MEDULLARY CARCINOMA OF THE SUPRARENAL GLAND  
(PHEOCHROMOCYTOMA)

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Carcinomas of the suprarenal glands are seldom seen, and of these the neoplasms of the medulla are the rarest. For this reason the following example of a tumor of the chromaffin tissues is reported.

CLINICAL HISTORY

The patient was a twenty-seven-year-old white woman who during the past four years had been suffering from intermittent episodes of vomiting associated with severe headaches. There had also been rather severe persistent constipation and periods of great weakness.

Three years earlier an appendectomy had been performed because of the various gastrointestinal complaints, but the operation afforded no relief. The blood pressure was consistently low. The patient had never had abdominal pain prior to the last admission.

On admission the temperature was 101–102° and the chief complaints were vomiting and severe headache. The patient's condition did not appear alarming until the third day. Although her skin had been cold and clammy, with profuse perspiration at times, she always stated that she felt warm. At four o'clock on the morning of the third day she cried out, complaining of severe pain in the region of the umbilicus. Her condition soon became critical and her physician found her in shock; pulse 168, and blood pressure scarcely obtainable. Stimulants were given and the usual measures taken to combat shock, but the patient failed to rally. She died at 10:30 A.M., at which time the pulse was 180 and temperature 105.6° F. As is evident, but few of the symptoms characteristic of tumors of the suprarenal medulla were present.

1 Under the auspices of the Research Fund Committee.
Autopsy

The body was that of a rather emaciated woman weighing about 130 pounds. No rigor mortis was present.

There was a four-inch scar on the abdomen in the right mid-portion. The large intestine was adherent to the anterior wall about the old appendiceal scar. The surface of the peritoneal cavity was glistening.

The pyloric end of the stomach was adherent to the lower portion of the liver. The stomach was greatly dilated and some small areas of erosion were present, but there was no evidence of ulceration. Inspection of the lower portion of the cecum showed the appendix stump adherent to the lateral wall.

The liver was of normal size and consistency, except that the right lobe was somewhat compressed by a suprarenal mass. On section, the liver appeared to be normal. The gallbladder was dilated and emptied with difficulty.

The spleen was small and hard, normal in color and other respects.

![Image: Gross Specimen: Sagittal Section Showing the Encapsulated Tumefaction Compressing the Kidney]

The tumor is cystic and exceedingly vascular.

Just above the right side of the kidney was a large mass measuring 15 × 10 × 7 cm., involving the right suprarenal gland and touching the lower border of the right lobe of the liver. The kidney itself was only about one-third larger than this tumor, which measured 11 × 7 × 2 cm. On cut section a definite capsule was visible, which was fibrous and enclosed areas of hemorrhage. Most of the neoplasm had undergone a cystic degeneration. The tissue was friable, soft, and infiltrated with blood. The more solid portions were of a lemon-yellow color. The mass pressed upon the upper portion of the kidney and did not infiltrate that organ. The kidney was laterally placed, the capsule stripped with difficulty, and there was a slight scarring of the surface. The cortex was uneven, striations were fairly well marked, and the medullary portion was infiltrated with a great deal of fat.

Sections from the kidney showed no metastases, nor was the kidney involved by local invasion at the point of contact with the tumor. The kidney showed a moderate arteriosclerotic lesion.

Microscopically the suprarenal tumor was seen to consist of large granular cells with clear cytoplasm. The growth was diffuse and exceedingly vascular. In portions there was some adenomatous arrangement but the desmoplastic reaction was meager.
FIG. 3. Low-power Photomicrograph showing islands of cells separated by vascular stroma

FIG. 4. High-power Photomicrograph showing lack of stroma between tumor cells, their syncytial arrangement, and variations in size and shape
Microscopic examination of the other organs showed nothing of note.

The diagnosis was medullary carcinoma of the suprarenal gland or pheochromocytoma. A chemical examination of the tumor revealed 2.2 grams of epinephrine per 100 grams of tissue.

**DISCUSSION**

The fact that a wide difference in type, characteristics, and clinical course exists between tumors of the suprarenal cortex and those arising in the medulla finds its explanation in the embryologic origin of the gland. The cortical portion is derived from the splanchnic mesoderm and is contemporary in its development with the mesonephron. The chromaffin cells of the medulla are derived from the ectoderm and have a common origin with cells comprising the sympathetic nervous system. The morphology and the physiological activities of cortical and medullary tumors of the suprarenal gland bear out this double origin, the more rapidly growing cortical tumors being accompanied by changes in the sex characteristics, while many of the medullary tumors resemble in microscopic structure the neurogenic tumors found elsewhere in the body derived from the chromaffin or sympathetic structures.

The primitive cells from which the cells of the adult suprarenal medulla arise likewise serve to produce those growths of the sympathetic nervous system referred to in general as neuroblastomas, both types being derived from a common ancestral group of cells, the sympathogonia. Harbitz tabulated the neuroblastomas as follows: (1) tumors consisting of fully differentiated nerve tissue with ganglion cells and nerve fibers, usually termed ganglioneuroma or genuine neura; (2) tumors made up of chromaffin cells in the sympathetic or parasympathetic tissues, termed paraganglioma, mostly of an epithelial nature; (3) tumors composed of undifferentiated sympathogonia or more differentiated nerve cells, the so-called malignant neuroblastomas, relatively frequent and important growths, whose real nature has been understood only in recent years. He adds that transitional and mixed forms are often encountered, as might be expected from the manner in which the sympathetic system and the suprarenal medulla are developed. The malignancy seems to decrease in proportion to the advanced stage of differentiation and the increasing age of the host, while, on the other hand, the differentiation of the embryonic tissue into ganglioneuroma and chromaffin tissue increases in proportion to the age of the individual.

In 1910, James H. Wright showed that the origin of the neuroblastic type of tumor is in the sympathetic nervous system, and it is to him we owe the name neuroblastoma. The growths, he says, are made up of numerous closely packed, small, atypical cells, with deeply staining round or oval nuclei. Their protoplasm is scanty. In appearance they are like the embryonic, undifferentiated cells of the sympathetic nervous system. Between the cells neural fibers form a finely fibrillated network. No ganglion cells are present. The arrangement often suggests a rosette, the pale, feebly staining center composed of numerous fibrillae, surrounded by radiating cylindrical cells, similar to the structure of certain gliomas of the retina and central nervous system.

On the other hand, the chromaffin-cell neoplasm offers a special problem to the pathologist concerned with tumors of the suprarenal medulla. From
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the sympathogonia, the pheochromoblasts and, in turn, the chromaffin cells are formed. This name has been given to these cells because, when they are mature, their chemical nature is such that treatment with chrome salts causes them to develop a brown color. This accounts for the color associated with adrenalin, which is the specific product of these cells. Pick, in 1912, suggested that tumors arising from these cells should be called pheochromocytomata, but the term “chromaffin-cell tumor” is often used. The neoplasms rarely form metastases and cause death by their physiological activity rather than by mechanical effects.

The papers by Belt and Powell and Rabin sum up the clinical and pathological knowledge of the subject. Two years ago Belt and Powell published a case of chromaffin-cell tumor, with special emphasis upon the clinical symptoms. Reviewing the literature, they found that in the majority of the reported cases the patients manifested signs and symptoms indicating an instability of the sympathetic nervous system, often including paroxysmal sympathicotonia. Chief among these signs and symptoms were hypertension, or paroxysmal hypertension, glycosuria and periodic attacks of tachycardia, vasoconstriction and vasodilatation of the peripheral vessels as shown by pallor followed by flushing of the skin, headache, nausea, vomiting, nervous manifestations with sensations of constriction in the epigastrium, dyspnea, suffocation, or choking. When subjected to surgical procedures these patients manifested an unusual susceptibility to shock. Pulmonary edema and hypertrophy of the heart were the most frequently associated pathological findings.

Belt and Powell’s own patient manifested what they recognized after her death as “a very characteristic and significant history of paroxysmal sympathicotonia.” The preoperative diagnosis was hypernephroma. In preliminary preparation the patient was given three-fourths of a grain of ephedrine hypodermically, and later a spinal anesthetic, 150 mg. of neocaine. The reaction was so violent that the operation was never done, and it was only at necropsy that chemical examination of the tumor tissue revealed an epinephrine content of 2 grams to 100 grams of tissue.

A review of the literature enabled Belt and Powell to tabulate 23 cases of benign pheochromocytomata, accounts of which had been published between 1910 and 1933. The “definite clinical syndrome” observed in their own case proved to have been present in all those collected, and they considered it “possible to explain all the outstanding signs and symptoms, as well as the postmortem findings of these patients, on the basis of the release into the blood stream of excessive quantities of epinephrine.”

The most complete discussion of pheochromocytoma is found in the paper published by Coleman B. Rabin in 1929. His article includes a bibliography complete up to the time of publication and a brief but excellent summary of previous papers. Rabin states that the first report of a medullary tumor of the suprarenal gland that may be considered a pheochromocytoma was that of Berdez (1892), who described a vascular, encapsulated tumor within the medulla of the right suprarenal gland. Like most of the tumors reported subsequently, it did not replace the entire medulla, but was demarcated from the remaining normal medullary tissue. Two years previously Perley had reported such a tumor, but his description of it was too meager to make one
certain of its nature. Manasse, in 1893, reported a tumor observed by him three years previously, which showed the characteristics of a pheochromocytoma. He found the typical hyaline inclusions that are seen in the normal suprarenal medulla, noticed some cells which he considered as probably ganglion cells and also noted tumor cells in the suprarenal veins. Three years later he reported a second case in which he demonstrated the chrome reaction in the cells composing the tumor. Marchetti was the first to describe a bilateral pheochromocytoma of the suprarenal medulla, in 1904. Suzuki recorded three cases, one of which was the first reported as occurring in conjunction with neurofibromatosis. He also noted the presence of sympathetic cells. Laignel-Lavastine and Aubertin in the same year noted the occurrence of melanoderma in their cases. Neusser and Wiesel, in 1910, reported the unusual occurrence of this tumor in a two-year-old child, who had the vascular changes of an epinephrine sclerosis, and at the same time they included a case of Kolisko’s, the first in which signs of vasomotor instability were noted. The first tumor of this nature to be removed at operation was that of Masson and Martin. The patient died of shock, which the authors considered incommensurate with the severity of the operation.

Consideration of the literature leads to the inevitable conclusion that the statement made by Grollman in his recently published book, *The Adrenals*, is correct; that is that the usual clinical course of all tumors of this type is progressive with rapidly fatal termination. Yet the fact that Porter succeeded in removing a growth at first thought to be a tumor of the cortex, but later recognized as a chromaffin-cell growth, with recovery and survival of the patient, and that Charles H. Mayo has a patient still alive seven years after operation, should give hope that increasing knowledge of this particular neoplasm, with earlier diagnosis and prompt surgery, may result in lessening the present high mortality rate.

**BIBLIOGRAPHY**

The following papers include all important references to the subject:

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