STUDIES ON TUMOR METASTASIS

VII. METASTASIS TO THE PINEAL GLAND

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Reports of tumor metastasis to the pineal gland are exceptionally rare, perhaps because of little systematic post-mortem study. Primary tumors are apparently much more frequent and have been carefully studied (1).

The first instance of metastasis is that reported by Förster (2) of Göttingen in 1858. The patient was a thirty-seven-year-old male with cancer of the lung (possibly esophagus) and widespread metastases which included the pineal gland. The pineal was reported the size of a small hazelnut. Its microscopic appearance was not described. In the next case, reported by Church (3) in 1869, the primary tumor was also apparently a cancer of the lung which was widely disseminated.

In the course of a discussion of splenic metastases, di Biasi (4) mentioned involvement of the pineal by metastasis from cancer of the breast in a sixty-nine-year-old female. This carcinoma was recurrent and involved the lymphatic channels of both the pleura and the lungs, with metastases to the spleen, bone, kidney, adrenals, lymph nodes, pelvis, mediastinum, axillary and cervical regions, thyroid, pituitary, and the pineal.

In none of these three reported cases is any change referable to disturbed physiology of the pineal gland noted.

In view of the rarity of this condition, the report of an additional case appears justified.

CASE REPORT

A single woman, sixty years of age, entered the Palmer Memorial Hospital on the service of Dr. G. A. Leland, complaining of a lump in her right breast, of a year's duration. Since this mass caused no pain, she had paid no attention to it until, about five months ago, she noticed that the skin was reddened, roughened, and scaling, with beginning ulceration. About four months before admission, intermittent hematuria developed, and within the last month small lumps had appeared over the skin of the entire body. There had been a loss of weight of about twenty pounds during the past year. X-ray examination of the skeleton showed central regions of rarefaction here and there, bordered by areas of increased density. The patient died twelve days after admission, having been given supportive treatment only.

Autopsy

Autopsy was done by Dr. Joseph Porter one and one-half hours post mortem. Anatomical diagnoses: Carcinoma simplex of right breast with metastases to the lymph nodes of the axillary, cervical, mediastinal, mesenteric, para-aortic, pancreatic, and inguinal regions; also to the skin, practically all large bones, the opposite breast, pericardium, myocardium, pleura, lungs, spleen, accessory spleen, liver, gallbladder, adrenals, kidneys, ureters, bladder, uterus, tubes, ovaries, vulva, esophagus, stomach, pancreas, serosa of the entire gastro-intestinal tract, peritoneum, omentum, mesentery, diaphragm, meninges, cerebrum,

The essential autopsy findings were as follows:

**Body:** The body was that of an emaciated, elderly female. The skin over the right breast was thickened and hard, and showed some scaling, with irregular, shallow ulceration, the whole lesion measuring about 9 cm. in diameter. The nipple was apparently negative. There was marked thickening of the skin of the anterior axillary fold. Scattered over the surface of the entire body were numerous small, raised nodules; many of these were easily visible, while others could merely be felt. These nodules varied from 2 to 4 mm. in diameter. There were, in addition, two large, flat foci covering an area up to 3 cm. in diameter, one just to the right of the midline above the umbilicus and the other at the costochondral junction on the left side. The skin was dry and wrinkled; there was no icterus. Numerous hard nodules were palpable in both axillae and inguinal regions. The right chest was somewhat flattened, while the left side bulged considerably and flared outward. The left breast was firm and nodular, but there were no definite skin changes over it. Rigor mortis was absent, and there was only a slight degree of post-mortem lividity.

**Head:** The left eyelids, particularly the upper, were much thickened and firm to palpation. The scalp, reflected by mastoid-to-mastoid incision, appeared negative. The calvarium, removed in the usual manner, also appeared to be negative. No definite foci of bone erosion were discovered. However, transmitted light revealed a few foci in which the bone appeared slightly thickened.

**Brain:** The brain weighed 1200 gm. and showed some thickening of the arachnoid, beneath which there was a moderate amount of somewhat turbid fluid. The outer surface was negative. The brain was sectioned by the technic of Virchow and was negative throughout.

**Pituitary:** Negative.

**Pineal:** Slightly enlarged, measuring $1.1 \times 0.8 \times 0.5$ cm.; firm and partly calcified.

**Venous Sinuses:** Negative.

**Middle Ears:** Negative.

**Primary Incision (Y type):** Incision revealed about 1 cm. of dark yellow fat over the abdomen. Cutaneous nodules, gray to white, rather granular and hard, appeared in most instances to be located just beneath the epidermis, causing slight bulging except for those instances previously described where the nodules were flat. The right breast showed a firm, gray to white, very hard tumor which measured up to 1.5 cm. in thickness from skin edge to inner aspect, replacing the entire breast, but not extending into the underlying muscle. A chain of hard, quite firm, granular nodes led into the right axilla. The left breast contained nodules of pearly-white, rather smooth tissue. Many firm nodes, varying in size, were found in the left axilla.

**Peritoneal Cavity:** The peritoneal cavity contained 450 c.c. of slightly turbid, dark yellow fluid. Studying the serosal surface of the entire gastro-intestinal tract were numerous firm nodules about 2 to 3 mm. in diameter. In some places there was moderate congestion of the serosa of the intestine. The omentum stood out prominently; on palpation a hard rim of tissue could be felt coursing along the vessels, but not invading them. A loop of jejunum, which extended down into the pelvis, was kinked upon itself and was adherent to the anterior wall of the sigmoid. Numerous small nodules were scattered over the ovaries, tubes, and part of the fundus of the uterus. These swept up anteriorly over the dome of bladder. The foramen of Winslow was patent and the lesser peritoneal cavity negative. The diaphragm was at the level of the 4th interspace on the right, of the 6th rib on the left, with scattered firm nodules.

**Pleural Cavities:** Each pleural cavity contained about 350 c.c. of clear yellow fluid.

**Pericardial Cavity:** The pericardial cavity contained about 25 c.c. of clear yellow fluid.

**Heart:** The weight of the heart was 270 gm. There were a few small, firm nodules on the epicardium. The fat which extended along the vessels was indurated. On section the myocardium was firm, brown, and rather homogeneous. On the inner aspect, in the columnae carneae, were scattered small flecks gray to white in color and about 1 mm. in diameter. The mitral valve was somewhat firmer than usual and in about its mid-portion, at the edge of the leaflet, contained a somewhat granular, red, ulcerated zone 3 cm. in di-
ameter. Otherwise the valves were negative. The coronaries were smooth and elastic throughout.

Lungs: The right lung weighed 310 gm., the left 340 gm. The upper lobes of both were markedly emphysematous. The alveolar spaces stood out clearly as translucent, small, circular zones. The lower lobes of both lungs were somewhat congested and showed moderate atelectasis, particularly posteriorly. The upper lobes were grayish-white and dry, the lower ones somewhat purple. A few scattered miliary nodules were palpable, with an occasional nodule measuring up to 2 or 3 mm. in diameter.

Spleen: The spleen weighed 190 gm. and was quite hard; the capsule was tense and partly covered by grayish-yellow fibrin. On section the organ presented a rather smooth, homogeneous appearance, mottled gray to dark brown in color. The trabeculae were not appreciably thickened and there were well demarcated, rounded, gray, translucent zones measuring up to 5 mm. in diameter. An accessory spleen, 1.5 cm. in diameter, contained a small gray nodule in its center.

Pancreas: The weight of the pancreas was 130 gm. Numerous firm lymph nodes were attached to the outer surface and on section gray, slightly granular zones up to about 2 mm. in diameter were seen scattered about. In its mid-portion, the pancreas felt much firmer than usual and showed some obliteration of the normal lobular markings.

Gastro-Intestinal Tract: The inner surfaces of the entire digestive tract were negative. The outer surfaces, from the esophagus down, were studded throughout with fine, firm nodules, 2 to 3 mm. in diameter, which appeared to be limited chiefly to the serosa.

Liver and Gallbladder: The liver weighed 1800 gm. Its outer surface was smooth and of a mottled brownish-yellow color. The edges were somewhat rounded and on section the parenchyma appeared rather brown, with fine, somewhat hazy gray foci. An occasional granular, yellowish-gray focus was present, measuring up to 6 mm. in diameter, hard and rarely showing necrosis in the center. There was also a well demarcated focus, 5 mm. in diameter, containing blood-filled spaces. The gallbladder contained a few implants on the serosa. The mucosa was normal, the ducts patent.

Adrenals: Both adrenals contained nodules from 1 to 2 cm. in diameter with an occasional larger focus in which a portion of the entire thickness of the gland was replaced by tumor.

Kidneys and Ureters: The right kidney weighed 130 gm., the left 170 gm. The capsules stripped easily, leaving a smooth brownish surface with an occasional gray opaque focus 1 to 2 mm. in diameter. The cortex was normal, measuring up to 6 mm. The medulla showed some compression, especially on the left, where the calyces were moderately dilated, thickened, and slightly granular in places. There was a small amount of blood-tinged urine in both pelves. The right kidney pelvis showed a slight degree of dilatation. The ureters were firm, not dilated; the lumina were small and on section appeared to be surrounded by white firm tissue.

Bladder: Fresh blood clot filled the bladder. The wall was thickened and hard in an area 6.5 cm. in diameter, over the dome. The serosal surface here was covered by numerous small nodules. The wall measured up to 1 cm. in thickness, and the mucosa was roughened, reddish-gray, and granular. The ureteral orifices were negative except for slight congestion of the adjacent mucosa.

Genitalia: The uterus was normal in shape and size; it measured 6 \times 5 \times 3 \text{ cm.} The fundus was partly covered by a few gray, opaque nodules. The myometrium and endometrium were negative, as was the cervix. The tubes contained a few flattened nodules on the surface. The serosa was congested. The right ovary measured 3.5 \times 3 \times 2 \text{ cm.}, and was replaced by a hard, gray, granular tissue. The left ovary was small, the surface wrinkled and partly covered by small nodules. The vaginal wall also contained a few small nodules.

Lymph-nodes: A chain of hard nodes, granular, gray, and opaque, ran along both sides of the neck. Similar nodes, up to 2 cm. in diameter, were found in both axillae, in the inguinal region, about the pancreas, along the hepatic duct and mesentery, and about the aorta. The mesenteric lymphatics were hard, white, and swollen. Nodes about the bronchi were also enlarged and firm and contained black pigment.

Veins: Negative.
Aorta: The aorta contained yellow elevated foci in the abdominal portion, one or two of which showed slight ulceration. It retained a fair degree of elasticity.

Thyroid: Negative. Weight 8 gm.
Parathyroids: Negative.

Bones: The second to the fifth lumbar vertebrae showed almost complete replacement by tumor, which was white, opaque, and firm.

Ribs: Slight roughening of the outer surfaces was observed.

Pelvic Bones: Normal exteriorly.

Microscopic Examination

Heart: A great number of tumor cells were diffusely scattered throughout the stroma and epicardial fat and in many instances had concentrated about the capillaries. The cells varied in shape and size; many had indented round or oval nuclei rich in chromatin with a large nucleolus. Multinucleated tumor giant cells were frequent and many cells were vacuolated, a few even of the signet-ring type. With the phosphotungstic-acid hematoxylin stain the cytoplasm appeared finely granular, slightly yellow.

Lung: In one section of the lung the tumor was seen growing about the bronchioles and vessels. Scattered alveoli contained leukocytes, fibrin, and phagocytic mononuclear leukocytes, while a few bronchioles were filled with polymorphonuclear leukocytes. In another section there was a fair-sized nodule in the pleura, the center of which was necrotic. The cells were compactly arranged, forming sheets, and were quite regular in size and shape. There was no gland formation, however, and a few veins and lymphatics were filled with neoplastic tissue. The bronchial wall contained much tumor. Several bronchial lymph nodes were replaced by metastatic cells.

Spleen: In the spleen were large foci of tumor cells in compact sheets and small foci about the central arteries and growing diffusely in the capsule. The cells were fairly uniform in size, with a small, well-defined nucleolus and acidophilic cytoplasm. The sinusoids were filled with tumor in some places while an occasional large vein showed masses of neoplastic cells advancing into the lumen. The accessory spleen also contained foci of metastatic tumor.

Pancreas: Scattered about in the stroma were a few tumor cells. These were invading the adjacent fat and in some instances appeared to be replacing the insular tissue. One section of the pancreatic duct showed extreme infiltration of the adjacent stroma, invasion of lymph nodes, and many arterioles, veins, and lymphatics.

Esophagus: Tumor cells were present in the submucosa.

Stomach: The stomach showed large patches in which tumor had replaced the mucosa. In one or two foci exceptionally large giant cells were seen. Tumor cells were also spreading deep in between the muscle fibers.

Small Intestine, Colon, and Rectum: In both the small and large intestine were serosal tumor implants, most extensive in the rectum. The mucosa of the colon and rectum showed extensive invasion. Serosal implants produced a fairly heavy stroma.

Liver: The liver contained a large metastatic focus of tumor with necrotic center and a diffuse, compactly arranged distribution of tumor, especially about central zones. In some instances a whole lobule was replaced, while in other places only the inner portions. One section contained a number of vessels of moderate size filled with blood and lined by flattened endothelium, a few of which contained thrombi and tumor cells.

Gallbladder: The wall of the gallbladder showed diffuse tumor infiltration.

Adrenals: In the adrenals the sinusoids were plugged by cords of tumor cells. There was also a moderate number of tumor cells in the adjacent fat.

Kidney: Foci of metastatic tumor were seen beneath the kidney capsules and about some vessels. An occasional hyalinized glomerulus was seen, and there was focal congestion of capillaries in the medulla.

Ureter: There was diffuse scattering of tumor cells in the walls of the ureters, and extensive infiltration in adjacent tissue, wherein small groups of cells formed masses projecting into lumina of vessels and lymphatics.

Bladder: The bladder wall was heavily invaded by tumor. Some cells were also seen in muscle bundles, and in some places the mucosal epithelium was replaced by tumor cells.
Ovaries: The ovaries were almost entirely replaced by diffuse tumor.

Uterus and Cervix: Diffuse tumor metastasis was seen in the uterus. The endometrium was atrophic. There was some dilatation of the cervical glands.

Tube: The fallopian tubes were infiltrated by tumor, which produced thickening of the plicae.

Mesentery: The mesentery showed extensive infiltration with tumor cells; also the vessel walls and lumina. Several lymph nodes were entirely replaced by metastatic cells.

Lymph Nodes: Several nodes were present, all of which contained a great deal of tumor. One node was studded with several irregular, hyalinized foci, about which occurred moderate fibrosis and deposition of a finely granular, brownish-black substance. Under the Nicol prism many granules were doubly refractile and some long, slender, and needle-like.

Aorta: The intima of the aorta was thickened and there was a slight increase in the vascularity of the media. In adjacent tissue was much tumor, which was seen invading several nerves.

Thyroid: Negative except for some atrophy.

Right Breast: The right breast consisted of dense collagenous tissue with tumor cells distributed irregularly among the fibers, invading the underlying muscle and plugging nu-
numerous lymphatics. The cells varied in size and shape, but for the most part were round or oval, with slightly eosinophilic, granular cytoplasm and a round or oval basophilic nucleus with prominent nucleolus. Mitoses were not common but many giant cells were seen. There was no semblance of gland formation. In many places the tumor was continuous with the duct epithelium.

Left Breast: In the left breast fibrosis was less dense and in a few places normal breast tissue still persisted.

Skin: Nodules were present in the corium, but the epidermis was not invaded. Cells were irregularly distributed throughout the deeper layers of the corium and subcutaneous fat.

Vertebra: In the spine the entire marrow space was filled with tumor which carried a delicate stroma. Necrosis had occurred in the center of some masses. Bony trabeculae were thickened and in some places the marrow space was filled with fine fibrous stroma. There was no evidence of hematopoiesis.

**FIG. 2. PORTION OF SECTION REPRODUCED IN FIG. 1, SHOWING CHARACTER OF TUMOR CELLS**

Phosphotungstic acid hematoxylin. × 200.

Brain: The cortex contained one or two small foci of metastatic tumor and a diffuse scattering of cells in the pia and arachnoid. The basal ganglia showed the tumor spreading along the perivascular lymphatics.

Cerebellum: The cerebellum was widely infiltrated by tumor cells, both in the cortex and molecular layer. One section of the medulla showed a few tumor cells in the meninges.

Pituitary: There were a few tumor cells scattered about in the anterior pituitary lobe and several foci of necrosis in which the architecture was well preserved and the cytoplasm and nucleus formed a pink mass. There were a few polymorphonuclear leukocytes in some of these necrotic zones. At the junction of the anterior lobe and the posterior lobe was a large focus of tumor cells in one section.

Pineal: The pineal gland was almost completely replaced by metastatic tumor cells. There were, however, a few typical cells still persisting, as well as scattered calcified foci. Section showed normal brain tissue fading off into tissue characteristic of the pineal gland with fairly numerous concretions (Fig. 1). There was marked infiltration of the pineal substance with epithelial cells in small clusters and singly, of the signet-ring type (Fig. 2). In most places, the pineal structure was entirely replaced except for the inclusion of scattered concretions. Apparently little stroma was carried by the tumor, but it infiltrated the tissue diffusely.
DISCUSSION

This case presented no evidence of disturbance in sexual characteristics, as would be expected from the fact that the patient was well past the menopause. Evidence of physiologic change has not been noted in the other reported cases of metastasis to the pineal.

In view of the histologic appearance of this tumor, the question of a possible gastric origin might be raised. In view of the history, however, and the character of the lesion of the breast, it seems more likely that we are dealing with a primary breast tumor with widespread metastases than with a gastric cancer, in spite of the marked resemblance of the individual cells to those of the linitis plastica type of carcinoma of the stomach.

Metastasis to the pineal, then, may be regarded as simply an anatomic curiosity. In the few cases in which it has occurred, widespread distribution of metastases has been noted, so that chance hematogenous deposit is most likely.

SUMMARY

A case of carcinoma of the breast with metastasis to the pineal gland is reported. This is the fourth metastatic pineal tumor recorded in the literature.

Note: Since the above report was put in type, a fifth case has been encountered, in a white adult male with multiple metastases of a malignant melanoma primary in the thigh. A small focus of tumor was present in the pineal gland.

REFERENCES