PARS INTERMEDIA BASOPHIL ADENOMA OF THE HYPOPHYSIS *

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Recent reviews of Cushing's pituitary basophilism (Tesseraux,[1] Brauer,[2] Pardee,[3] Bland and Goldstein,[4] and others) indicate that the rôle of the hypophysis in this syndrome is far from being settled. There are certainly many cases of this type in which no basophil adenoma is demonstrable, and some without any hypophyseal tumor of any kind. The 2nd case reported by Ulrich [5] is an example where no evidence of adenoma could be found in any organ. Practically all cases, however, show some hyalinization of the basophils as described by Crooke.[6] Statements to the effect that there is hyperplasia of the basophils of the anterior lobe, but no distinct adenoma, must be taken with considerable reservation because of the failure to recognize the irregular distribution of these cells normally, the lack of quantitative methods (Rasmussen [7]) and insufficient examination of the gland.

Many basophil adenomas have been found without being accompanied by so-called pituitary basophilism (Kraus,[8] Costello,[9] and Susman [10]). Close [11] reported a case where the only symptom common to pituitary basophilism was high blood pressure. The syndrome has occurred in cases purported to show acidophil adenomas of the hypophysis (Reichmann,[12] Konschegg,[13] and Horneck [14]), and where the hypophyseal tumor was strictly chromophobic (Fuller and Russell [15]), or chromophobic with a few scattered basophils (Crile, Turner and McCullagh [16]). The case reported by Bettoni,[17] in which the anterior lobe was almost completely occupied by a chromophobic adenoma, probably belongs in this general category. In a number of instances it has been impossible to be definite as to the basophilic character of the tumor. In the 1st case reported by Ulrich,[18] slight indications of the basophilic character of the granules could be obtained only with great effort and then only in a few of the larger cells. In all recent extensive lists of cases there are several in which the type of adenoma was not clearly established.

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A high percentage of cases with the syndrome of pituitary basophilism have either an adrenal cortical tumor or distinct hypertrophy of the adrenal cortex. McQuarrie, Johnson and Ziegler [19] have emphasized the fact that the electrolyte pattern of the plasma in most respects may be diametrically opposite to that found in Addison's disease, and hence suggest "hypercorticoadrenalism" as the most expressive name of the syndrome. This is further strengthened by the studies of Jores,[20] and by Anderson and Haymaker,[21] who found evidences of increased adrenal cortical hormone in cases of Cushing's disease. Bauer [22] is rather emphatic that the syndrome is a form of interrenalism, while Kraus [8] argues that both the hypophyseal and adrenal changes are compensatory in nature, secondary to fat metabolism and associated metabolic disturbances. Various differential diagnoses between adrenal cortical hyperfunction, basophil adenoma of the hypophysis and arrhenoblastoma of the ovary have been attempted (Goldzieher and Koster [23]), but great difficulty still exists as is shown by a case (Norris [24]) presenting a malignant ovarian tumor. The report by Walters, Wilder, and Kepler [25] on the suprarenal cortical syndrome represents the situation well. A very recent case (Pons and Pappenheimer [26]) with the "classic" features of so-called pituitary basophilism showed neither a basophil adenoma nor hyalinization of the basophil cells and was finally designated "renal hyperparathyroidism."

It is, therefore, advisable to record all basophil adenomas of the hypophysis so that their significance may be better understood. Apparently it is necessary to allow for a fair percentage of chance coincidence. The cases reported here are of special interest because the adenomas appear to have arisen from the same source as the basophilic cells that normally invade the neural lobe. Since these invading basophils normally differentiate from the pars intermedia (Rasmussen,[27] Roussy and Mosinger,[28] Plaut,[29] and Lennon [30]) we are apparently dealing with pars intermedia tumors. The migration of basophilic cells into the neural lobe has been greatly discussed in recent years, particularly in connection with hypertension (Cushing [31, 32]). Ahlström,[33] Gómez Marcano,[34] and Leary and Zimmerman [35] present additional data that have been interpreted as supporting more than mere chance correlation between the invasion and hypertension. Yet Gómez Marcano does

not consider that a constant relation exists between the degree of basophilic invasion and the height of the blood pressure. Most observations, however, do not favor any relation (Kraus,[36] Spark,[37] Biggart,[38] Berblinger,[39] Butt and Van Wart,[40] Seecof,[40] Boyd,[40] Hawking,[41] Scriba,[42] Plaut,[29] Parsons,[43] and Rasmussen [44]), although a few of these authors think there is some connection between the abundance of basophils in the *anterior* lobe and high blood pressure. Again, Kraus thinks this basophilic invasion may be related more directly to adiposity than to blood pressure, particularly in eclampsia.

In connection with diffuse basophilia of the anterior lobe and its relation to blood pressure, it should be noted that only in the reports by Hawking [41] and Rasmussen [44] were the cells enumerated, and both these studies show that the increase in percentage of basophils in essential hypertension is not regular enough to be regarded as possessing etiological significance.

The following cases are presented as additional evidence that great caution is still necessary in estimating the effects of basophil adenomas of the hypophysis.

Case Reports *

Case 1: The tumor was found unexpectedly at autopsy in a well developed 77 year old white male who was admitted to the University of Minnesota Hospital May 10, 1937 because of nocturia, urgency, incontinence and loss of weight of 9 months duration, although he had had mild urinary symptoms for many years. Slowness of speech and comprehension had been evident for a year. Occasional edema of the ankles occurred. The blood pressure 1 year before admission was 260/90 mm. Hg. He had slight dyspnea but no other cardiorespiratory symptoms.

On admission the systolic blood pressure ranged from 200–260 mm. Hg., and the diastolic from 115–150 mm. Hg. An occasional extra systole was noted. Pitting edema of the ankles was present. The prostate was moderately enlarged. Residual urine amounted to 750 cc. and contained traces of albumin and numerous blood cells but no sugar. The blood showed 85 per cent hemoglobin, 10,300 leukocytes and 62 per cent neutrophils. The blood urea nitrogen was 22 mg.; phenolsulphonephthalein 44 per cent; Wassermann negative.

Within 2 days there developed thickness of speech, dropping of left side of mouth, deviation of the uvula and tongue, modified reflexes and

* We are indebted to the Department of Surgery, University of Minnesota, for permission to publish these cases.

weakness of the left extremities. The electrocardiogram indicated auricular fibrillation and ventricular extrasystoles. A cystostomy was done a week later and the prostatic condition greatly improved. Symptoms of cerebral thrombosis persisted and the patient died on the 18th day.

Autopsy Findings

The autopsy was performed 45 minutes after death. The body was emaciated, 171 cm. in length and weighed about 115 pounds. A subcutaneous lipoma 4 cm. in diameter was present in the left hypochondriac region. The heart weighed 430 gm. and showed slight left ventricular hypertophy but no fibrosis of the myocardium. The mitral and aortic valves, coronary arteries and the root of the aorta showed moderate senile atheromatosis. The kidneys were quite smooth and weighed 130 and 150 gm. respectively. The parenchyma was pale and slightly fibrous. Microscopic sections revealed slight senile arteriosclerotic changes but no hypertensive changes. Moderate bilateral hydronephrosis and hydroureter were present. The bladder was markedly trabeculated. There was moderate hemorrhagic cystitis. The lateral lobes of the prostate were slightly hypertrophied, there was a fibrous median bar formation, and sections showed irregular nodular adenocarcinomas. The adrenals were normal. The left testis was markedly atrophic. The thyroid was small, brown and fibrous with an adenoma (3 by 3.5 by 4.5 cm.) at the left lower pole. This adenoma contained a cyst measuring 2 cm. in diameter with a calcified wall. The parathyroids were normal. No thymic tissue could be seen.

The blood vessels at the base of the brain were sclerotic and greatly reduced in size. After injection with formalin the brain was found on section to contain numerous small cystic areas in the region of the right internal capsule and a few in the left side. On the right was a fairly large area of softening involving the internal capsule and basal nuclei. Microscopic examination revealed no cellular reaction around these cavities. Some were of recent origin.

The upper aspect of the sella turcica appeared to be normal but dissection uncovered a tumor about 1.5 cm. in diameter adherent to the right side of the hypophysis and attached to its lower pole. The adenoma extended underneath the right internal carotid

artery (Fig. 1), and depressed the roof over the right side of the sphenoid sinus, but did not appear to have invaded the bone at any point. Discovery of this neoplasm stimulated a more careful examination of the body for further evidences of endocrine disorders, but the body build, muscular development and hair distribution were all normal. There was no evidence or history of obesity, purple striations or acromegaly. After serial sections of the hypophysis showed the tumor to be a basophil adenoma, the records were carefully checked but no signs or symptoms indicative of pituitary basophilism existed, except the high blood pressure.

The hypophysis was somewhat asymmetrical on account of the pressure of the tumor on the right side. The tumor was cut so that part of it remained attached to the hypophysis and the rest was removed with the internal carotid artery. Both blocks of tissue were fixed in formalin, cut at 5 μ and stained with the Mallory-Heidenhain and hematoxylin-eosin stains. A rather sharp boundary line, which gradually merged into the connective tissue capsule of the anterior lobe more anteriorly, separated the new-growth from the anterior lobe (Fig. 2). As the series of sections were followed toward the lower pole the tumor became denser, large nodules of strongly basophilic cells appeared (Fig. 3) and there was continuity with a great mass of similar cells that infiltrated the neural lobe (Fig. 3).

A careful study of serial sections indicates that the outgrowth has been from the lower pole of pars intermedia — a region where basophilic invasion of the neural lobe is prevalent. The cells in well preserved portions of the adenoma are identical with the cells not only in the adjacent neural lobe but also in remote regions of this lobe (Fig. 2) where they have unquestionably been derived in the usual manner from the pars intermedia. The cells are variable in size. None are excessively large. They are distinctly granular but only occasionally vacuolated. A high power view of the area marked + in Figure 3 is shown in Figure 5. Much of the tumor contains only small, irregular basophilic islands (the dark areas in Figure 4) in which the cells are degenerating and contain only a few basophilic granules. The intervening region consists of a loose network of connective tissue invaded by neutrophils and containing some scattered indifferent cells with little or no cyto-

plasm and cells in various stages of degeneration. In limited areas there is diffuse hemorrhage and fibrin formation. As a whole the tumor is poorly vascularized. There is a small indifferent staining region in the anterior lobe (Figure 2, just below the end of the leader to the anterior lobe) which appears to be degenerative. No hyalinization of the basophils is present.

Comment: Owing to the advanced age of this individual, one would hesitate to associate the high blood pressure with the basophilia. The probability of mere chance coincidence would appear to be too great. It should also be recalled that hypertension is not uncommon in acromegalia which is due to acidophil adenoma. Jéquier [45] found this to be true in over a third of the cases. Hypertension has been found in 60 per cent of acromegalic females over 40 years of age. The literature is well reviewed by Houssay.[46]

CASE 2: A white female, 55 years of age, was admitted to the University of Minnesota Hospital Nov. 22, 1937, with a strangulated umbilical hernia. Because of the condition of the patient no physical findings, except those immediately connected with the hernia, were obtained. She was operated upon immediately. Some dark loops of intestine near the hernial sac became progressively better in color, showed active peristalsis, and were, therefore, returned to the abdomen and the hernia repaired. The systolic pressure was down to 70 mm. Hg. Transfusion of 700 cc. of blood and 800 cc. of normal saline brought the systolic pressure to 90 mm. Hg. where it stayed. The patient was cyanotic and was put in an oxygen tent but expired the same day.

Slightly less than a year preceding death the patient was examined by a local physician because of dyspnea and a fainting spell. Her weight at that time was 225 pounds and the blood pressure was 204/96. The lower parts of the legs were edematous. The urine was free from sugar and albumin. Six months previously she had been examined by another physician during an acute attack of influenza. The hypertension and dyspnea were evident at that time. The heart sounds were slightly irregular and rather weak. A moderate number of granular casts were present in the urine.

Obesity and hair on the face appeared shortly after the birth of her first child, 33 years ago. She had three normal children subsequently and continued to menstruate regularly till 51 years of age. She even menstruated once when 54 years of age.

Autopsy Findings

The autopsy was performed about an hour after death. The body was very obese, 168 cm. in length and about 210 pounds in

weight. The obesity was marked on the trunk and upper portions of the extremities. There was slight edema of the legs and numerous varicose veins. Papillomas up to 1 cm. in diameter were present on the right labium majus, the inside of the right thigh, the right nipple, and small ones were present on the upper eyelids. A heavy growth of thick stiff hairs was present around the mouth and on the chin. Purple striae were clearly evident on the abdomen. The outward features were characteristic of Cushing's pituitary basophilism so that the body was carefully examined for further evidences of this syndrome.

The umbilical hernia had been repaired and was in good condition and there was no peritonitis or ascites, but about 6 feet from the ileocecal valve was a segment of small intestine 10 cm. long which showed early gangrene. The abdominal subcutaneous fat was 6 cm. in thickness. The heart weighed 575 gm. There was marked ventricular hypertrophy on the left and slight hypertrophy on the right. The myocardium of the anterior portion of the left ventricle showed a moderate degree of old spotty fibrosis but no large infarction. The valves were normal. The foramen ovale was closed. Atherosclerosis was moderate in the coronary arteries and much of the aorta. There was a stone 7 mm. in diameter in the common bile duct and the gall bladder was tightly filled with about fifty stones. A moderate degree of fat replacement was evident in the pancreas. The kidneys were essentially normal on gross appearance but sections showed a moderate degree of hypertensive changes in the small arteries and arterioles. The adrenals were normal. The uterus weighed 225 gm. and contained about a dozen interstitial myomas up to 2 cm. in diameter. The cervix uteri was eroded and cystic. The uterine tubes and right ovary were normal. The left ovary was replaced by a multilocular cystic mass 7 by 8 by 10 cm. which contained clear yellow fluid. The wall of one of these cysts had a few early papillomatous growths. There were a few small cysts around the right ovary. At the lower pole of each lobe of the thyroid was an adenoma of the mixed type. The one on the left was 3 cm. in diameter and was calcified, while the one on the right was soft, pale in color, and measured 4 cm. in diameter. Sections of the thyroid indicated moderate atrophy and fibrosis with lymphocytic foci. The parathyroids were normal. No thymic tissue was visible.

The brain weighed 1210 gm. and showed nothing unusual beyond a moderate degree of sclerosis in the vessels at the base. The sella turcica was normal. The hypophysis weighed 0.682 gm. and except for a moderate degree of cupping on top gave no outward indications of any abnormality. It was fixed in formalin, sectioned serially and stained as in Case 1. A definite basophil adenoma about 3 mm. in diameter was found on the left side of the upper region of the pars intermedia and extending into the rim formed by the depression of the cerebral part of the upper surface of the gland (Figs. 7).

On microscopic examination the cells of the adenoma are found to be strongly basophilic, densely packed (Fig. 6), and to compress the upper left pole of the anterior lobe from which the adenoma is separated by a sharp boundary line in which are flattened colloid vesicles and other traces of pars intermedia (Figs. 7 and 8). At about the middle of the series it becomes less compact and merges into a stratum of basophilic cells which extends across the entire anterior portion of the neural lobe and enlarges at the right margin so that there is a more or less symmetrical bilobed basophilic area throughout the rest of the gland to the lower pole (Fig. 9). The cells of the adenoma proper (Fig. 6) present the structural features of the basophilic cells that normally migrate into the neural lobe. In the interior is an irregular fluid-filled space (Fig. 7) which has no definite wall. There are no indications of degeneration.

Numerous, small circumscribed masses of basophils (Fig. 10) are found throughout most of the anterior lobe, particularly in the upper part of the gland and near the pars intermedia. Larger areas of more diffuse basophilia are intermingled with the above so that there is an excess of basophilic cells in the anterior lobe also. An actual differential count of the cells of the anterior lobe showed that there were 39 per cent chromophobes, 30 per cent acidophils and 31 per cent basophils. The average percentage of basophils in females normally is about 7 per cent and they rarely reach 17 per cent.[7] There is no hyaline change such as is almost always evident in pituitary basophilism. This hyalinization is regarded by Crooke as an expression of altered physiological activity, while Severinghaus [47] thinks it is a degenerating process.

Comment: In spite of the adenoma and the excess number of

basophils in both lobes of the hypophysis and the presence of several of the characteristics of Cushing's syndrome, there were no menstrual disturbances, glycosuria, osteoporosis, hypertrophy of the adrenal cortex, or hyaline change in the basophilic cells of the hypophysis. The obesity had existed for nearly 33 years. Crooke and Russell would exclude this from the list of true pituitary basophilism.

At least 2 other basophil adenomas apparently originating from the pars intermedia are on record — the Raab-Kraus case and Case 6 (fatal eclampsia) reported by Cushing — both described in detail by Cushing.[32] They were wholly within the posterior lobe. A 3rd case, published by MacCallum, Futcher, Duff and Ellsworth,[48] is undoubtedly an anterior lobe tumor. It was strictly within the anterior lobe but posteriorly extended to the intermediate region. Their principal reason for considering it of pars intermedia origin was the mistaken idea that the copper hematoxylin method stains the basophils of the anterior lobe dark blue. The tumor by ordinary stains was basophilic but did not stain with copper hematoxylin. The facts are that it is the acidophils of the anterior lobe that stain deep blue with copper hematoxylin,[49] and neither the basophils of the anterior lobe nor those that arise from the pars intermedia take this stain strongly.

Summary

Two cases of basophil adenoma originating from the pars intermedia are described. In 1 case the only symptom at all referable to the hypophysis was high blood pressure. On account of the old age of this individual (77 years) the association of the adenoma with the hypertension is questionable. In the 2nd case a number of the major characteristics of pituitary basophilism (adiposity, striae atrophicae, hirsuties, high blood pressure, florid face) were present. In neither case were there any hyaline changes in the basophils.

There was considerable diffuse invasion of the neural lobe by basophils in both cases. The great bulk of data, however, does not indicate that there is any direct significant correlation between this invasion and hypertension.

REFERENCES

1. Tesseraux, H. Zur Kasuistik und Pathologie der Cushingschen Krankheit. *Endokrinologie*, 1936, **18**, 379–394.

2. Brauer, E. W. Zur Kenntnis des Morbus Cushing. *Endokrinologie*, 1936, **19**, 10–19.

3. Pardee, Irving. Pituitary basophilism of Cushing — syndrome of the basophilic adenoma. *Bull. Neurol. Inst. New York*, 1937, **6**, 183–198.

4. Bland, P. Brooke, and Goldstein, Leopold. Pituitary basophilism; a review of 42 verified cases, with a report of a personal case. *Surg. Gynec. & Obst.*, 1937, **65**, 644–656.

5. Ulrich, Henry L. Pituitary basophilism without adenomata anywhere. *Minnesota Med.*, 1936, **19**, 535–537.

   (See also de Jongh, C. L. Cushing syndrome (basophil adenoma of pituitary). *Nederl. tijdschr. v. geneesk.*, 1935, **79**, 1805–1811.)

6. Crooke, A. C. A change in the basophil cells of the pituitary gland common to conditions which exhibit the syndrome attributed to basophil adenoma. *J. Path. & Bact.*, 1935, **41**, 339–349.

7. Rasmussen, A. T. The proportions of the various subdivisions of the normal adult human hypophysis cerebri and the relative number of the different types of cells in pars distalis, with biometric evaluation of age and sex differences and special consideration of basophilic invasion into the infundibular process. *Proc. Assoc. Research Nerv. Ment. Dis.* (Session of Dec. 1936), 1938, **17**, 118–150.

8. Kraus, E. J. Morbus Cushing, konstitutionelle Fettsucht und interrenaler Virilismus. Nebst Bemerkungen über den "Diabète des femmes à barbe." *Klin. Wchnschr.*, 1934, **13**, 487–489.

9. Costello, Russell T. Subclinical adenoma of the pituitary gland. *Am. J. Path.*, 1936, **12**, 205–216.

10. Susman, William. Adenomata of the pituitary, with special reference to pituitary basophilism of Cushing. *Brit. J. Surg.*, 1935, **22**, 539–544.

11. Close, H. G. Basophil adenoma of the pituitary gland with renal changes. *Brit. M. J.*, 1935, **1**, 356–357.

12. Reichmann, V. Über ein ungewöhnliches Krankheitsbild bei Hypophysenadenom. *Deutsches Arch. f. klin. Med.*, 1919, **130**, 133–150.

13. Konschegg, Th. Über die Cushing'sche Krankheit. *Frankfurt. Ztschr. f. Path.*, 1935, **48**, 486–492.

14. Horneck, Karl. Zur Klinik des Morbus Cushing. *Ztschr. f. klin. Med.*, 1936, **129**, 191–197. (Same case as that of Konschegg.)

15. Fuller, C. J. Chromophobe adenoma of the pituitary associated with Cushing's syndrome; with a histological report by Dorothy S. Russell. *Lancet*, 1936, **2**, 181–183.

16. Crile, George, Turner, Henry, and McCullagh, Perry. Polyglandular disease. *N. Y. State J. Med.*, 1936, **36**, 475–484.

17. Bettoni, Italo. Distrofia adiposo-genitale con sindrome di virilismo e di diabete mellito; contributo allo studio della genesi del diabete neuroipofisario e dell 'insulino-sensibilita' in dette forme. *Arch. di pat. e clin. med.*, 1932, **12**, 50–75.

18. Ulrich, Henry L. A basophilic adenoma of the pituitary gland. *Minnesota Med.*, 1935, **18**, 73–77.

19. McQuarrie, Irvine, Johnson, R. M., and Ziegler, M. R. Plasma electrolyte disturbance in patient with hypercorticoadrenal syndrome contrasted with that found in Addison's disease. *Endocrinology*, 1937, **21**, 762–772.

20. Jores, Arthur. Die Bedeutung der Hypophyse für die Entstehung des Hochdruckes insbesondere der essentiellen Hypertonie. *Klin. Wchnschr.*, 1936, **15**, 841–846.

21. Anderson, E. M., and Haymaker, W. Prolonged survival of adrenalectomized rats treated with sera from Cushing's disease. *Science*, 1937, **86**, 545–546.

22. Bauer, Julius. Was ist Cushing'sche Krankheit? *Schweiz. med. Wchnschr.*, 1936, **17**, 938–939.

23. Goldzieher, M., and Koster, H. Adrenal cortical hyperfunction. *Am. J. Surg.*, 1935, **27**, 93–106.

24. Norris, E. H. Arrhenoblastoma, a malignant ovarian tumor associated with endocrinological effects. *Am. J. Cancer*, 1938, **32**, 1–29.

25. Walters, W., Wilder, R. M., and Kepler, E. J. The suprarenal cortical syndrome with presentation of ten cases. *Ann. Surg.*, 1934, **100**, 670–688.

26. Pons, J. A., and Pappenheimer, A. M. Renal hyperparathyroidism associated with Cushing's syndrome. *Puerto Rico J. Pub. Health & Trop. Med.*, 1937, **13**, 115–170.

27. Rasmussen, A. T. Origin of the basophilic cells in the posterior lobe of the human hypophysis. *Am. J. Anat.*, 1930, **46**, 461–475.

28. Roussy, G., and Mosinger, M. Sur le lobe intermédiaire de l'hypophyse. La fente hypophysaire et ses annexes, l'immigration de cellules glandulaires dans le lobe nerveux. *Compt. rend. Soc. de biol.*, 1934, **115**, 946–949.

29. Plaut, Alfred. Epithelial invasion in the posterior lobe of the hypophysis. *Arch. Path.*, 1936, **21**, 408.

30. Lennon, G. Gordon. The basophil cell of the hypophysis cerebri: stages in its life-history. *Edinburgh M. J.*, 1937, **44**, 94–99.

31. Cushing, Harvey. Posterior pituitary activity from an anatomical standpoint. *Am. J. Path.*, 1933, **9**, 539–548.

32. Cushing, H. Hyperactivation of the neurohypophysis as the pathological basis of eclampsia and other hypertensive states. *Am. J. Path.*, 1934, **10**, 145–176.

33. Ahlström, Carl Gustaf. Das Vorkommen basophiler Zellinfiltration in der Neurohypophyse bei hypertonischen Zuständen. *Klin. Wchnschr.*, 1935, **14**, 1456–1459.

34. Gómez Marcano, A. Der Hypophysenhinterlappen bei Hypertonie. *Klin. Wchnschr.*, 1935, **14**, 1525–1529.

35. Leary, Deborah C., and Zimmerman, H. M. Basophil infiltration in the neurohypophysis. *Am. J. Path.*, 1937, **13**, 213–228.

36. Kraus, E. J. Über die pathogenetische Bedeutung der Basophilie der Hypophyse, insbesondere für die Eklampsie. *Med. Klin.*, 1935, **31**, 1641–1642.

37. Spark, Charles. Relation between basophilic invasion of the neurohypophysis and hypertensive disorders. *Arch. Path.*, 1935, **19**, 473–501.

38. Biggart, J. H. Some observations on the basophil cells of the human hypophysis. *Tr. Edinburgh Obst. Soc.*, 1934–35, **55**, 113–124.

39. Berblinger, W. Die Basophilen in Adenohypophyse und Neurohypophyse bei essentieller Hypertonie und bei Eklampsie. *Endokrinologie*, 1935, **16**, 19–38.

40. Butt, E. M., and Van Wart, Roy M. A histopathological study of one hundred hypophyses. *Am. J. Path.*, 1935, **11**, 891–892. (Corroborated by Dr. Seecof of Montreal and Dr. Boyd, then of Winnipeg.)

41. Hawking, Frank. Differential cell counts of the pituitary gland in hypertension and endocrine disturbances. *J. Path. & Bact.*, 1936, **42**, 689–702.

42. Scriba, Karl. Die basophilen Zellen des Hypophysenhinterlappens und ihre Beziehungen zur Hockdruck und zur Eklampsie. (Zugleich ein Beitrag zur Frage: Hat der Mensch eine dem tierischen Zwischenlappen vergleichbare Pars intermedia?) *Virchows Arch. f. path. Anat.*, 1936, **297**, 221–251.

43. Parsons, Robert J. The pituitary gland and its relation to age, hypertension and pathological processes: a study of 107 unselected pituitaries. *M. Papers, Christian Birthday Vol.*, 1936, 366–405.

44. Rasmussen, A. T. The relation of the basophilic cells of the human hypophysis to blood pressure. *Endocrinology*, 1936, **20**, 673–678.

45. Jéquier, Michel. Acromégalie et tension artérielle. (A propos d'un cas de tumeur hypophysaire.) *Ann. d'anat. path.*, 1936, **13**, 179–188.

46. Houssay, Bernardo A. Hypophysis and blood pressure. *New England J. Med.*, 1936, **214**, 1086–1092.

47. Severinghaus, Aura E. Cellular changes in the anterior hypophysis with special reference to its secretory activity. *Physiol. Rev.*, 1937, **17**, 556–588. (See also *Proc. Assoc. Research Nerv. Ment. Dis.*, 1938, **17**, 69.)

48. MacCallum, W. G., Futcher, T. B., Duff, G. Lyman, and Ellsworth, Read. Relation of the Cushing syndrome to the pars intermedia of the hypophysis. *Bull. Johns Hopkins Hosp.*, 1935, **56**, 350–365.

49. Rasmussen, A. T. Copper hematoxylin, a stain for the acidophils of the human hypophysis. *Proc. Soc. Exper. Biol. & Med.*, 1936, **34**, 760–762.

DESCRIPTION OF PLATES

PLATE 59

FIG. 1. Case 1. Drawing of the hypophysis and adenoma in relation to the internal carotid arteries. Viewed from above. The lateral margin of the tumor underneath the right carotid artery is indicated by a broken line.

FIG. 2. Case 1. Microphotograph of a horizontal section through the hypophysis and part of the adenoma, which is closely applied to the right side of the hypophysis but sharply separated from the latter at this level. A large number of basophilic cells have invaded the neural lobe quite remote from the tumor. A small, circumscribed degenerating area is seen at the end of the leader in the anterior lobe.

FIG. 3. Case 1. Microphotograph of a horizontal section through the lower pole of the hypophysis at about the middle of the adenoma which is continuous with the basophils of the pars intermedia, which completely encircle the neural lobe at this level. A conspicuous nodule of strongly basophilic cells in the adenoma is indicated by a white +. Except for such nodules the tumor is for the most part loose like the lower third of the figure. At slightly lower levels, where there is no longer any evidence of the neural lobe, the continuity between the adenoma and the pars intermedia is even more evident, but an illustration from this lower level would be less informative than the one here reproduced.

FIG. 4. Case 1. Microphotograph at a higher magnification showing that portion of the tumor which is in contact with the internal carotid artery. The wall of the artery is shown in the lower part of the figure. The irregular scattered dark areas are mostly degenerating basophils.

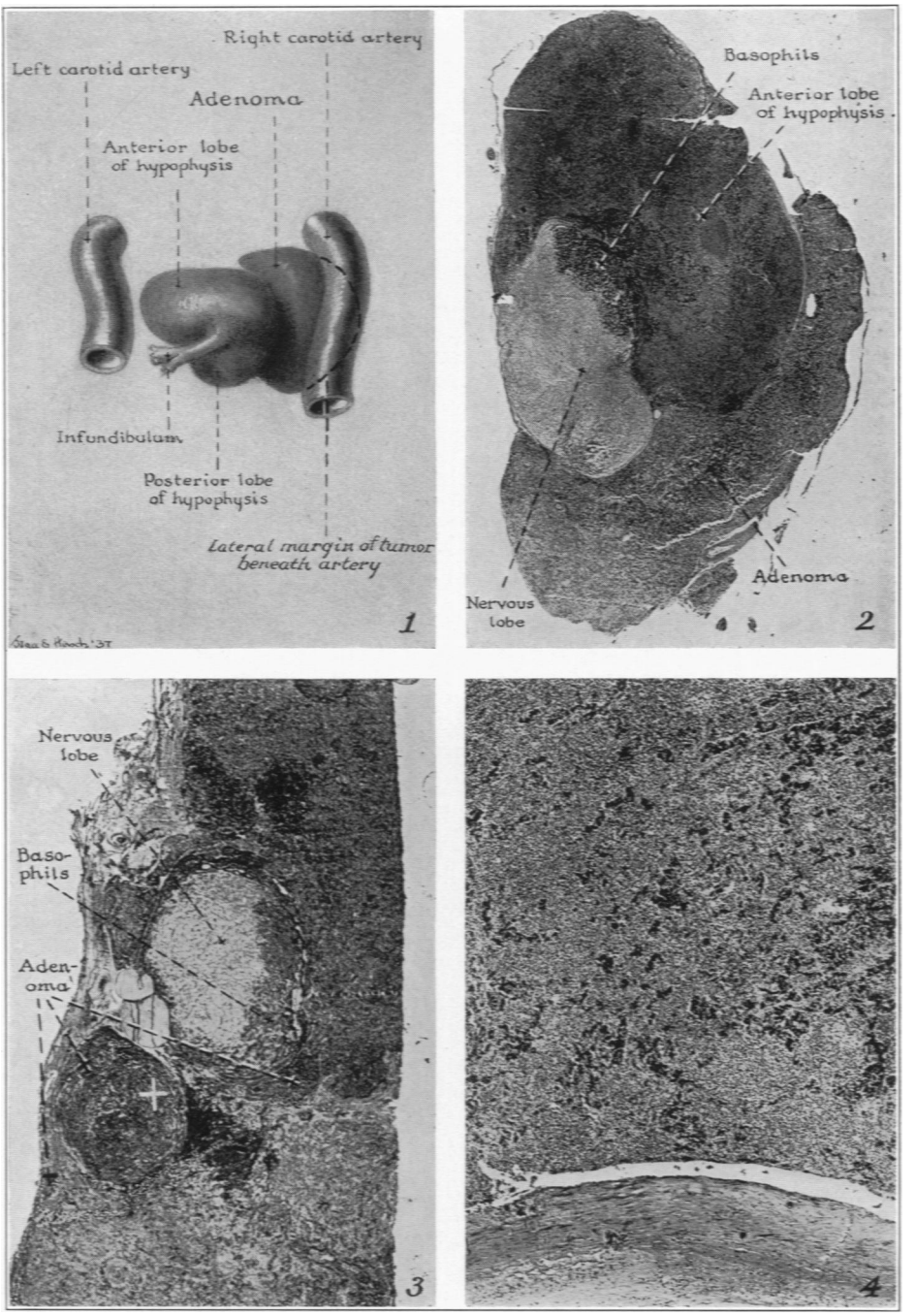

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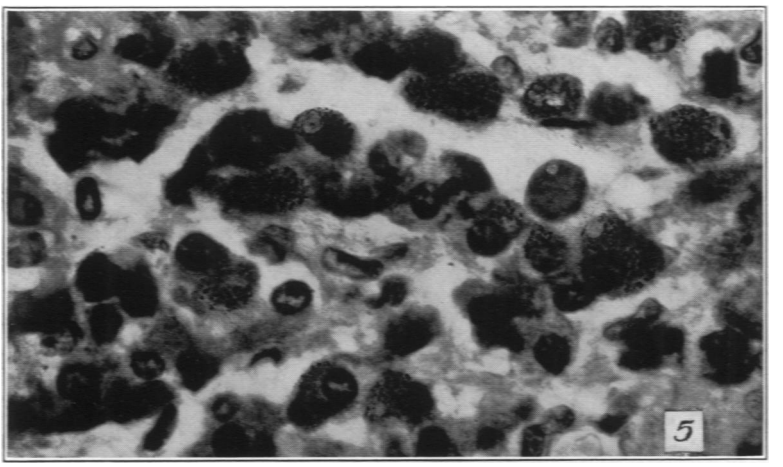
PLATE 60

FIG. 5. Case 1. High power view of the area in Fig. 3 marked with a white +. The cells are variable in size and in degree of granulation and only occasionally vacuolated. In structure and staining reaction these cells are indistinguishable from the basophils that normally differentiate from pars intermedia and more or less invade the neural lobe.

FIG. 6. Case 2. Microphotograph of the center of the basophil adenoma shown in Fig. 7. The cells are small, closely packed and moderately rich in granules. Palisading around the blood vessels is rarely evident. There are no indications of active degeneration.



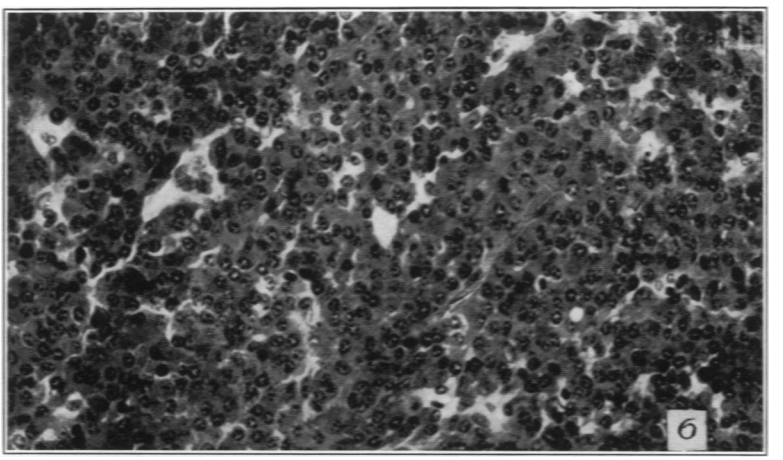


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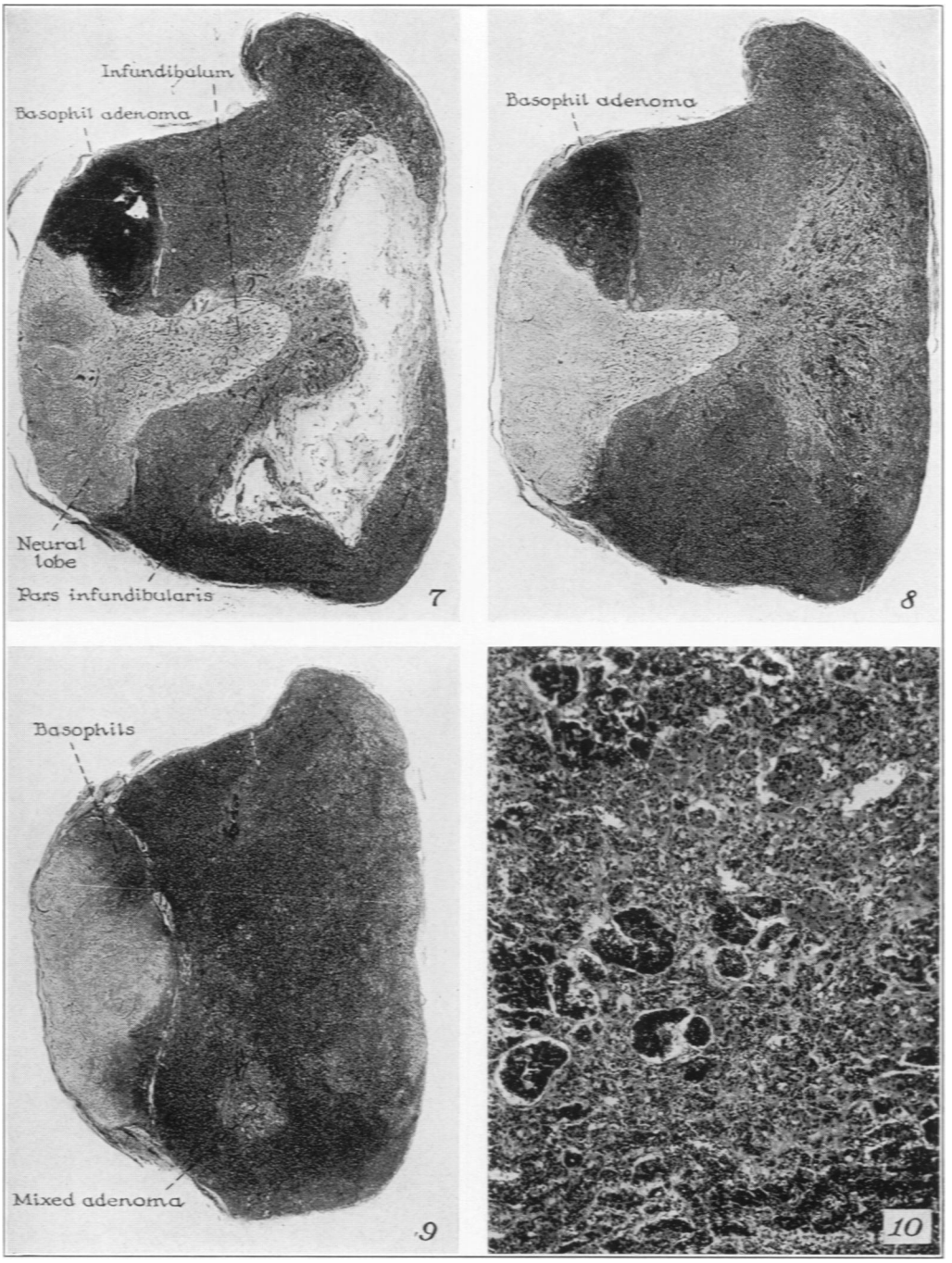
PLATE 61

FIG. 7. Case 2. Microphotograph of a horizontal section through the upper rim of the hypophysis showing the location and general dimensions of the basophil adenoma. Part of the residual lumen and other evidences of the boundary between the anterior lobe and the pars intermedia are still present and indicate that the tumor is strictly within the posterior lobe.

FIG. 8. Case 2. Microphotograph of a horizontal section about a millimeter lower than Fig. 7 showing the adenoma in the same relative position.

FIG. 9. Case 2. Microphotograph of a horizontal section through the middle of the hypophysis and entirely below the adenoma where it has been replaced by a looser mass of basophilic cells derived from the pars intermedia, into which the tumor gradually merges. Diffuse basophilic invasion is present at this and all lower levels on the other side as well and to a lesser extent in the intervening region. In the anterior lobe is a small area having the appearance of a mixed adenoma containing many weakly basophilic cells.

FIG. 10. Case 2. Microphotograph of a typical area of the anterior lobe of the hypophysis showing numerous small circumscribed masses of deeply basophilic cells. Normally such groups of cells are not rare but there is an excessive number in this specimen.



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