AMYLOID TUMOURS OF THE ORBIT*

BY

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THE complex of diseases known as amyloidosis is characterized by the accumulation of a peculiar structureless material in the walls of capillaries and arterioles, and in the surrounding tissues. The aetiology is obscure, but is apparently related to a disturbed metabolism which results in the deposition of a protein material rich in sulphated mucopolysaccharides. Several varieties of the disorder are recognized, but as yet there is no satisfactory classification of its categories. Systemic amyloidosis may be primary or secondary. The primary type may occur either in a familial or a sporadic form; secondary systemic amyloidosis may complicate other diseases, as for example, multiple myeloma. Localized amyloid tumours may follow chronic inflammation and destruction of tissues such as that occurring with trachoma, but also may arise without known antecedent.

In ocular structures, amyloid tumours of the lid and conjunctiva have been reported with sufficient frequency that they may no longer be considered ophthalmic curiosities (Elles, 1945; Ashton and Rey, 1951; Agarwal and Shrivastav, 1958; Mathur and Mathur, 1959; Hameed and Nath, 1960; Guerri and Wiesinger, 1960; Picó, 1961; Richlin and Kuwabara, 1962; Madangopal, 1962; Behal, 1964; Stansbury, 1965). In the files of the ocular pathology department at this hospital (representing the accessions of the past three decades) there are twelve cases of amyloidosis involving the conjunctiva, nine of which were verified with special stains. In nine of the twelve cases there was no known antecedent, and in the other three a history of repeated pyogenic conjunctivitis over a period of several years was obtained.

Until recently, there have been no cases of amyloid tumours of the orbit in our files, and indeed, such an occurrence seems to be extremely rare; for this reason, the two cases which have been recognized at this institute are being placed on record. Correspondence with authorities at the Registry of Ophthalmic Pathology of the Armed Forces Institute of Pathology, Washington, D.C., indicates that there are no known similar cases on record there.

Information regarding amyloidosis of the orbit in the ophthalmic literature is scant. Falls, Jackson, Carey, Rukavina, and Block (1955) reviewed the world literature dealing with hereditary primary systemic amyloidosis, and reported six additional cases; they noted that bilateral exophthalmos may occur among the ocular signs. Handousa (1954) described the case of a man with proptosis of thirteen months' duration who proved to have localized intra-orbital amyloid, and Coats (1915) reported a unique instance in which amyloidosis of the conjunctiva had spread to the orbital tissue and dural sheath of the optic nerve.

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Case Reports

Case 1.—A 27-year-old woman of Chinese parentage complained of a swelling in the outer portion of the left upper lid which had been present for 2 years (Fig. 1), and which had recently enlarged slightly, causing a stinging sensation. General health and past medical history were unremarkable. Ocular examination revealed a subcutaneous mass in the region of the lacrimal gland, the palpable portion of which was smooth, ovoid, and about 1 cm. in diameter. The mass was fixed, but the skin moved freely over it; the conjunctiva in the upper fornix was normal in appearance. Manual separation of the lids did not cause the mass to present beneath the conjunctiva. There was slight limitation of abduction of the left eye. Ocular examination was otherwise unremarkable, revealing only mild degenerative retinochoroidopathy consistent with the patient's high myopia.

She was referred to Dr. A. B. Reese by Dr. T. A. S. Boyd, and was admitted to this hospital. Routine physical examination, complete blood count, and urine analysis were unremarkable. Stereoscopic radiography of the skull and orbits was within the normal range; in particular, no abnormalities of the left lacrimal fossa were noted. An orbitotomy with removal of the lateral wall was performed, revealing a mass in the lacrimal fossa with three smaller satellite-like nodules along the posterior border. The mass and its nodules, together with the periosteum of the lacrimal fossa, were removed, leaving bare bone which did not appear to be involved.

FIG. 1.—Case 1. A 27-year-old woman with a small mass in the left lacrimal fossa.

FIG. 2.—Case 1. Medium-power photomicrograph of a section stained with haematoxylin and eosin. Acellular hyaline material infiltrates the walls of the blood vessels and surrounding tissues.

Microscopic examination of the sections showed areas of an acellular material infiltrating connective tissue and surrounding the lobules of the lacrimal gland (Fig. 2). The amorphous matter was perforated by tiny cracks and crevices, disrupting its homogeneity. The walls of some of the blood vessels were infiltrated with this substance, and the cells of the acini in some of the lobules of the gland were largely replaced, leaving only nuclei adjacent to the lumina. The amorphous material stained pink with haematoxylin and eosin, reddish-purple with periodic-acid-Schiff, orange with Congo red, and bluish-purple with Masson's trichrome. Foreign-body giant cells were not noted. The diagnosis of amyloid tumour was confirmed by Dr. R. Lattes, Professor of Pathology, College of Physicians and Surgeons, Columbia University.

Post-operatively the patient has complained of some dryness of the eye and diplopia when looking to the left. There has been no recurrence of the lesion in the 4 years since excision.

Case 2.—A 60-year-old Caucasian man noted prominence of the right eye in 1960, at which time a mass was palpated in the upper nasal quadrant of the right orbit. There was a complaint of diplopia, but visual acuity was not decreased. A partial excision of the mass was performed through an anterior incision at another hospital, and the microscopic sections were read as "granulomatous pseudotumour". A therapeutic trial of systemic steroids produced no improvement.

Post-operatively the proptosis recurred, progressing relentlessly, and the patient was referred in 1964 to Dr. A. B. Reese by Dr. E. Levine. At that time he showed advanced proptosis of the right eye with deviation of the eye down and in (Fig. 3). Temporally in the palpebral aperture beneath the conjunctiva there was a large mass extending superior and posterior to the globe with a firm nodular surface. The eyeball was fixed and immobile.

FIG. 3.—Case 2. A 60-year-old man with proptosis of the right eye which had slowly progressed for four years. A firm mass was palpated in the upper and temporal portion of the orbit.

General physical examination, complete blood count, and urine analysis were unremarkable. Radiographs of the skull and orbits were interpreted as showing marked enlargement of the right orbit with increased density of soft tissue. Temporally the bone of the orbit was thin and bulged into the temporal fossa.

A biopsy of the orbital mass was performed through a lateral canthotomy. Microscopically there was partial replacement of the connective tissue by irregularly shaped aggregations of a brightly eosinophilic substance without determinate form (Fig. 4). The areas of eosinophilic material were partially surrounded by foreign-body giant cells. Perivascular inflammatory infiltrates were present, and the walls of some of the arterioles showed hyaline thickening. Staining reactions were similar to those described for the first case; in addition, crystal violet was employed, with which the islands of amorphous deposits stained metachromatically purple. The diagnosis of amyloid tumour was confirmed by Dr. R. Lattes. Tissue culture of the specimen by Dr. G. Ehrlich resulted in growth of cells without recognizable production of amyloid material.

FIG. 4.—Case 2. Medium-power photomicrograph of a section stained with haematoxylin and eosin. Areas of amorphous deposits are partially surrounded by multi-nucleated foreign-body giant cells.

Dr. M. R. Murray kindly reviewed fixed specimens of the tumour after explantation *in vitro*, and made the following comment:

"One can trace the emigration of many cells from tumour nodules of the explant into the growth zone. These cells tend to be discrete, elongated, or even ribbon-shaped, with a single, round, or oval nucleus (Fig. 5). Frequently, the hyperchromatic nuclei show one nucleolus, but many of them have two or several nucleoli. No amyloid is visible. Although the outgrowth has a mesenchymal cast superficially, it is probably not stromal in origin. Epithelial cells have been known to grow in this habit, but that it not usual. The nuclear picture is epithelioid or neoplastic. I have little doubt that these are tumour cells".

FIG. 5.—Case 2. Medium-power photomicrograph of fixed specimen of tumour explant growing *in vitro*, showing discrete elongated cells with hyperchromatic nuclei containing one to several nucleoli. Lower centre, the explant from which the cells are derived.

If the author may be permitted a comment relative to Dr. Murray's analysis, it is probable that the lesion in this patient represents a true neoplasm rather than a localized metabolic or vascular disturbance following inflammation.

Four days later a partial excision of the tumour was performed through a wide lateral canthotomy. The tumour had a plastic consistency somewhat resembling a yellowish rubbery substance, and conformed to the surface of the globe and to the roof of the orbit. Once a plane of dissection had been established the tumour could be peeled away from these structures quite easily. The lateral rectus muscle had been replaced. The lesion infiltrated the posterior orbital structures and could not be entirely removed.

An extensive medical evaluation was carried out by Dr. C. J. D'Alton. Stereoscopic radiographs of the chest showed multiple nodular parenchymal densities of the left lung. The following studies were unremarkable: skin testing with tuberculin, histoplasmin, coccidioidin, and blastomycin; serum levels of protein-bound iodine, glucose, uric acid, cholesterol, alkaline phosphatase; erythrocyte sedimentation rate; electrophoresis of serum proteins; stool guaiac test; hepatic scan with radio-active gold; radiological studies of the gastro-intestinal tract (upper and lower gastro-intestinal series and barium enema); intravenous pyelogram; and biopsy of the rectal mucosa for amyloid.

The final diagnosis was amyloid tumour of the right orbit and probable amyloid tumours of the left lung. Metastatic carcinoma to the lung could not be ruled out, although the extensive medical examination did not produce evidence for a primary neoplasm. Diagnostic biopsy of the pulmonary nodules would have been of academic interest only, and was not carried out.

Comment

In the first case the tumour occurred in the region of the lacrimal fossa and showed minimal progression for two years after it was first noted. In the second case the mass

infiltrated the orbit and progressed inexorably until the globe was severely proptosed and firmly fixed. At the time of orbitotomy, the tumour appeared to be composed of a rubbery, yellowish substance which conformed to the contours of the orbital roof and globe; a plane of dissection was established between the mass and these structures, and it was peeled away without difficulty. However, the lesion extended to the apex of the orbit, and could not be entirely removed.

Treatment of amyloid tumours of the orbit by local excision may prove to be curative in the case of small isolated nodules. With larger and more infiltrative masses, removal will almost certainly be followed by recurrence, and repeated local excision may be required.

Biopsy of the tumour in the second case three years before the patient was seen at this hospital had been interpreted as "granuloma", undoubtedly due in part to the presence of the large foreign-body giant cells. Such cells are characteristic of certain amyloid tumours, and may lead to confusion in pathological diagnosis. It is possible that amyloid tumours of the orbit are not quite so rare as supposed, and that they have been similarly misdiagnosed in the past. The appearance of amorphous areas in microscopic sections from suspected pseudotumours of the orbit should suggest the possibility of amyloid disease. Special staining is then of great assistance in arriving at an accurate diagnosis. The hyaline-like areas stain red-orange with Congo red, and red with periodic-acid-Schiff. With crystal violet, amyloid characteristically stains a metachromatic purple colour, while the other tissue elements are blue.

Summary

Amyloid tumours occurred in the orbit in two patients. There was no proptosis in one, but in the other proptosis was severe. Local excision of the masses was performed in each case.

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