A CASE OF INFANTILISM ASSOCIATED WITH PITUITARY NEOPLASM *

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Illness depending on pituitary disturbances is becoming more frequently recognized. The case of infantilism here reported is presented as an example of an interesting condition worthy of addition to the records of pituitary disorders.

CASE REPORT

History.—H. H., male, aged 26 years, occupation errand boy, weight 70 pounds; height 3 feet 8 inches, entered the Royal Victoria Hospital on account of headaches, vomiting and vertigo. He was a full term healthy child of 9 pounds at birth, and grew quite normally and naturally until the age of 10 years; he has not grown any since. As long as he can remember he has had attacks of vertigo, and at times double vision. About every month he was troubled with an attack of severe frontal headache, which sometimes darted through to the occiput; it was as a rule much worse during the day than at night. Vomiting was another distressing symptom which later began to trouble him. It usually accompanied the headache, was explosive in quality, occurred sometimes after meals, but often independent of them. These attacks of headache, vertigo and vomiting would last two or three days, and between them he was comparatively well, and able, when he grew a little older, to do work as an errand boy. Within the past year or so these attacks have become more frequent, and at times more prolonged. Stiffness of the muscles of his legs have been also observed by him during this time, and objects appeared to move up and down, and very often appeared double to him. His voice and mental development never got beyond that of a boy of 10 years, and his appearance shortly before his death was of a fleshy boy of that age; it could hardly be credited that he was 26 years old.

Examination.—The general contour of his body was suggestively feminine; his head was large and his forehead slightly prominent. He was mentally bright for a boy; he was sexually as a boy of 10; he had no desire to associate with young men of his actual age; his amusements were boyish—tops, marbles and such toys. His skin was pale; on the face it had a distinct yellowish tinge, not by any means jaundiced; the subcutaneous fat was well marked. There were no lymph-node enlargements. His thyroid was not palpable. There was slight fulness of the mammary glands, no distinct enlargement, but on palpation in that situation the tissues were distinctly firmer to the touch than the surrounding structures. There was no hair on his body. The hair of his head was dry, straight and coarse. His genital organs were those of a boy. His chest was slightly barrel-shaped, well formed, symmetrical. His pulse averaged 68 to the minute, of regular rhythm, but low tension. His blood-pressure was 90 to 100 mm. of mercury.

There were no pathological reflexes present, no strabismus, nor nystagmus, but double optic neuritis developed shortly before his death. He was under observation off and on for three months, but his headache, vertigo, etc., ceased after his first few days in the hospital. His last entrance to the hospital was five days before his death; his headaches were severe (uncontrollable by the usual remedies), and vomiting was frequent; muscular twitchings of the legs and arms

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were present and he was very dull mentally. His urine for the first time was found to contain abnormal constituents: specific gravity was 1.012, no albumin or sugar, but acetone in abundance, and a trace of diacetic acid. His temperature had ranged from 97 in the morning to 99 in the evening throughout his stay in the ward, rose to 101 twenty hours before his death.

Necropsy.—Examination of the body was made four hours after his death. An undersized male; apparent age 12 years. Diffuse, light-yellow pigment in skin of face. Scanty eyebrows. Teeth were excellent and well formed. Eyes were gray; pupils were equal and slightly dilated; eyelashes long and curved. Chest was prominent, and the skin was absolutely white. Breasts contained some fat. There was no hair on the body at all. Abdomen was prominent and fat. Genital organs were small. The testicles had descended.

The scalp was thin, and stripped readily from the skull, which was thin and transparent. The dura was not adherent. The blood-vessels of the dura were congested. There was an excess of fluid between the dura and the brain. There was no thrombosis of the sinuses. The sella turcica was widened, and the pituitary was greatly enlarged; it was tensely distended, particularly the portion nearer the brain. The infundibulum and stalk were likewise distended. The portion of the pituitary which fitted into the sella turcica was 2.3 cm. from before backwards, and vertically it measured 2.5 cm. It was accidentally incised during removal, and about 10 c.c. of bright yellow fluid, which was found to contain numerous cholesterin crystals, escaped. The wall of the cyst was thin and adherent to its inner surface. In the region of the posterior lobe were three or four small, soft, rounded, gelatinous-looking masses. At the bottom of the cyst in the locality of the anterior lobe was a mass of soft, light-yellow, very friable material, the remains of a degenerated anterior lobe. The wall of the cyst in this locality was thicker and contained calcified material. The stalk of the pituitary was widely distended, and was hollowed out continuous with the infundibulum, so that there was a free communication between the cystic pituitary and the third ventricle. On section of the brain it was found that the anterior portion of the left cerebral hemisphere was hollowed out in the white matter, and contained a turbid yellowish cholesterin-containing fluid. The margins of the cavity were ill-defined. Projecting into it from behind was a jelly-like mass of reddish color continuous with the chorioid plexus, forming a soft watery mass as large as the pituitary itself. The posterior horn of the left lateral ventricle was not dilated, and its walls were normal. The posterior horn of the right lateral ventricle was dilated, though its walls were normal in appearance. The right chorioid plexus was small, apparently normal; in the neighborhood of the velum interpositum the white matter showed numerous punctate hemorrhages; the same condition was seen in the velum itself and in the posterior portion of the corpus callosum.

Sections of rounded masses found in the cystic pituitary show new growth consisting of slender branching lines of cells separated by a highly myxoid stroma, very rich in well-formed capillaries. The cells at the edge of the columns are columnar, those in the center polymorphous, they are more or less vacuolated. Some of the stroma cells are spindle-shaped, some are drawn out into multiple processes. A few lymphocytes and allied cells are scattered here and there around the capillaries. The tumor at the anterior part of the chorioid plexus shows the same characters, save that the processes of cells frequently include spaces filled with colloid material, in a few places resembling thyroid colloid. In a few instances there seems no doubt that this change is the result of liquefaction of the myxomatous tissue already mentioned.

Diagnosis of tumor: cystic endothelioma.

Section of the cyst wall shows a fibro-cystic change, with here and there small areas of necrosis, while others show evidences of having been infiltrated with blood.

Sections taken from the floor of cystic pituitary in the region of the anterior lobe showed a large number of degenerated cells in which no nuclei are visible,

and whose cytoplasm usually stains very faintly with hardly an indication of the cell outline. A few cells are present which have a small dark-staining nucleus. A great deal of light yellow pigment is seen throughout the section. No blood-vessels are seen and no trabecular framework. The anterior lobe was therefore much degenerated.

The chest is well formed; the *Angulus ludovici* of the sternum is prominent. The costal cartilages are not calcified. The bone-marrow of the sternum is pale and scanty. The subcutaneous fat was 2.2 cm. in thickness and light yellow in color; the great omentum was full of fat. The diaphragm reached the level of the upper fourth rib on the right side, and the lower fourth rib on the left.

The thyroid was not enlarged; it is homogeneous. The right lobe measured 2.5 by 2.3 cm. The left 2.3 by 2 cm. and the weight of the organ was 5.5 grams.

Sections show acini of varying size, rounded in shape and lined by a single layer of cells with deep-staining nuclei, and distended with colloid material. The lining cells in some of the acini have a flattened appearance. There is no fibrosis, but excessive colloid.

Microphotograph of tumor in the chorioid plexus; showing the lines of epithelioid cells inclosing spaces, some filled with colloid matter, others with myxoid tissue. (Low power magnification.)

A large thymus, particularly the left lobe, was present; it was equal in size to what would be found in a child. Sections showed abundance of lymphoid tissue and Hassall's bodies were numerous. The proper cells were well defined and fat spaces were moderately abundant.

The liver weighed 650 grams, and measured 19 by 12 by 5 cm.; it was quadrilateral in shape, rather flabby; the surface was smooth, mottled with anemic areas; differentiation was poor. The connective tissue was not increased; the cut surface was firm; the blood-vessels were empty. Microscopic examination showed no noteworthy abnormality.

The pancreas measured 15 by 3 by 1.5 cm. It was soft and pink in color and natural on microscopic examination.

The spleen weighed 60 grams and measured 8 by 6 by 2.3 cm. The organ was firm; the surface was smooth and was purple red in color. Malpighian bodies

were hardly visible. The trabeculae were not conspicuous and the pulp was firm histologically.

Right kidney weighed 75 grams; it measured 8 by 5 by 1.9 cm. Juvenile in size. The width of cortex was 7 cm.; medulla 1 cm. The capsule stripped easily; the surface was smooth and lobulated; the differentiation of cortex was good; the glomeruli were visible. The pelvis and the ureter were normal. Left kidney weighted 70 grams and had same characters as right. There was some cloudy swelling of the tubular epithelium.

The adrenals averaged 5 by 1.2 by 0.3 cm. The weight of both was 6 grams. They were atrophic in appearance; the cortex was pale in color; differentiation was good; the pigment was pale and sharply marked. The medulla was gray, and no necessary perivenous cortical tissue was present. Sections disclosed some vacuolation of the cells of the reticulate portion.

The testes were very small and waxy looking. Sections showed a preponderance of interstitial tissue, some of which was fibrous and some hyaline; the tubules were small in size, had little or no lumen, and were lined by a single layer of nucleated cells with a relatively small amount of cytoplasm. Many of the tubules here were replaced by fibrohyaline tissue. Very few interstitial cells are seen (cells of Leydig).

The other organs showed no abnormality.

SUMMARY OF FINDINGS

This case showed some remarkable features. Briefly, the clinical manifestations were: Marked underdevelopment of the skeleton and organs. "Infantile" development of the mental system. Brain tumor symptoms (headache, vomiting and optic neuritis). Feminine contour of body. Evenly distributed adiposity. Absence of body hair. Infantile genital organs. Low pulse-rate. Low blood-pressure. Subnormal temperature. Slight myxedema. Terminal changes in urine.

At necropsy: Cystic degeneration of the pituitary, with complete disappearance of the posterior lobe, and only a few degenerated cells representing the anterior lobe; free communication through the pituitary stalk with the third ventricle. Neoplasm of the chorioid plexus extending into the pituitary. Internal hydrocephalus. Excessive colloid material in thyroid.

Vacuolation of the fasciculate layer of the adrenals.

Underdevelopment of the testes.

Small sized organs of the body generally.

Discoloration of the fatty tissue.

COMMENT

Infantilism has been written about chiefly by the French school of medical observers; they have a voluminous literature on the subject, and recognize distinct types. Conjectures have in many instances been made as to its causation, but few cases are recorded in which an autopsy examination disclosed the nature of the disturbance. Byron Bramwell, in his clinical studies, reports an interesting living case of infantilism, which agrees in most particulars (especially the age) with ours; it was supposed that the pituitary was at fault.

We have, however, a number of symptoms in our case which have been usually associated with the type of pituitary disturbance known as hypopituitarism. These symptoms are adiposity, absence of body hair, tendency to female bodily characteristics. Absence of sexual sense; subnormal temperature; low pulse-rate and low blood-pressure, although this latter symptom is supposed to be due to some disturbance of the adrenal; it may be that the adrenal is disturbed because the pituitary is disturbed. Also the slight myxedema changes may have resulted from a thyroid change, secondary to a primary pituitary disorder.

The outstanding feature clinically in this case was the infantile characteristics in a male, aged 26 years, and pathologically the marked pituitary changes. I have been unable to find in the literature another case in which a cystic pituitary communicated with the third ventricle through a hollowed out infundibulum and stalk. Such a condition is normal in a few of the lower vertebrates, but in man as well as the other members of the higher vertebrates it is not. The occurrence of a relatively benign neoplasm in the chorioid plexus and of masses exhibiting the same characteristics on the walls of the cystic pituitary, as well as the clinical history, point toward a congenital origin for this abnormality. There may also exist a connection between the function of the pituitary and the chorioid, as there may also be an embryological relationship between the chorioid and the posterior lobe of the pituitary body.

Neoplasms in the pituitary have been often reported. The enlargements of the anterior lobe seen so frequently in cases of acromegaly have been often due to a new growth as well as to hypertrophy of the entire lobe. The type of neoplasm found in this case is rare. We have been unable to find any mention in the literature of finding this type of neoplasm in the chorioid and pituitary in the same case. Ziegler mentions a condition occurring in the pituitary to which he gives the name "cystic endothelioma," the description of which agrees very closely with our case.

Farnell describes an interesting change in a pituitary tumor removed at autopsy from a female, aged 43, whose symptoms commenced when 36 years old, with headache, vomiting and optic neuritis, as well as cessation of menses. To quote some of his description of the findings:

> Semicystic mass 3 cm. in diameter continuous with the hypophysis and partially obliterating foramen of Munro. Both lateral ventricles dilated. Gritty granular material and numerous small cysts found in the tumor as well as colloid material. Microscopically it had an adenopapillomatous structure, and the older cells of the growth showed tendency to degeneration. Internal cells of papillae showed calcareous changes.

He conjectured that:

> Its median position and nodal relation to the neuro-enteric canal, its continuity with the hypophysis, strongly suggest its histogenic relation not only to the buccal epithelium, but to the mandibular type composing the enamel-forming

organ of the tooth, hence its designation as a hypophyseal cholesteatoma, and also an adamantoma comparable to those tumors developing in the jaws from dental epithelium.

It may be seen from this interesting case that the pituitary is not immune to pathological conditions of an obscure nature. The suggestion as to the origin of the tumor in Farnell's case may be quite correct, and the name appropriate, yet it would be obviously impossible to collect within the confines of one small article all the obscure tumor formations of this organ. Suffice it, at any rate for the present, to say that our case presents another unusual type of tumor formation probably congenital in origin, and that for some unexplainable reason it produced in the pituitary change which brought about in some obscure manner, physical and mental departures from the normal.

Many views have been presented about pituitary disturbances since Marie, in 1885, made his interesting observation connecting pathologic changes in the pituitary with acromegaly; it was not, however, until a few years ago, 1905, that Frölich recognized another type of pituitary disorder resulting in disturbances different from those occurring in acromegaly. Briefly stated, the principal changes in this condition were: in females, adiposity and ceasing of menstruation; in males, a tendency toward the acquirement of female bodily characteristics, with impotence.

Recent histological studies confirm what was previously held, that there are at least two distinct types of cells in the anterior or glandular lobe of the pituitary body. It is conjectured, principally from their anatomical situation, that these two types have distinct and separate functions, and probably discharge the products of their metabolism into the different channels, the one into the cerebrospinal fluid, the other into the blood. The posterior lobe of the pituitary is composed of modified brain tissue, and in its action on blood-pressure it resembles the adrenal, although there are some important differences.

Even from this brief recital of the more outstanding anatomical features of the pituitary, it may be seen how rich the possibilities are for conjecture regarding its functions. It is not to be wondered at that this well-protected and isolated organ has only in recent years excited the curiosity of the research worker. While something has been accomplished, much remains to be done. It was only natural to expect that at the beginning of the work many unusual findings were recorded; there is much obscurity yet surrounding our knowledge of the functions of the pituitary. It is, however, fairly well established that the conditions of gigantism and acromegaly are due to changes of the anterior lobe of the pituitary. If the disturbance occurs before growth is completed gigantism appears; if after, acromegaly results.

It is also thought that the condition described first by Frölich (generally termed hypopituitarism) is caused by some unknown change, principally in the posterior lobe. The case already outlined would help to support such hypothesis. There was no posterior lobe discovered at autopsy, and the remains of the anterior lobe were in a state of degeneration. The central symptoms existing from his earliest remembrances, and subsiding after rest in bed for a few days, indicate a congenital origin for the brain findings. It is probable that the changes usually associated with thyroid and adrenal disturbances, and present to some extent in this case, may be attributed primarily to the pituitary.

As to the mental underdevelopment, it is difficult even to offer conjectures as to its causation. Only the fact was obvious that it was the mental development of a child and not that of a man of 26 years.

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