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TUMOR OF THE HYPOPHYSIS IN A CASE OF ACROMEGALY *

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The importance to health of the integrity of the pituitary gland is now unquestioned. Experimentalists and clinicians are busy elucidating its physiology and pathology, in order that rules may be formulated for the diagnosis and treatment of its various disorders. Meanwhile surgeons are perfecting new practical methods of approach to the hidden gland at the base of the brain, thus robbing hypophysectomy of many of its dangers. The literature of the past few years has been enriched by a number of valuable articles and monographs on the theoretical and practical aspects of hypophyseal disorders, which must be consulted by those wishing to get a general view of the subject. My contribution is the report of a case of acromegaly with post-mortem findings, which I had the privilege of studying for about seven years. I shall attempt, if possible, to correlate the features of this case with the latter-day teachings on the hypophysis.

REPORT OF CASE

History.—The patient, a Canadian lake captain, 49 years old and unmarried, was first seen in September, 1903. Father died of some lung trouble at 71; the health history of other members on this side of the family is unknown. The mother, in good health at 79 years, stated that her parents died at 82 and 85 respectively; a sister had a "stroke" at 70 and died several years later; her other children are healthy and she never knew of any nervous diseases in her entire family. Birth and early physical and mental development of patient were normal. With the exception of an attack of tonsillitis when 2 years old and of two attacks of lumbago during adolescence, there were no complaints previous to the present trouble. He always had good habits; never smoked nor drank to excess. Though sexually moderate, he did not escape a mild case of gonorrhea and, later, a chaneroid with bubo; but he never acquired syphilis. During his boyhood and early adolescence he was tall and slim. Figure 1 shows him at 35. At this time he was still within normal proportions with reference to height and weight. Soon after this picture was obtained, however, he began to gain in weight, and we discover in him the fully-developed acromegaly type at the age of 44 (Fig. 2).

Present Complaint.—At my first examination the family were agreed that the disease had not lasted over eight years. The patient placed much emphasis on two incidents which

occurred shortly before the development of his symptoms, and he holds these responsible for his troubles. First, during a stormy voyage on the lake he was overtaken by fright and confusion of such nature that he was obliged to yield the command of the vessel to his first officer. The second incident which he regards as the principal cause of his disease was an infected vaccination wound on his left arm, from which he suffered in 1894. Shortly after the infection had subsided, he noticed peculiar nervous "spells," during which he held his breath and snored for a few seconds; there was said to have been some discoloration of the lips, but no frothing at the mouth during these attacks. Consciousness was never lost during any of the seizures. In the autumn of 1894 the attacks changed in character, not only motor, but also sensory and vasomotor phenomena occurring; added to the snoring and pause in respiration there developed "creepy," chilly feelings, followed by hot flushes and sweatings. Occurring at long intervals in the beginning, the "spells" became more frequent later, until toward 1897 major attacks of epilepsy also made their appearance. During a period of seven months, in 1895, the patient found himself in a condition of physical and mental inertia. He was somnolent, apathetic, could not recognize familiar objects and persons and was unable to attend his natural wants. Slowly he emerged from this lethargy; he began to take short walks in the open and to care once more for his person. At this time and subsequently an insignificant physical or mental effort was usually sufficient to bring on a state of exhaustion. In 1896 many nervous spells of the variety already described occurred, which were modified to the extent that each attack was either followed or initiated by a smacking of lips and trembling of face, usually accompanied by a lachrymose outery of "Oh my, oh my!" In 1897 the first major attack of epilepsy was noticed; there was the short tonic, followed by a longer clonic convulsion, with frothing at the mouth, biting of the tongue, and complete relaxation of the vesical sphincter. Similar attacks continued to recur mostly during the early morning hours. They were always preceded by "creepy," chilly feelings in the fingers; often, however, the latter constituted the entire attack, which then terminated by yawning and profuse perspiration, but without convulsions. A prominent symptom was severe headaches, which have occurred at irregular intervals since the lake accident—for the patient the beginning of his disease. Very intense at first, the cephalalgias became less severe and less frequent toward the end.

Physical Examination.—Patient is about 6 feet tall, presents a clumsy posture and a gait betokening lack of energy. His face is coarse and large, the lower jaw massive and protruding beyond the upper; the lips and nose are thick, the nasolabial folds accentuated. The eyes are deeply set, eyebrows coarse, and supra-orbital arches prominent. While the lower portion of the forehead bulges out considerably, the upper end appears to be retreating; the malar bones are large. The fingers are sausage-shaped and the hands resemble a spade, all the tissues—bones, muscle, fat and skin—being excessively developed. The feet show similar excess in the growth of both soft and osseous structures. Kyphosis is marked in the cervicodorsal region. Both clavicles and the sternum are considerably enlarged. The genitals are under-

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sized and the libido and sexual power are absent. Except for the heart, which shows slight tachycardia, the viscera are normal. The voice is low-pitched, the speech slow, guttural and monotonous. The tongue, indented by the teeth, is extremely large and fills the mouth almost completely, thereby exciting an increased flow of saliva. The thyroid is not palpable.

At various times early in my observation I found in the urine phosphates, urates and traces of sugar, but no albumin. Somewhat later I failed to detect sugar, and discovered the phosphates only occasionally. Polyuria, polydipsia and polyphagia were symptoms more or less present during the entire

Fig. 1.—Patient at 35, still within the normal growth proportions.

Fig. 2.—Patient at 44. Typical acromegaly appearance.

Fig. 3.—Hypophyseal tumor growing in all directions, more especially on the left side.

course of the disease. A blood examination revealed nothing beyond a slight secondary anemia.

Nervous Examination.—There is no paralysis, tremor or ataxia. The tendon reflexes are reduced in the upper extremities; the knee-jerks are barely elicitable, the Achilles jerks absent. Babinski's toe phenomenon and Oppenheim's foot sign cannot be obtained. The sensory examination reveals negative findings throughout. The special senses show no anomalies. Hearing, taste and smell are normal. An examination for visual disturbances fails to disclose hemiopic or central vision disorders. As I could not prevail on the patient to visit an ophthalmologist for purposes of perimetric and ophthalmoscopic examination, I am compelled to use rough

tests for the visual fields, which yield negative findings. Ophthalmoscopically, the optic nerve appears within the normal limits of health, neither congested nor too pale. That the patient has remained an inveterate newspaper reader almost to the end would lend support to the last statement. The pupils react to light and in accommodation, though rather sluggishly.

Mentality.—Forgetfulness, apathy, absence of mental concentration and a puerile state of mind are constant features. The patient is an indefatigable collector of newspaper clippings from the advertisements of quacks and charlatans, who appeal strongly to his enfeebled mind. On certain days he develops attacks of somnolency, which interrupt all serious occupation with the patient. He thinks a Roentgen-ray examination unnecessary and cannot be induced to go to the laboratory.

Subsequent History.—During the two years previous to his death the major epileptic attacks had become rare, but instead the *petit mal* seizures had become more frequent. In addition there developed great difficulty in swallowing, regular choking spells impeding the process of feeding. The troubles of deglu-

Fig. 4.—Optic chiasm, very much attenuated, surrounded on all sides by tumor mass.

tation diminished about three or four months before death, but the patient became more somnolent and weak; the memory was almost a blank; he was childish, confused and unable to answer simple questions. The patient died in coma July 27, 1910, at the age of 56, having been a sufferer from acromegaly for about fifteen years.

Necropsy.—Permission was granted to examine the brain, but none of the other organs. The important finding was a large tumor in the hypophyseal region, which had grown in all directions (Fig. 3). In its continuous growth, the neoplasm had destroyed the posterior clinoid processes and extended upward as well as downward. While the sphenoidal sinuses were also found infiltrated with tumor tissue, the principal mass grew laterally and upward. As a result of this upward extension the optic chiasm had become attenuated and flattened into a cup-shaped structure (Fig. 4), measuring 2 by 1.5 cm. Laterally the neoplasm grew from the sella toward the uncinate gyri, both of which were thus compressed, but especially the left one. Still further extending into the inferior horns of the lateral ventricles, the tumor produced a considerable degree of irritation hydrocephalus,

which was more marked on the left side (Fig. 5). The irregular mass, with its numerous protuberances occupying the entire interpeduncular space, was of a dirty-gray color and had but little cohesiveness; after a few days' hardening in formalin solution it began to fall apart. It measured approximately 6 cm. in its transverse, 4 cm. in the sagittal and 3 cm. in the longitudinal diameter.

Microscopically there are seen a few groups of deeply staining cells (chromophils) scattered among numerous others that stain but feebly (Figs. 6 and 7), (chromophobes), with colloid masses here and there. Part of the tumor shows irregular rows of cylindrical epithelium, having the typical appearance of secreting cells, with their darkly stained protoplasm to one side and the lighter portion to the other (Fig. 8), a picture resembling a secreting gland. The brain not having been especially prepared for the granular stain, the existence of granule cells could not be ascertained with certainty, though Dr. Dean Lewis, who kindly examined and stained for me some specimens from this tumor, believes that he recognized some of the cells on which he and Benda have laid so much stress. When I first examined the tumor the

Fig. 5.—Bilateral hydrocephalus, more marked on left side. Infiltrating masses seen in left lateral ventricle.

diagnosis of sarcoma was uppermost in my mind, because the growth consisted largely of round cells with little or no stroma. On consulting the literature, however, and especially Benda's and Lewis' writings, I came to the conclusion that the neoplasm belonged to the adenomatous variety of hypophyseal tumor.

Summary.—As a result of a psychic trauma or an infection a male patient at the age of 41 develops symptoms of acromegaly, accompanied by attacks of petit mal epilepsy; somewhat later there are added somnolency, cephalalgias and change of character. Though presenting the classic picture of acromegaly the patient never suffered from any of the usual visual disorders of this disease, such as hemiopia and central scotoma. In the course of time, however, attacks of major epilepsy and uncinate fits supervene and the patient dies about fifteen years after the beginning of the first symptoms, having lived the life of a vegetating automaton for many years. The post-mortem examination then reveals a large adenoma, which had pushed up the optic chiasm, extended into the lateral ventricles and incidentally caused a bilateral hydrocephalus, more marked on the left side.

CONCLUSION

The peculiar distribution and extent of the tumor may explain many of the symptoms in this case. The proliferation of glandular tissue leads one to suppose that there must also be a corresponding increase in the function of such tissue. Assuming with Benda,¹ Lewis²

Fig. 6.—Magnified 180 diameters. Tumor consisting of (a) chromophobe cells, with few (b) chromophil cells interspersed.

Fig. 7.—Magnified 450 diameters, showing (a) large and (b) small cells; also (c) colloid material.

1. Benda, C.: Beiträge z. normalen u. pathologischen Histologie d. menschlichen Hypophysis cerebri, *Ber. klin. Wehnschr.*, 1900, xxxvii, 1205; *Deutsch. med. Wehnschr.*, 1901, xxiii, 536; *Pathologische Anatomie d. Hypophysis*, *Handb. d. path. Anatomie d. Nervensystems*, 1904, p. 1418.

2. Lewis, D. D.: Hyperplasia of the Chromophil Cells of the Hypophysis as the Cause of Acromegaly, with Report of a Case, *Bull. Johns Hopkins Hospital*, 1905, p. 157; A Contribution to the Subject of Tumors of the Hypophysis, *The Journal A. M. A.*, Sept. 17, 1910, p. 1002.

and Cushing³ that the skeletal overgrowth of acromegaly is conditioned by a hypersecretion of the anterior portion of the hypophysis, we certainly had the structures from which such secretions might have been derived. As the tumor continued to grow, the hyperactivity was converted into hypoactivity—the chromophil gave way to chromophobe cells. Then it was that we discovered the existence of adiposity, myasthenia, and loss of sexual power. As may be observed in the microphotographs, the tumor masses consist almost entirely of chromophobe cells, while the chromophil cells—the real secreting structure—seem to have almost entirely disappeared. Apparently there was a stage of immoderate stimulation followed by one of exhaustion. This interpretation harmonizes with the modern teaching on the causation of acromegaly. While the theory of hypophyseal activity receives but scant support from my case, more can be said under the heading of neighborhood symptoms on which Cushing in his monograph

Fig. 8.—Magnified 110 diameters. (a) Irregular rows of cylindrical epithelium, resembling glandular structure; (b) scattered round cells like sarcoma.

puts great emphasis. We may recall that the patient developed *petit-mal* attacks at first, and, as the tumor continued to grow toward the uncinate gyri, there also appeared attacks which were accompanied by a smacking of the lips and movements as though the patient were tasting some unpleasant substance. These were probably *petit-mal* seizures belonging to the type which Hughling Jackson described long ago as uncinate fits—caused by the extension of the growth to the uncinate convolutions. The attacks of *grand-mal* epilepsy must also be considered as neighborhood symptoms. They were most probably caused by the varying fluid content in the ventricles compressing the brain against the skull, thus producing cortical irritation. To the invasion of the frontal lobe by the tumor must be attributed the

mental changes, somnolency and puerile behavior—symptoms frequently noted in acromegaly. The absence of visual disturbances in my case can be explained from the appearance of the optic chiasm, as may be observed in the photograph. The chiasm appears thinned out, but widened; evidently the neoplasm compressed this structure very slowly, thus permitting gradual accommodation to pressure, while the tumor itself showed a tendency to extend laterally, rather than to grow in an upward direction.

A symptom which may throw some additional light, as every such case must, on the interrelationship existing between the various glands of internal secretion, was the complete absence of a thyroid gland in my patient. Possibly in taking up the work of the thyroid, the hypophysis continued to grow and functionate beyond the physiologic needs, with the resulting formation of a large adenoma.

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INTESTINAL SAND

REPORT OF A CASE WITH CHEMICAL ANALYSIS OF SAND *

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Laboulbène¹ reported the first case of intestinal sand in 1873. He found a sandy substance in the feces resembling brown or yellow sand, which he believed was of vegetable origin. Since that time there have been many reports of cases in which intestinal sand was associated with one or more clinical manifestations, and attempts have been made to show that the sand was a part of various forms of diathesis.

More recently Myer and Cook² studied the literature on the subject and came to the conclusion that intestinal sand was not a part of any clinical entity but that, in their own case, it resulted from the ingestion of bananas. They found that after eating bananas sand invariably appeared in the feces after twenty-four hours and often continued for several days. It came in large quantities at first (from 1 teaspoonful to 1 tablespoonful) and gradually diminished in amount. If the feces were not manipulated too much, the grains were often found in chains. These chains correspond in arrangement and shape to the cylindrical cells in the milk-ducts of the banana. These cells contained highly refractive resin balls or masses, which were suspended in a fluid rich in tannin.³ They believed that these resin balls were affected by the secretions of the stomach and intestine in such a way that the resin was hardened and an insoluble tannate formed. They were unable, however, to reproduce the sand by artificial digestion or by placing the banana in fecal material.

I have examined many hundreds of stools both in the gross and under the microscope during the past five years and have seen only two cases with intestinal sand. Both of the patients denied having eaten bananas within several months. The stools of many other children, who had eaten bananas, failed to show intestinal sand.

* Presented before the American Association for the Advancement of Clinical Investigation, Washington, D. C., May, 1913.

1. Laboulbène: Bull. de l'Acad. de méd., November, 1873.

2. Myer and Cook: Intestinal Sand; the Banana One of Its Sources, Am. Jour. Med. Sc., 1909, cxxxvii, 383.

3. Bury: Vergleichende Anatomie bei Phanerogamen und Farne, 1877, pp. 153, 160, 451, quoted by Myer and Cook.

3. Cushing, H.: The Hypophysis Cerebri; Clinical Aspects of Hyperpituitarism and of Hypopituitarism, THE JOURNAL A. M. A., July 24, 1909, p. 249; The Functions of the Pituitary Body, Am. Jour. Med. Sc., 1910, xxxix, 473; The Pituitary Body and Its Disorders, J. B. Lippincott Company. This excellent monograph contains the recent literature on the hypophysis.