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***Subject:* PITUITARY TUMORS**

1. Review of Literature,
   EUGENE HICKMAN, M.D.,
   Resident in Radiology
2. Presentation of Cases
   CHARLES HUNTER, M.D.,
   Resident in Radiology
3. Diagnosis and Treatment,
   WM. E. ALLEN, JR., M.D.
   Director, Department of Radiology,
   Director, The Tumor Clinics

REVIEW OF THE LITERATURE: *Dr. Hickman*

NINETY per cent of all pituitary tumors can be diagnosed by radiology alone. In most cases, a routine skull series is all that is needed, special procedures being reserved for the more bizarre cases. In cases with homonomous field defects, pneumoencephalography may be used to exclude a lesion of the temporal lobe or a lesion interfering with the visual apparatus due to pressure on the optic radiations posterior to the optic tract. Pneumoencephalography is also of value in cases of pituitary tumors with choked discs, without endocrine, ophthalmologic or roentgenologic bone changes. In these cases the presence of an adenoma encroaching on the third ventricle, producing internal hydrocephalus and choked discs may be revealed. Carotid angiography may prove useful in cases in which an adenoma has broken out of the sella laterally, causing homonomous or other atypical visual field defects plus third nerve palsy. It is used to differentiate a tumor from an anuerysm of the circle of Willis or the internal carotid artery. The value of radioisotopes in the diagnosis of pituitary tumors remains questionable, but is at present being investigated.[1]

The chromophobe adenoma, usually attracts attention radiologically by a ballooning of the sella turcica. The floor is depressed and thinned, the posterior clinoid processes and dorsum sella are displaced posteriorly and are also thinned. Sharpening and shortening of the anterior clinoid precesses may be observed, and the tuberculum sella may be displaced upward and appear quite sharp. The anterior floor of the sella is occasionally extensively decalcified and the tumor outlined by air in the sphenoid sinus. The skull is usually small with the bones of the vault and skeleton slightly undeveloped. There is usually no increased intracranial pressure or calcification.

The eosinophilic adenoma, which is responsible for gigantism and acromegaly, produces sellar enlargement in the same manner as the chromophobe adenoma, but to a lesser degree. In addition, the paranasal sinuses are usually hyperdeveloped, especially the maxillary and frontals. The mandible is increased in size with prognathism. The vertebrae, pelvic bones and long bones are also increased in size. The long bones may have long bulbous ends with exostoses developing at the tendon attachments. In gigantism, the long bones will be increased in length and breadth; and the epiphyses are open beyond the usual time for closure.

Mixed adenomata enlarge the sella, and the bony changes are those described above, depending on the relative proportion of chromophobe and eosinophilic elements.

The basophilic adenoma, which is usually only about one to five millimeters in size, produces no enlargement of the sella although the floor of the dorsum sella may be decalcified. The bones of the skull and the skeleton in general may show decalcification. Compression of one or more vertebrae is common.

Adenocarcinoma cannot be differentiated radiologically from adenoma.

The craniopharyngioma, which usually occurs

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in patients under fifteen years of age, commonly produces a generally enlarged and partly eroded sella. Calcium deposits may be seen as flecks slightly above and extending into the sella. The skull is usually rather small with the bones of the vault appearing thin. Separation of the sutures and increased convolutional impressions may be evident as a result of increased intracranial pressure.

Irradiation has proved a satisfactory primary method of treatment for both chromophobic and eosinophilic adenoma, the over all good results ranging about 70 per cent,[2] the criteria being a decrease in intracranial pressure and improvement in vision. Endocrine manifestations remain unaltered.[3] Survival times of 1 to 170 months are reported.[2]

Although treatment of pituitary basophilism is quite unsatisfactory by any method, remissions following roentgen irradiation are greater in number than those by any other method.[4] Definite improvement in forty-two cases reviewed was 38 per cent.[4] It seems generally agreed that radiation is of no value in treatment of cystic pituitary tumors,[5,6,3,2] in which group 20 per cent of all pituitary tumors will eventually fall.[6] No cases of attempted irradiation treatment of craniopharyngioma or carcinoma of the pituitary were found in the literature reviewed, possibly due to the acceptance of previous teaching that such treatment is to no avail.

During the past ten years, the trend has been to use irradiation as primary therapy whenever the reduction of vision is not marked and has not been rapid.[7] Primary surgery has shown 10-15 per cent mortality in the average neurosurgical clinic.[5,8]

In cases operated following irradiation, irradiation has shown no adverse effects on either the result or technique of surgery.[7]

Post-operative irradiation in cases where surgery was the primary treatment, has been thought to lessen the incidence of recurrence.[5,3,7]

CASES: *Dr. Hunter*

Case I, a 37 year old married female was admitted to the hospital on March 1, 1952 complaining of generalized weakness, loss of energy, restlessness, headaches, vertigo, transient loss of vision and urinary frequency of 20 to 30 times during the day and 8 to 10 times during the night. She also suffered from constant thirst and had gained 20 lbs. in weight during the preceding thirty days. The patient had been in good health and working as clerk typist until 4 weeks prior to her admission to the hospital. There was nothing of significance in her past history.

Physical examination revealed a slightly obese, apprehensive female in no apparent distress. There was no enlargement of the jaws, clubbing of the extremities, hypertrichosis or other significant findings. The significant laboratory findings were in the urine which was pale with a specific gravity of 1005. It was negative for sugar, albumin and acetone. Radiographs of the skull revealed thinning of the posterior clinoid processes with fragmentation probably due to erosion. The floor of the sella turcica in the posterior half was roughened, irregular and deepened probably due to a space occupying, bone eroding soft tissue mass. The roentgenologic impression was pituitary tumor.

The Ophthalmologist in consultation reported no evidence of intraocular pathology. He concluded that in view of the positive x-ray signs and negative eye signs he could assume that the tumor was an eosinophilic or a basophilic adenoma and not a chromophobic tumor. Perimetric studies revealed a diminution on the visual field of each eye.

The patient was referred to the department of radiology for deep x-ray therapy. A tumor dose of 5640r was delivered to the pituitary gland. An ophthalmologic examination one month after the completion of the x-ray treatment and another three months later revealed progressive improvement in the visual fields. The patient has been seen regularly in the follow up clinic with marked improvement in her other symptoms, especially the headaches and urinary frequency. When last seen on October 25, 1952 she had no symptom or complaint and was working successfully full time on a new position as clerk typist. Later radiographs of the sella turcica revealed no change in the appearance of the process.

Case II, a 44 year old widow was admitted to the hospital on July 26, 1950 with a diagnosis of toxic goiter. The patient's past history revealed that she had had a progressive enlargement of the thyroid gland over a period of ten years with associated irritability, tremors, loss of weight in spite of increased appetite, left frontal headaches, tinnitus, vertigo and a decrease in visual acuity for which she had worn glasses. In recent months prior to admission she had noticed exophthalmos, paresthesis, decrease in libido, polyuria and polydypsia. The patient had had a hysterectomy and an appendectomy in 1946 and an amputation of the right first toe following a crushing injury at a forgotten date.

Physical examination revealed a well developed, well nourished female in no apparent distress. The blood pressure was 152/110. The skin was unusually thick, exophthalmos was present which was more prominent on the left. The optic discs were pale, old exudates were present and visual acuity diminished. The thyroid gland was enlarged and nodular. The hands were unusually large and thick for a woman. The heart was enlarged. Reflexes were normal. The significant laboratory findings

were, urine, clear, specific gravity 1028, Sugar 4 plus, Albumin 1 plus, Blood sugar 410 mgm per 100 cc., basal metabolic rate + 18 and electrocardiographic tracing, left ventricular hypertrophy. X-ray examination of the skull revealed the floor of the sella turcica deepened and eroded with thinning of the posterior clinoid processes probably due to a pituitary tumor. Perimetric studies revealed a generalized constriction of the visual fields with a defect in the superior nasal and temporal fields, suggesting a mass encroaching on the inferior aspect of the optic chiasma such as a pituitary adenoma. Electroencephalographic studies suggested the possibility of a deep midline lesion. Radioactive iodine excretion studies revealed 70 per cent excretion. The patient was referred to the department of radiology to receive deep x-ray therapy for a pituitary tumor. She was given a tumor dose of 4940r. There was subjective improvement for one month following this course of therapy with a decrease in the severity and frequency of the headaches and improvement in visual acuity. Perimetric examination at this time showed a definite defect in the superior fields but some expansion in the medial and lateral fields. It was decided to give additional irradiation to the pituitary gland and 1000r was given. The patient has been seen regularly in the follow up clinic and has shown progressive improvement. When last seen October 20, 1952 her visual fields had widened, her diabetes was under control by diet and insulin and she complained of only an occasional mild headache.

DIAGNOSIS AND TREATMENT: *Dr. Allen*

The pituitary gland consists of two lobes, an anterior, a posterior and an intervening para intermedia. The anterior is of glandular origin, and contains both chromophobic and chromophilic cells. These latter cells may be either eosinophilic or basophilic depending upon the manner in which they take up certain dyes. The posterior lobe is of nervous origin. It is derived from a downgrowth of the floor of the third ventricle and is composed of nerve cells. Epithelial cells comprise the para media. The anterior lobe is concerned with growth and sexual development, the posterior lobe with the development of fat and carbohydrate metabolism.

Pituitary tumors are not rare, they constituted 18 per cent of Cushings series of brain tumors. Those tumors which are primary in the gland consist of four major types, three adenomas and one anlange. The adenomas may be chromophobic or chromophilic with two varieties of the latter, the eosinophilic and the basophilic. The eosinophilic type tumor is characterized by gigantism if the neoplasm is present before epiphyseal closure and acromegaly when it occurs in adults. There also may be present large hands and feet, prominent jaws, an enlarged head and paranasal sinuses. Bitemporal cuts in the visual fields due to pressure on the optic chiasma and headaches are usually present. Glycosuria is not an infrequent sign. Case II is an example of this type tumor.

The effects of the basophilic adenoma are glandular in origin. The tumor itself is usually small. The outstanding signs are changes in the facies, hypertrichosis, hypertension, purplish stria, obesity, osteoporosis and sexual dystrophy.

The signs and symptoms of the chromophobic tumor are due entirely to its size. Headaches, hypopituitarism due to pressure atrophy and bitemporal visual defects may occur. Diabetes insipidus may result from pressure causing the diuretic activity of the anterior lobe to be unchecked by the anti-diuretic activity of the posterior lobe. Case I is an example of a tumor of this type.

The fourth type is the Rathke pouch tumor or the craniopharyngiomas. These tumors by pressure may depress pituitary function, cause defects in the visual fields, disturbances in water and carbohydrate metabolism and may even cause hydrocephalus from pressure upon the third ventricle.

The diagnosis of these tumors requires close co-operation between the internist, neurosurgeon, radiologist and ophthalmologist. The major clinical signs and/or symptoms are headaches, dizziness, scotoma, failing vision, diminution in visual fields, gain in weight, enlargement of the hands and feet, acromegaly and diabetes insipidus.

Positive radiographic signs may be entirely absent. Scout films should be made of the skull and detail spot films of the sella turcica in both the lateral view and in the occipital view projected through the foramen magnum. The most frequent direct radiographic sign of a pituitary neoplasm is alteration in the size and shape of the sella turcica. Other direct evidence is atrophy or erosion of the dorsum sella and posterior clinoid processes, unilateral erosion of the floor of the sella which may extend into sphenoid sinus and calcification in the tumor or wall of a cyst. Atrophy of the anterior clinoid processes may occur but is relatively infrequent.

The indirect signs are the secondary signs of

increased intracranial pressure such as diastasis of sutures, convolutional atrophy and dilated venous channels. These signs are rather infrequent as these tumors seldom grow large enough to cause them.

Three basic methods have been used in the treatment of these neoplasms, surgery, irradiation and surgery followed by post operative irradiation. The mortality in surgery varies from 10 to 15 per cent. This method of treatment is definitely indicated in the Rathke pouch tumors, cystic type tumors, when signs of hemorrhage into a tumor are present, when blindness is imminent, when there is increasing intra cranial pressure and cases where there is a failure to respond to irradiation.

There is no mortality when irradiation is the method of treatment, 90 per cent of the eosinophilic and 50 per cent of the chromophobic type tumors can be expected to respond favorably to adequate dosage. Paterson recommends a tumor dose of 6000r in five weeks. He uses three lateral fields. Our method is to deliver a somewhat similar dose in the same period of time but through two lateral and supplementary frontal, intra orbital or occipital fields to bring the tumor dose up to the predetermined level.

Radon seed implanation according to the method of Northfield has proved generally unsatisfactory and is seldom used.

Irradiation should be started cautiously because of the possibility of cerebral edema during the initial stages of the treatment. Headache, nausea, dizziness or vomiting justify an immediate interruption of the treatment and the institution of the proper indicated therapy. We start our treatment with initial small doses and routinely use heavy filtration; Thoreous giving a HVL beam of 2.3 mm copper. Epilation in the treated areas occurred in both of our cases; however in each instance a full growth of hair has returned due we believe to the use of heavy filtration. The beams must be directed so as to avoid the lens and frequent visual field studies are advised.

The success of the treatment is shown by the loss of the headaches, decrease in urinary frequency, an increase in urinary concentration in diabetes insipidus and most important, improvement in the visual fields. Changes in the body outline, weight and appearance are unreliable and may be due to other causes.

In Davidoffs series of 59 cases, 36 or 61 per cent responded satisfactory to surgery, 34 of these were of the chromophobic type and 2 were of the eosinophilic variety. He treated another series of 88 cases by irradiation giving 3 or 4 courses, 4 to 8 weeks apart and 3000r in air per course. 43 or 49 per cent of these cases showed a satisfactory response. 25 of 59 of the chromophobic type and 18 of 29 eosinophilic. Kerr in a series of fifty cases gave 8 to 9000r in air in a single course completed in 3 to 4 weeks. 36 or 70 per cent of his cases treated by this method responded satisfactory. 26 of 37 chromophobic and 8 of 11 eosinophilic type.

Case one in our series was treated in a single course delivering a tumor dose of 5640r in four weeks. Case two was treated in two courses. During the first course a tumor dose of 4940r was delivered to the pituitary gland in five weeks. After an eight week rest an additional dose was administered to the case receiving the two courses.

Both cases have shown a similar satisfactory response and no recurrence to date. Cases have been followed as long as fifteen years after irradiation without a recurrence.

REFERENCES: *Dr. Hickman*

1. LOVE, G.: Diagnosis and Surgical Treatment of Pituitary Tumors: Surg. Cl. of N. Am. 32: 1005-1016; 1952.
2. KERR, D.: Irradiation of Pituitary Tumors; Am. Jour. of Roent. and Rad. Ther. 60: 348-359; 1948.
3. EVANS, W. G. and G. PICCIOTO: Chromophobe Adenoma of the Pituitary: Br. J. Rad. 21: 330-336; 1948.
4. SOSMAN, M. C.: Cushing's Disease — Pituitary Basophilism: Am. J. Roent. 62: 1-31; 1949.
5. BUSCHKE, F.: Radiotherapy of Pituitary Adenoma: West. Jour. of Surg. 58: 271-278; 1950.
6. CANTRIL, S. T. and F. BUSCHKE: Roentgen Therapy of Pituitary Adenoma: West. Jour. of Surg. 54: 403-407; 1946.
7. HORRAX, G. and H. F. HARE, J. L. POPPEN, L. M. HURXTHAL, and O. Z. YOUNGHUSBAND; Chromophobe Pituitary Tumors, II Treatment: J. Clin. Endocrin. Metab. 12: 631-641; 1952.
8. MUFSON, J. and S. S. BLANKSTEIN: Roentgen Therapy of Pituitary Adenoma: Wisconsin Med. Jour. 45: 680-685; 1946.
9. YOUNGHUSBAND, O. Z. and G. HORRAX, L. M. HURXTHAL, H. F. HARE and J. L. POPPEN: Chromophobe Pituitary Tumors, I Diagnosis: J. Clin. Endocrin. and Metab. 12: 611-630; 1952.