PROGRESSIVE EXOPHTHALMOS FOLLOWING THYROIDECTOMY; ITS PATHOLOGY AND TREATMENT

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The exophthalmos which is characteristic of a certain type of goitre usually subsides following operative treatment of the gland; ordinarily it is not a matter of any great concern to the surgeon, nor does it require special treatment. In occasional instances, however, this protrusion of the eyes may not subside after operation and may then constitute a disturbing residual symptom of the disease. In still other instances exophthalmos after thyroidectomy becomes progressive and the literature is filled with instances in which this has occurred. Among the reports of particular interest are those of Zimmerman,[1] Burch,[2] and Roeder and Killins.[3] This condition has resulted, in extreme instances, in total blindness. Enucleation of the eye is often necessary because the protrusion advances to such a degree that the lids are no longer able to cover the cornea, and desiccation, abrasion and ulceration with infection result from exposure. Some of these patients show choking of the discs and atrophy of the optic nerves, though this is by no means an invariable accompaniment of the exophthalmos. Ophthalmologists have recommended various procedures for protection of the eye, such as suturing the lid and canthotomy. In other instances, operations upon the cervical sympathetics or the stellate ganglion have been tried upon the theory that the principal factor in the production of the exophthalmos is an overactivity of the sympathetic nervous system, producing its effect upon the involuntary muscles in the orbit. The operations upon the lid, as might be expected, have met with no success, and have had no effect upon the progress of the protrusion. Sympathetic operations likewise, while resulting in a slightly narrowed lid slit and a smaller pupil, have been quite inadequate and unsatisfactory.

An inquiry into the cause of the exophthalmos associated with hyperplastic goitre indicates that there is no concurrence of opinion as to the underlying mechanism. There have been numerous proponents of the idea that certain muscles supplied by the sympathetic nervous system have become overactive and, in one way or another, are responsible, not only for the exophthalmos, but for the wide lid slit and the lagging of the upper lid in following downward movements of the eyeball. The muscles of Müller,[4,5] Landström,[6] and Krauss,[7] all have been considered to play their rôles; the muscles of Müller and Landström by acting directly upon the globe, and the muscles of Krauss by constricting the ophthalmic vein so as to produce a venous engorgement, which secondarily has been responsible for the prominence of

the eye. Other explanations offered are that there is an increase of orbital fat or that there has been an œdema of the orbital fat, the reasons for which have not been made clear. Some writers have suggested that venous congestion in the orbital veins is the factor.

A recent experience has shown what has proved to be a satisfactory treatment for progressive exophthalmos and has revealed the pathologic changes which produced it.

CASE REPORT.—An unmarried, white woman, forty-seven years of age, was admitted to the University of California Hospital March 12, 1930, because of progressive exophthalmos and failing vision following thyroidectomy for exophthalmic goitre. Her past history was essentially negative until April, 1928; from April to July, 1928, she gained twenty-nine pounds. During July she became aware of some dyspnœa but medical examination was negative. She was given thyroid-ovarian-pituitary medication for two weeks and lost nineteen pounds. She was then well until November, 1928, when she had transient œdema of the ankles, noted in the mornings, and nocturia; examination at that time was said to reveal no evidence of cardiorenal disorder. At that time she again was given some thyroid-ovarian-pituitary therapy. She improved and remained fairly well for two months, at which time she noted some subconjunctival œdema and slight lacrimation; the urinary findings were normal. In January, 1929, her eyes had a somewhat staring appearance. There was neither history nor evidence of any infection in any part of the body. By the end of February, 1929, her eyes began to be prominent, and, with this symptom, the first evidence of tumor over the thyroid appeared. Shortly after this, she began to lose weight again, became nervous and developed a tremor, with moderate sweating. Palpitation on exertion was present. Her basal metabolic rate at this time was reported to be, on one occasion, 17-plus, and on another 23-plus. In May, 1929, she consulted a surgeon, who advised and performed thyroidectomy. Except for a moderate exophthalmos which was present at that time, there was no complaint referable to her eyes and her vision was normal. Upon leaving the hospital, she was considerably underweight but her nervousness was less and she was able to return to work in two months. Shortly after this, she noticed that her eyes were becoming still more prominent, and the upper lids became œdematous. In August, 1929, three months after operation and seven months before consulting us, she noted that her vision became blurred, and she was told by a physician whom she consulted that her optic discs were choked. At this time her basal metabolic rate was found to be minus-32. From this time on she received one-half grain of thyroid three times a day. Her vision slowly failed. In September she still was able to get around alone, and to write letters, but, by the last of October, she could not see well enough to do either of these.

Upon admission to the University Hospital, she presented an extreme exophthalmos. She was unable to close the lids completely; upon closure the lid margins remained about 2 millimetres apart. Both eyes were about equally prominent. Both upper and lower lids were puffy, the conjunctival sclera was œdematous and watery in appearance, the vessels of the sclera were somewhat injected and the movements of the eyes were limited in all directions, so that the range of movement was reduced to perhaps 25 per cent. of the normal; in addition, the patient was almost blind. She was unable, at a distance of six feet, to recognize anyone and could make out only the outline of a person standing at her bedside. The optic discs were slightly elevated and blurred at the margins, a considerable degree of atrophy had occurred, and minute hæmorrhages were present in the left retina close to the disc.

At that time it was felt that this patient might be suffering from an intracranial lesion, possibly a tumor, which was not only contributing to the exophthalmos, but was responsible for the changes in her optic discs, and the primary investigation was

directed toward determining the presence or absence of such a lesion. Her neurologic examination proved to be entirely negative and encephalograms confirmed the opinion that there was no gross abnormality in her nervous system; her spinal fluid pressure was normal. Measurements with an exophthalmometer read 34 on the right side and 32 on the left side.

It was decided that the protrusion of the eyes could not be explained on the basis of any intracranial lesion and there was no evidence of intraorbital tumor or arteriovenous aneurism. In view of the fact that the loss of vision was progressive and the exophthalmos still increasing, it was felt that a decompression of the orbit offered both an opportunity at once to relieve the exophthalmos and perhaps to determine its cause. A satisfactory explanation of the changes in the optic discs could not be made in the light of our present knowledge, but it was felt that they must be associated with whatever pathologic condition was producing the exophthalmos.

Operation.—April 7, 1930 a right frontal operation was performed. The dura was elevated from the orbital plate, which was then opened. The orbital roof was ronguered away widely to give a maximum decompression of the orbital content. The bone was removed mesially as far as the ethmoid and sphenoid cells, and anteriorly as far as the frontal sinus. Laterally the entire plate was removed, and posteriorly, it was removed to the greater wing of the sphenoid. The orbital content bulged markedly through this opening and obviously was under extreme tension. The orbital fascia was opened and the orbital content was exposed. Fat was visible toward the mesial and lateral sides of the orbit, but, upon palpation, it was evident that it was not under tension as contrasted with the tension within the cone of extra-ocular muscles which passed forward from their origin about the optic foramen to the globe. Upon palpation, the tension of this muscle cone was extreme. We felt that the explanation for the exophthalmos must lie here and decided to open through the muscle and to explore the retrobulbar space for the cause of the pressure. Small sutures were introduced into the levator superioris to act as retractors and the muscle fibres were split longitudinally. As the incision was continuously deepened, it was found that, instead of dealing with the normal muscle, perhaps 1½ millimetres in thickness, we were in a deep muscle mass, and the incision had to be deepened to about 1½ centimetres. This muscle was greatly increased in size, was perhaps a little paler than normal, and was distinctly fibrous. This splitting of the muscle was continued forward to the sclera, and its margins were retracted. We were then able to explore the retrobulbar space and the optic nerve as it entered the sclera. No veins and no fat were found within this space. The entire space was filled by this bulk of extra-ocular muscles. Small portions of the muscle were removed for microscopic examination.

With these findings before us, the explanation for the protrusion of the eye was clear. It was caused by an increase in muscle volume. The reason for the changes in the optic discs was not so easily seen. It was considered as a possibility that some constriction about the optic foramen by this same mass of muscle might be a factor in the disc changes. For that reason, it was decided to continue the decompression of the orbit to include the optic foramen and, with this in mind, the bony roof of the optic foramen was ronguered away. The muscle incision was then continued back to the point of origin of the muscle at Zinn's ligament—the fibroperiosteal ring about the optic foramen from which these muscles take their origin. The muscle splitting was continued back to include their origin and the optic nerve was exposed. The muscle became progressively more fibrous and even gritty to the knife and additional portions were removed from microscopic examination. Following the complete decompression of the orbital contents and the optic nerve, the dura of the frontal lobe was allowed to come down upon the orbital contents, the bone flap was replaced and the wound was closed. It was obvious at once, upon the conclusion of the operation, that the right eye had receded markedly. The following day there was considerable œdema of the

lid, which interfered with our judgment of the degree of protrusion. When the recession of the eye was at the greatest the measurements by the exophthalmometer registered 23, as contrasted with 32 prior to operation. During convalescence the right eye became slightly more prominent than it was on the day following operation, but at no time did it reach the previous degree of protrusion. The range of movements of the eye gradually increased; this was true for movements of the globe in all directions, and offered a marked contrast to the still limited movements in the left eye. At the end of one week after operation, it was obvious that the vision was returning rapidly in the right eye. Whereas, prior to operation, the vision was worse on the right, it had now become much better than on the left. In a short time the patient was able to read the addresses on letters, which represented an enormous increase in vision over her pre-operative state. The scleral œdema on the right side also decreased. The patient left the hospital in excellent condition, much pleased with the result.

She returned one month later, insisting that the same procedure be performed on the opposite side. This was done on May 28, 1930, and the patient was discharged two weeks later. At this second operation a procedure was performed identical to that on the right side, and with identical pathologic findings. Portions of the muscle were removed, and the optic foramen and orbital content decompressed. In addition, specimens from the left temporal muscle and from the thigh muscles were removed for the sake of comparison.

Microscopic examination of the extra-ocular muscles on both sides was identical and showed round-cell infiltration, marked œdema, destruction of the muscle fibres, complete loss of muscle architecture with increase in fibroblasts and generalized fibrosis. The temporal muscles and the thigh muscles were normal.

The general course following this second operation was identical with that of the first. There was immediate and marked recession of the left eye; later, a little more protrusion, which, however, did not nearly reach the pre-operative state. A gradual improvement in movements of the globe in all directions followed, with recession of the changes in the optic disc and improvement of vision. The patient has been seen at frequent intervals since that time, and the improvement in her appearance has been most striking. Apparently gradual recession of the eyes is occurring even at this time. She has regained excellent vision. In spite of the large orbital decompression on both sides, there is no lack of parallelism of the eyes and both move well in all directions. There is no diplopia. The œdema and congestion of the sclera have subsided and the lids are becoming less puffy. The optic discs, of course, show some degree of atrophy.

In explanation of the pathologic condition found, that is, the great volume increase in the extra-ocular muscles, pathologic examination would indicate that this is not a true hypertrophy, but rather that there was muscle swelling from œdema and that fibrosis followed. The factors which might serve to initiate this condition are most interesting to speculate upon. A search of the literature has revealed that a hypertrophy, or at least an increase in the volume of the extra-ocular muscles, has been found in other conditions than that of exophthalmos caused by thyroid disease. In these reports one is impressed by the frequency of general circulatory disorders and the possibility of some secondary circulatory disturbance in the orbital circulation. It is well recognized that in certain of the general diseases, particularly in nephritis and in mitral stenosis, exophthalmos is not infrequently seen. MacCallum and Cornell,[8] in experimental work, were unable to produce marked exophthalmos in dogs, but produced some slight degree of exophthalmos through stimulation of the sympathetic nervous system and increased it

slightly by tying the external jugular veins. Dr. Margarete Kunde,[9] of the Department of Physiology of the University of Chicago, has reported, in her experimental work upon rabbits, that exophthalmos could be produced if a thyroidectomy were performed upon three-weeks-old rabbits, if these rabbits were later fed with thyroid. No examination of the orbital contents has been reported in these animals. This we hope to present to you at a later time from our own and her experimental work. It is noteworthy that most of the patients who are described in the literature as suffering from progressive exophthalmos have had a normal or low basal metabolic rate as is the case in Doctor Kunde's experimental animals. The patient now reported had a low metabolic rate and had been given thyroid. Also it was noted that an unusually broad collar incision had been made at the time of her operation, and that both external jugulars had been tied. In view of the fact that the venous return from the orbit has a double channel to the systemic circulation, one by an intracranial route, and the other through communicating veins to the facial vein, this might be one factor in the production of the protrusion. The changes Brooks[10] reported in the presence of marked obstruction of venous return flow from muscles in the extremities were similar to those found in this case of progressive exophthalmos.

It is hoped that experimental work now under way may throw additional light upon the mechanism of these muscle changes and also add a link to our understanding of the circulatory changes seen in choking of the optic discs.

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