A CASE OF THREE NEOPLASMS

B. C. PORTUONDO, M.D.

(From the Department of Pathology, St. Louis University School of Medicine, St. Louis, Mo.)

Multiple primary malignancies are not of uncommon occurrence. Warren and Gates published a series of such cases, of which 243 showed two independent primary malignant neoplasms.

Various criteria have been proposed for the diagnosis of multiple primary malignant tumors. Billroth demanded that each tumor have an independent histologic picture, arise in a different situation, and produce its own metastasis. This would seem much too stringent, as one or more of the primary neoplasms may not have metastasized at the time the material is obtained for study. Warren and Gates postulate that each tumor must present a definite picture of malignancy, each must be distinct, and the probability of one being a metastasis of the other must be excluded. Thus, while Billroth makes an accidental occurrence—the production of metastasis—one of the essentials, Warren and Gates stress only the intrinsic characteristics of the neoplasms. This is obviously preferable, especially as the possibility of one of the tumors being a metastasis of another is ruled out. Other authors mention various criteria for determining the presence of multiple primary neoplasms, but these do not vary intrinsically from those of Warren and Gates.

It would seem that the majority of multiple primary malignant tumors involve the skin, the gastro-intestinal canal, or the reproductive system. Only a few hypernephromata are mentioned in Warren and Gates' report. Neoplasms arising within the cranial cavity are rare, and apparently there are no records of a pituitary tumor associated with neoplasms elsewhere. In the case here reported three dissimilar types of tumor were present. Two of these and a metastasis from the third were within the cranial cavity.

CASE REPORT

A white male garage worker, fifty-three years old, entered Firmin Desloge Hospital of St. Louis University on Feb. 20, 1936. He was in a semicomatose condition and his history was obtained from his wife.

About five years earlier the patient had begun to feel weak and listless and his ordinary activities tired him excessively. He consulted a physician, was told that he had low blood pressure, but continued to work. About fifteen months before admission he noticed dimness and blurring of vision, with double vision at intervals. An oculist was able to give him no help, and the visual disturbances became progressively worse, until by December 1935 he could hardly read the headlines in a newspaper. At that time, also, he began to suffer from distressing headaches from the frontal to the occipital region. On Dec. 17, 1935, he had a severe headache and pain in the right side of his head, which felt as though it had been struck. He did not lose consciousness but was in bed for three weeks. His speech became slow and slurring, and he manifested signs of difficulty in understanding. His face was pulled to the right side and his tongue deviated to the right for a week. There was no paralysis of the extremities. Attacks of vomiting, probably projectile, occurred, the vomitus containing blood. When the patient was again up and about he occasionally staggered to the
right but always corrected this quickly; the visual disturbances remained about the same. On Feb. 11, he awoke with severe headache and vomiting, which lasted about two days. At that time he first became dull, somnolent, and non-responsive to questioning. Occasionally involuntary voiding occurred.

The past history was insignificant. The patient had had typhoid fever in 1916 and had suffered from hay fever and asthma all his life. For the past four years he had been deaf in his right ear. A hemorrhoidectomy was done in 1935. His father died of apoplexy, his mother, still living, was an invalid. He had four siblings living and well. His wife and two children were also living and well.

The patient appeared well developed; he was in a semicomatose state, was aroused with difficulty, answering questions with a slow, slurring speech and dropping back to sleep. He was oriented for time and place, but appeared mentally dull and slightly irritable when aroused. His face showed a left-sided weakness. The left pupil was slightly larger than the right. There was a slight reaction to light but none to accommodation. Both optic discs were choked, but the left somewhat more than the right. The external ocular movements were normal. There was a history of a left homonymous hemianopsia. While the superior part of the left seventh nerve was normal, there was a weakness of its inferior portion. The tongue deviated to the right on protrusion. There was a slight stiffness of the neck. The fifth cranial nerve appeared normal. There were positive apposition and pronation on stroking the base of the palm of either hand. The left hand was weaker than the right. The abdominal and cremasteric reflexes were absent. There was astereognosis of the left hand. The right knee jerk was greater than the left. The left side showed a positive Chaddock sign.

The heart was slightly enlarged. The pulse was 76 and the blood pressure 110/92. The sounds were clear and distinct with no thrills or murmurs. There were no areas of dullness over the chest and no rales were heard. The breath sounds were clear and distinct. The abdomen showed no tenderness, nor were any abdominal masses palpable. The percussion note showed the usual variations.

A blood count showed red cells 3,540,000 per c. mm.; white cells 9150 to 16,750 per c. mm. The differential count (Schilling) was as follows: juvenile forms 2 per cent; stab forms 9; segmented forms, 78; monocytes 3; lymphocytes 8. The non-protein nitrogen was 33 mg. per 100 c.c., and the blood sugar 90 mg. per 100 c.c. The Wassermann and Kahn tests were negative.

The urine was amber in color and its specific gravity was 1.018. It contained no sugar or albumin. Two or 3 white blood cells per low-power field and an occasional cellular and hyaline cast were observed.

Ventricular puncture and ventriculography, Feb. 25, showed internal hydrocephalus, involving the anterior and posterior horns as well as the third ventricle. No cerebellar tumor was found at operation, but the gyri were widened and swollen.

The patient failed to rally following operation and was unconscious until his death, Feb. 29, 1936. The temperature ranged from 100 to 104.4° F.

Necropsy was performed about six hours post mortem by the author and C. W. McNamara.

The pericardial cavity was slightly displaced to the left and contained about 1 c.c. of a thin, clear fluid. The coronary arteries showed some tortuosity and fibrous tissue thickening. All the chambers of the heart were of the usual size and shape and lined by a thin, smooth, intact endocardium. No thrombi were encountered. The musculature was somewhat soft and paler than normal. The intimal surface of the aorta contained some irregular, raised, yellowish plaques of atherosclerosis.

The diaphragm reached the level of the third interspace on the left and of the second on the right side. The linings of the pleural cavities were thin, shiny, and intact, with no fluid, exudate, or hemorrhage. The lungs were heavier than usual, of a gray-black color and reduced in size. There was a diminution of crepitation throughout, and the cut surface revealed a wet, purplish-red parenchyma. The mucosa of the bronchi was reddened, and some grayish yellow tenacious fluid was found in their lumina.

The peritoneal cavity had a thin, glistening, intact lining and contained no fluid, hemorrhage, or exudate. The inferior margin of the liver was found at the level of the sixth right interspace. The other viscera occupied their usual positions.
The entire gastro-intestinal canal had a thin wall and a thin, velvety, intact mucosa showing the usual regional markings throughout. The liver had the nutmeg appearance of passive hyperemia, with a thin capsule covering a smooth surface. The gallbladder was thin-walled and all ducts were patent. The pancreas was firm and well lobulated throughout.

The spleen was moderately enlarged and soft. The cut surface showed a dark mulberry-colored parenchyma which could easily be scraped away.

The adrenals were of the usual size and shape, the cortex thin and of an ochre yellow color; the medulla showing cystic degeneration.

The left kidney was of the usual size, shape, and color, with a thin capsule which stripped easily. The cut surface revealed congestion of all vessels and the usual cortico-medullary proportions. The right kidney was enlarged and of a bizarre shape due to the presence of a firm mass on the postero-lateral aspect opposite the hilus. This mass was irregularly round, with a maximum diameter of about 6 cm. Its cut surface was of a yellowish hue and it contained many areas of softening and of hemorrhage, giving it a variegated
appearance. The central portions of the tumor were softened. The renal vein was invaded by masses of tumor. The ureters and bladder showed no dilatation; their vessels were not injected nor their walls thickened. The prostate was slightly enlarged, firm and smooth throughout.

There was some injection of the vessels of the thin, glistening meninges. The usual amount of a thin, clear cerebrospinal fluid was encountered. In the middle cranial fossa the

![Fig. 3. Cerebellum Showing Area of Hemorrhage](image3)

sella turcica was enlarged, the clinoid processes were absorbed, and the diaphragma sellae was stretched to cover a rounded, bulbous mass extending about 2.5 cm. above the margins of the pituitary fossa. The tumor was roughly oval in shape with a diameter of about 3 cm. It was not definitely encapsulated. The surface was smooth and the consistency apparently gelatinous. The mass was of a light amber color throughout. It had no connection with the basis cerebri.

The gyri of the brain were slightly flattened, while the sulci were shallower than usual. The optic chiasm was slightly displaced to the right. The optic tracts were more widely separated and the medial aspects somewhat atrophic. The right tract was much smaller than the left.

In the angle between the pons and the cerebellum, on the right side, was a soft, rounded tumor about $3 \times 3$ cm., in close relationship to the facial and auditory nerves. While the external surface of the neoplasm was of a grayish white color, the internal surface had a yellowish cast streaked with bands of a more translucent appearance. The tumor lay in a shallow fossa in the brachium pontis of the right side.

![Fig. 4. Photomicrograph of Cerebellum Showing Metastasis of the Hypernephroma. × 60](image4)
The lateral ventricles were moderately dilated but lined by thin, intact membranes. In the left lobe of the cerebellum was a hemorrhagic cyst about 3.5 cm. in diameter, containing a laminated chocolate-brown blood clot. Extending from the cyst was a broad area of hemorrhagic necrotic tissue which permeated the vermis to reach the anterior portion of the right cerebellar lobe.

Blocks of tissue of the usual size and shape were fixed in 10 per cent formalin for about five days, imbedded in paraffin, cut at 7 micra and stained with hematoxylin and eosin. The pituitary tumor was fixed in Zenker-formol for twenty-four hours, washed in running tap water for another twenty-four hours, imbedded in paraffin, and cut at 7 micra. The sections were stained with Kindell's modification of the eosin methyl-blue stain of Mann.

Sections of the right kidney showed a tumor rather poorly separated from the renal parenchyma by bands of adult fibrous tissue. It was composed mainly of masses and large alveolar groups of loosely packed polyhedral cells, with a distinct cell membrane, fairly
abundant cytoplasm, characteristically clear or finely vacuolated, and small round or oval vesicular nuclei. Many areas showed degeneration, necrosis, and hemorrhage. Pleomorphism of the cells of the neoplasm is shown by the presence of plump fusiform cells, large pyriform cells, and small round ones. None of these types showed any definite arrangement. The lumen of the renal vein contained masses of these same anaplastic cell types.

Sections of the tumor from the cerebellopontine angle showed it to be composed of long, spindle-shaped cells arranged in whorls. These cells had long, oval, pale, vesicular nuclei and bipolar eosinophilic cytoplasmic strands. Some palisading of the nuclei was observed. In the central portions of the tumor were only a few scattered spindle-shaped cells in an edematous, reticular background.

The sections of the hemorrhagic area in the cerebellum showed hemorrhage surrounded by large, round or polyhedral cells which appeared to contain much lipoid material. Their stroma was scanty. The cells showed an alveolar grouping of solid cords divided into masses by thin septa.

The pituitary tumor was composed of small round or polyhedral cells, fairly deeply staining, growing in small alveolar clusters separated by thin, tenuous fibrous tissue septa. The volume of cytoplasm and of nucleus was about equal. The cytoplasm appeared as finely granular. The cells showed no tubular nor any acinar formations but some pseudo-
rosettes about blood vessels were found. Mitotic figures were quite rare. While the stroma was scanty, the tumor was quite vascular. Stained with Kindell's modification of Mann's eosin methyl-blue, the neoplastic cells did not appear as definite eosinophils, basophils, or chromophobes.

**DISCUSSION**

This case exhibits three separate neoplasms. The hypernephroma is, in all probability, an example of a cell rest becoming neoplastic. The acoustic neurofibroma may also have had its origin in a cell rest which became active. Sternberg points out that the acoustic and some other cranial nerves arise from the neural ridge at a time when the tissues are comparatively undifferentiated. The complexity of some acoustic neurofibromata he believes is due to cellular inclusions. That this is applicable to the neurofibroma of this case is shown by the varied histological picture. The peripheral areas contained many whorls of spindle-shaped cells, while in the more central portions there were only a few spindle-shaped cells in a stroma composed of cells having small round nuclei and a fusing of membranes to form a tenuous background. The carcinoma of the pituitary would seem to have no demonstrable relationship with any cell rest.

From the history it would appear that the acoustic neurofibroma was of about four years' standing. The visual disturbances were marked a year and a half prior to death, which indicates that the pituitary tumor was large enough at that time to cause ocular signs and symptoms. The weakness, listlessness and hypotension may have been due to the hypernephroma, and since these symptoms were of some five years' duration it would seem that the kidney tumor had been present about that length of time. The cerebellar metastasis may have been responsible for the slow slurring speech and the staggering gait. These occurred only about two months prior to death, which would indicate that the metastasis may have occurred at that time. It may have been present longer without causing enough destruction of cerebellar tissue to produce signs.

Since two of these neoplasms may have had their origin from cell rests, it would seem that the same factor may have been operative in producing neoplasms in both instances. Just what this factor was is unknown. The added presence of the hypophyseal carcinoma would seem to suggest a special tendency to neoplasms, and it may be that this was the decisive factor.

**SUMMARY**

A case is reported of three independent neoplasms in one subject, a hypernephroma of the right kidney with a cerebellar metastasis, a carcinoma of the pituitary, and an acoustic neurofibroma of the right sixth cranial nerve. Both the hypernephroma and the neurofibroma may have been of cell rest origin.

It appears interesting that the hypernephroma, its cerebellar metastasis, and the acoustic neurofibroma all occurred on the right side of the body.

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