orbital roof and incision of Tenon's capsule a large red vascular tumor overlying the globe and lying in the superior lateral side of the orbit was removed together with some muscle that had to be sacrificed.

The pathologic diagnosis was hemangioendothelioma, and reexamination of the previous surgical specimens resulted in the same diagnosis.

Postoperative course was uneventful, and the patient was dismissed on the 8th postoperative day. Extraocular movements of the left eye were depressed in all directions, and ptosis, +3, was present. Visual acuity and fundi were unchanged. The patient was last heard from in July 1963, at which time there was no evidence of recurrence of the tumor.

Case 3. In March 1941, a 27-year-old woman was first seen in the ophthalmologic section because of painless unilateral proptosis of 3 years' duration and decreased vision for several weeks in the right eye. A diagnosis of thyroid disease had been made elsewhere 1 year before, and she had received a course of radiation therapy.

Examination revealed that extraocular movements were limited only on upward rotation; no bruit or thrill was present; external examination gave normal results; Hertel exophthalmometric readings were O.D. 28 mm. and O.S. 16 mm.; and funduscopic revealed papillodema on the right and a normal disk on the left. Routine laboratory studies were noncontributory, and a diagnosis of thyroid disease was ruled out. Roentgenograms of the skull and optic canal were normal.

A tumor, measuring \(3 \times 2.5 \times 2.5\) cm., lying to the temporal side of the optic nerve and behind the globe, was removed by the Krönlein operation. The optic nerve was normal.

The pathologic diagnosis was highly malignant hemangioendothelioma.

Postoperative course was uneventful, and the proptosis and papillodema receded.

The patient returned to the ophthalmologic section in November 1944, because of increasing proptosis and a marked decrease of vision in the right eye. Hertel measurements were O.D. 24 mm. and O.S. 15 mm. Films of the skull were normal.

Through an anterior orbitotomy an encapsulated tumor, measuring \(1.5 \times 1.0 \times 1.0\) cm., was removed from the superior lateral aspect in the posterior third of the right orbit.

Postoperatively, there was complete ptosis, and the nerve head was white.

The patient returned again in April 1945, because of increasing proptosis associated with pain, nausea and vomiting.

Enucleation of the right eye and subtotal exenteration of the orbit with application of radon seeds were performed. The posterior half of the orbit was filled with a tumor.

The patient returned once more in November 1945, because of rapid deterioration of vision in the left eye over a 2-week period. Visual acuity was 3/60. Visual-field examination revealed a temporal hemianopsia. Results of external and funduscopic examinations were normal.

A right transfrontal craniotomy was performed with total removal of the intracranial tumor up to the optic foramen. The right optic nerve was divided and removed, but the optic canal was not opened for fear of making a communication from the cranial subarachnoid pathways into the open orbit.

The pathologic diagnosis, including that for the previous surgical specimens, has been amended to hemangioendothelioma.

Postoperative radiation therapy was administered, and the patient was dismissed on the 37th postoperative day.

Death occurred in March 1946.

Case 4. A 50-year-old woman came to the ophthalmologic section in January 1954, because of unilateral exophthalmos in the right eye of several weeks' duration.

Examination revealed weakness of upward rotations, grade 2; normal visual acuity; normal fundi and visual fields; and Hertel exophthalmometric measurements of O.D. 23 mm. and O.S. 17 mm. Neurologic findings were normal. The patient was thought to have a hyperophthalmopathy of Graves' disease. Clinically, she was euthyroid; a small, firm thyroid was palpable. The basal metabolic rate was +2 per cent, and protein-bound iodine measured 5.7 \(\mu\)g per 100 ml. of serum; further laboratory results were noncontributory. Roentgenograms of the skull and optic canals were negative. Treatment with Lugol's solution was prescribed and the patient was dismissed.

The patient returned in October 1954, because of a further increase in proptosis and severe chemosis and periorbital edema on the right. Further paresis of the extraocular movements was present. Hertel measurements were O.D. 30 mm. and O.S. 15 mm.

In view of the progress of the exophthalmos in spite of therapy, decompression of the orbit by the transcranial route was performed. At operation, the roof of the orbit appeared vascular and thinned out, and when the periorbita was incised
a tumor was found which was thought at first to be a meningioma. Most of the tumor was removed.

The pathologic diagnosis was malignant hemangioendothelioma. Review of these slides shows the growth to be a hemangiopericytoma.

The patient was given a heavy dose of radiation therapy postoperatively, and at the time of dismissal the Hertel measurements were O.D. 16 mm. and O.S. 18 mm.

However, she returned in March 1955, with glaucoma in the right eye. Control could not be obtained with medical management, and therefore in April evisceration of the right eye was performed.

The patient returned again in May 1963, because of tenderness about the right antrum. Roentgenograms revealed destruction of the bony wall of the antrum and a soft-tissue mass in the antrum. Biopsy revealed fibrosarcoma, grade 3. Microscopic sections of this tissue and the previous surgical specimens revealed them to be different tumors, and the question was raised whether the present tumescent growth might be secondary to the massive radiation therapy received previously.

Radical resection of the upper jaw and further exenteration of the orbit were performed.

The postoperative course was uneventful, but the patient returned in October 1963, because of bleeding in the orbital cavity. A large red mass was seen growing from the dura mater covering the frontal lobe. Removal of the dura mater was not attempted, because of the danger of meningitis. In spite of the questionable value of further radiation and of the risk involved, the patient at this time is receiving radiation therapy.

Pathologic Features of Hemangiopericytoma

Grossly, the tumor is solid and usually well encapsulated, and it resembles closely a meningothelialomatous or fibroblastic meningioma. There are, however, no constant gross features to aid in its diagnosis.

The microscopic features, by the use of hematoxylin and eosin and reticulin stains, are diagnostic, even though the tumor may vary somewhat in different areas (Figs. 3 to 8). In general, the tumor is characterized by closely packed, twisted, and deformed cells, the nuclei of which vary from round or ovoid to elongated spindle shapes, forming swirls
and frond-like projections in the intervascular spaces. These swirls and fronds compress and distort the multitudinous vascular channels. Characteristically, the tumor cells are oriented around blood vessels and fill the spaces between them, each pericyte or cluster of pericytes being enclosed by fibers of reticulin. The tumors in many instances may be conspicuously vascular; in other instances the blood vessels may be collapsed or slit-shaped or appear as nonpatent vascular buds barely suggested by their elongated endothelial cells, which in all instances are entirely normal in appearance. Only a single layer of endothelial cells lines the vascular channels. A stain for reticulin is necessary to bring out the characteristic arrangement of tumor cells lying entirely outside the vascular sheath of blood vessels. A study of intracranial hemangiopericytomas seen at the Mayo Clinic was carried out in an effort to grade the tumors on a histologic basis, the grading being done in the histologic degree of malignancy and the amount of formation of reticulin. The gradation had some value in determining prognosis, but the series was not large enough or the follow-up period long enough to permit a statistical analysis.

**Differential Diagnosis**

Hemangioendotheliomas and hemangiomas may be solid grossly but usually are cystic, whereas the hemangiopericytoma is solid. Microscopically they may imitate the hemangiopericytoma in hematoxylin and eosin stains because the lining endothelial cells are often flattened, the surrounding proliferating cells are often rounded, and lipoid-containing cells usually are present. However, by means of silver stains the reticulin will be seen to enclose both the flattened and the rounded cells, indicating that they are endothelial cells, while in the hemangiopericytoma the mantle of rounded cells will be outside the vascular sheath and will have in most instances a fine meshwork.

![Fig. 5](left). Case 1. Detailed view of plump, spindle-shaped pericytes, demonstrating their arrangement about small capillaries. An occasional mitotic figure was found in the sections. Hematoxylin and eosin, X350.

![Fig. 6](right). Case 4. Loosely arranged plump pericytes associated with numerous capillary vessels that exhibit an unusually prominent wall. Hematoxylin and eosin, X165.
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Fig. 7 (left). Case 4. Cellular area of tumor shown in Fig. 6. The plump, closely packed cells have compressed occult capillaries. Hematoxylin and eosin, X350.

Fig. 8 (right). Case 4. Moderately undifferentiated fibrosarcoma that arose in the postirradiated area of the orbit and maxilla 8½ years after irradiation. Hematoxylin and eosin, X175.

of reticulin around individual cells.

Meningioma may be difficult to distinguish from hemangiopericytoma on the basis of tissue stained with hematoxylin and eosin. However, intercellular reticulin is not present between the cells of the meningotheliomatous meningioma. The angioblastic meningioma of Cushing and Eisenhardt and the hemangiopericytoma of Stout are probably identical tumors.²,¹²

In essence, there are 3 outstanding histologic features of the hemangiopericytoma: (1) perivascular patterns of growth of the tumor; (2) pattern of reticulin showing the tumor cells to be outside the vascular sheath and enclosed by the reticulin; and (3) the presence of normal endothelial cells in the great proportion of blood vessels.

Comment

Hemangiopericytoma of the orbit is a relatively rare tumor, as is evidenced from the paucity of reports in the literature. However, because of the ubiquitous distribution of capillaries, the neoplasm occurs in many sites throughout the body, most commonly in the soft tissues¹,¹⁴,¹⁷ but also intraspinally,¹⁸ in the meninges of the brain,¹² and in the brain itself.²,¹⁶ The pathogenesis of the hemangiopericytoma is somewhat obscure. It may be considered established that the hemangiopericytoma is the result of an abnormal proliferation of cells normally present in the external mural layer of capillaries, whether they are pericytes specifically or not.

The clinical importance of the hemangiopericytoma lies in its potentially malignant behavior as demonstrated in some instances by the rapidity of recurrence and by the infiltrative growth. In the 4 cases reported plus the 8 in the literature, multiple operative procedures for recurrent hemangiopericytoma were carried out in 8. Distant metastasis was not experienced in our 4 patients, although the death of 1 patient
resulted from intracranial extension via the foramen of the optic nerve. Radiation therapy and implantation of radium had little or no effect on the tumor, although 1 patient (Case 1) enjoyed a lengthy period of freedom from increase in the size of the tumor. Most reports on hemangiopericytomas make little reference to irradiation and its effect. Radiation therapy is used when surgical removal is incomplete or when the neoplasm is inoperable and palliation is desired. Kent and Mujahed and associates expressed the belief that radiation therapy is effective; because of the high incidence of recurrence, they advocate its use in the postoperative period. Kauffman and Stout, however, stated that this form of therapy was, at best, only palliative. Friedman and Egan concluded that the lethal dose in soft-tissue hemangiopericytoma is high as did Fink and Oberman, but the latter believed that a dose of the magnitude advocated by Friedman and Egan was too likely to cause damage to tissue and that the evidence that such a dose would be tumoricidal was insufficient. Postirradiation sarcoma of bone, while admittedly rare, must be considered as a late complication of irradiation (Case 4). The treatment of choice is surgical excision.

Evaluation of Orbital Tumors

Although the diagnosis of an orbital tumor can often be made with relative ease, the nature of the tumor is often unknown until the lesion has been examined microscopically. At the Mayo Clinic the evaluation of masses within the orbit is the primary responsibility of the ophthalmologist. The best surgical approach to such tumors often lies within the realm of the neurosurgeon, and thus the problem becomes one of joint responsibility. Vascular tumors of the orbit are the tumors occurring most commonly, and a presumptive diagnosis often can be made before operation. Such a diagnosis often is aided by roentgenography. Routine roentgenograms are used in the search for an orbital tumor, augmented by views of optic canal and orbital views, basal views, and occasionally tomograms. Orbital pneumography has rarely contributed to our knowledge of intracranial tumors. Pneumoencephalography and angiography usually are used to detect intracranial extension of an orbital tumor. In recent years, however, angiography has been of increasing value in outlining vascular tumors in the orbit (Fig. 1a). Recently Holman and Bullard described the "subtraction read-out technic" in the analysis of various roentgenographic studies using contrast media. This technic results in the "reading-out" of overlying bone and soft tissue which often obscure the tumor; this provides more detail of the shadows of the contrast medium and facilitates the study of fine vessels and tumor stains (Fig. 1b).

Summary

Four cases of intraorbital hemangiopericytoma removed by the transcranial approach have been presented, together with a review of the literature. The outstanding histologic features of the tumor are as follows. The tumor cells are oriented around blood vessels and fill the spaces between them. Staining for reticulin reveals that the cells are outside the vascular sheath and that each pericyte or group of pericytes is enclosed by reticulin. The endothelial cells of the blood vessels are normal in the great majority of vessels.

The clinical importance of the hemangiopericytoma lies in its potentially malignant behavior as demonstrated in some instances by the rapidity of recurrence and the infiltrative growth. The treatment of choice is surgical excision of the tumor.

References


