MALIGNANT GRANULAR CELL MYOBLASTOMA INVOLVING THE URINARY BLADDER

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THIS IS A REPORT of a granular cell myoblastoma involving the urinary bladder which exhibited the histologic characteristics of a benign neoplasm in its primary manifestation and yet metastasized widely, causing death.

It seems necessary to identify the tumor which we choose to call granular cell myoblastoma and explain the reason for using this name, which is not the one most commonly employed. The tumor type was first described by Abrikossoff, in 1926, and called by him myoblastic myoma (myoblastenmyom). In 1931, he published a second paper in which he described the histologic features of four different varieties of the tumor: (1) The typical form made up of round, egg-shaped, or elongated myoblasts from 20 to 25 microns long with granules but without longitudinal or cross striations; (2) a variation of the first type in which some cells show longitudinal or cross striations; (3) an hypertrophic form with cells from 40 to 160 microns and sometimes multinucleate. These first three groups are all composed of granular cells and all are benign tumors. (4) Malignant myoblastic myoma in which the myoblasts are not granular, but assume atypical aspects and vary in size so that the tumor resembles a polymorphous sarcoma. He had no personal experience with this fourth group but cited the case of von Meyenburg as an example of it.

The observations of Abrikossoff have been repeatedly confirmed but most unfortunately subsequent authors have elected to use the term myoblastoma indiscriminately for all four of Abrikossoff's groups without emphasizing the important histologic and clinical distinctions between the first three benign groups and the fourth malignant group.

This omission becomes serious when Howe and Warren warn us that myoblastoma is more often malignant than is generally supposed, since five of their ten cases behaved like malignant tumors, without making it perfectly clear that all of the malignant tumors belonged to Abrikossoff's fourth group of myoblastomas.

Indeed, until the case here reported was observed by us we were firmly convinced that no example of a malignant primary granular cell myoblastoma belonging to any of Abrikossoff's first three groups had ever been recorded None of Howe and Warren's malignant cases do so, nor do any of the ten malignant cases which they have culled from the literature. One of us (A.P.S.) has studied these ten cases and is convinced that none of them, in its primary manifestation, belonged to Abrikossoff's first three groups. In Morpurgo's second case, the *metastases* resembled the metastases of the case we are about to report but the primary tumor was quite different.

We feel, therefore, that tumors belonging to Abrikossoff's first three groups, since they are almost all benign, should be labelled clearly with a distinctive name so that they will not be confused with the other forms of striated muscle tumors most of which are malignant. For this reason we choose to use the name "granular cell myoblastoma." This is not new, since it has already been employed by Lattes and Horn and Stout, and it appeals to us as eminently reasonable and necessary. It is beyond the scope of this paper to discuss the propriety of using the term myoblastoma for Abrikossoff's fourth group, but we may be permitted to regret that he ever chose to include it with his first three groups since it has provided such a potent source of confusion.

Case Report.—D. Y., white, male, age 31, single, a pressman, was first seen by one of us (A. R.) on March 29, 1943. According to the mother he had been a deaf mute since the age of one when he had cerebrospinal meningitis. In 1937, he had had osteomyelitis of the left ankle following injury, for which he was operated upon twice. He had had diurnal frequency every two to three hours and nocturia at least once for many years. There had been painless hematuria, with urinary frequency every hour, for 11 days before admission.

Physical Examination.—The subject was a young deaf mute, quite emaciated and anemic. The heart was normal in size, with a pounding apex beat and loud sharp systolic and rough diastolic murmurs heard over the aortic and pulmonic valves. The lungs were clear. The abdomen was scaphoid in type. Liver, spleen and kidneys were not felt. A large, very firm, smooth, nontender mass was felt in the lower abdomen as far up as the level of the anterior iliac spine, extending on the right to the iliac and pubic bones and into the true pelvis. B. P. 120/54. The urine was port wine in color and essentially negative except for the blood. Rectal examination revealed a very large, firm, immobile, smooth mass filling almost the entire true pelvis and more prominent on the right than on the left. The upper limit of the tumor mass could not be reached by palpation through the rectum. Preliminary roentgenograms of the kidneys and bladder showed obliteration of the kidney outlines by gas. There was a rather wide separation of the symphysis pubis. Attempt at cystoscopy failed. A No. 21 F. sound could be passed but was deflected far to the left. Rectal palpation, with the sound in the urethra, showed a normal prostate and left seminal vesicle. The large mass palpated to the right of the prostate was highly suggestive of an unusual type of tumor that appeared to arise from either the right lateral lobe of the prostate or the right seminal vesicle. A No. 16 F. Coudé rubber catheter was passed into the bladder and only a small amount of slightly blood-tinged urine was withdrawn. The patient was immediately sent to the Adelphi Hospital, with a tentative diagnosis of an unusual giant-sized sarcoma involving the bladder, prostate and right seminal vesicle.

At the hospital an intravenous pyelogram, reported by Dr. Asa B. Friedman, revealed a functionless right kidney. The left renal function was normal and the pelvis showed slight hydronephrosis. The lower third of the left ureter was lifted upward by a deformity of the bladder (Fig. 1). The crescentic-shaped bladder was markedly deformed by a large, smooth, regular, oval mass that filled the major part of the bladder area and seemed extrinsic to the bladder. The bladder itself showed a small capacity and was pushed far upwards and to the left, overlying the left anterior superior spine of the ilium. A roentgenogram of the chest was negative.

The blood showed 62 per cent Hb., R. B. C. 3,210,000; W. B. C. 9,400, 76 per cent polys., 19 per cent lymph., 5 per cent mononuclear. Blood sugar 95.4 mg. per 100 cc., urea nitrogen 158, creatinin 1.3.

Owing to the unusual type and size of the tumor mass a celiotomy was considered

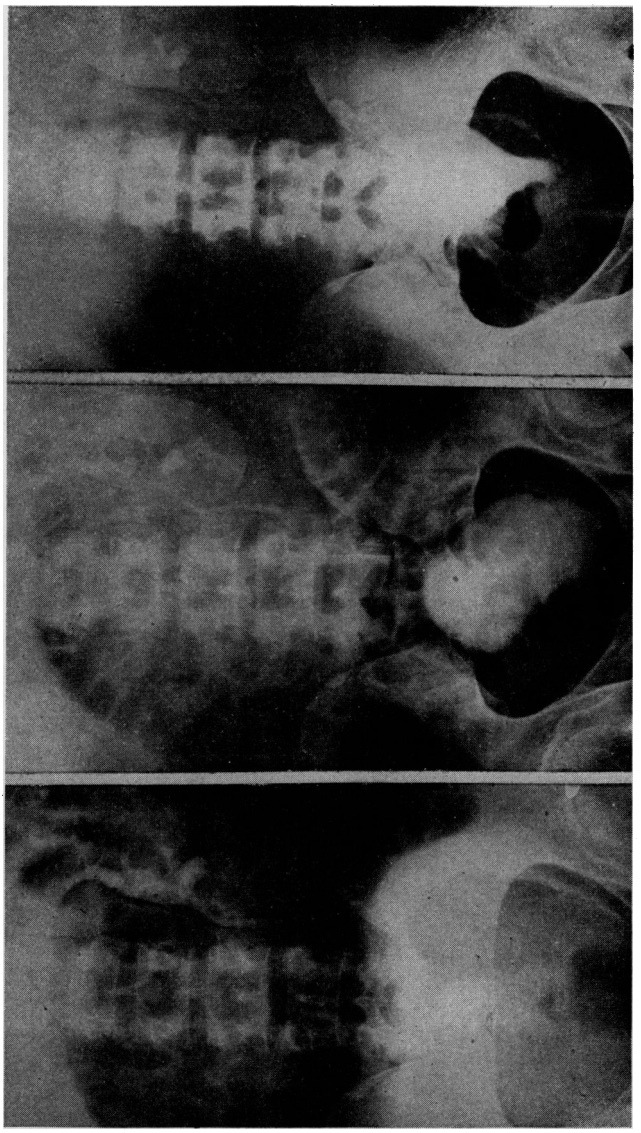

FIG. 1.—Intravenous pyelograms to show progress of the tumor. The one at the left was taken March 30, 1943—before operation. The right kidney is functionless; the left normal except for slight hydronephrosis. The bladder outline is semilunar and pushed far to the left. The center pyelogram was taken May 17, 1943—six weeks after operation. The bladder now appears more normal in contour and location. The pyelogram at the right was made May 5, 1944—13 months after operation. The bladder is pushed upwards and its pear shape indicates encroachment around its neck and base. The lower end of the left ureter has a bizarre relation to the bladder neck. The kidney findings remain essentially unchanged.

preferable to a perineal approach, even though it was thought at the time that we were dealing with a sarcomatous tumor arising from the right seminal vesicle.

Operation.—April 1, 1943 (A. R. and R. A. R.) : Under spinal anesthesia, a midline incision extending from the umbilicus down to the symphysis pubis was made. The tumor mass was exposed and found to be smooth, well encapsulated, of hard rubbery consistency, heart-shaped, and about the size of a large grapefruit. It was tightly wedged into and filled the entire right iliac fossa, the right false and true bony pelvis and pressed against the sacrum. At its contact with the urinary bladder, which was thinly stretched across the upper left border of the tumor, the neoplasm lost its distinct demarcation which characterized the rest of the mass and apparently merged imperceptibly with the musculature of the bladder which was torn into during the enucleation of the tumor from this area. The entire mass was carefully enucleated from its surrounding tissue bed by blunt dissection. A number of large vessels leading directly into the mass were ligated and cut. A tiny area which was intimately adherent to the upper part of the right external iliac vein was dissected away with the radio knife in an attempt to prevent extension of the growth and at the same time avoid tearing into the vessel. The apex of the mass was in the region of the right seminal vesicle. The longitudinal tear into the right wall of the bladder offered an opportunity for careful study of the interior of that viscus, which, aside from the deformity in outline, was otherwise normal in appearance. The bladder neck was normal, though pushed far up and to the left. No enlargement of the prostate was discernible and only the left ureter orifice was seen. Careful search for the right ureter orifice failed to locate it, nor could the right ureter be recognized in the right pelvis either during or after the removal of the tumor mass.

The longitudinal rent in the bladder was repaired and sutured around a Pezzar catheter and five cigarette drains were placed into various areas of the tumor bed and around the bladder. The wound was closed in layers, and the patient returned to his bed in good condition.

The postoperative course was slow but uneventful. The Pezzar catheter fell out on the 13th day and he started voiding per urethram on the 23rd day. On several occasions the suprapubic sinus reopened but it closed eventually, and he was discharged from the hospital with the wound and fistulous tract almost entirely healed on May 24th.

Because of a suspicion that the right ureter had been accidentally tied off and cut during the operation, an intravenous pyelogram was taken April 21st, three weeks after operation. It showed good function in the left kidney which was apparently normal but again no dye was visible in the right kidney. No visualization of the bladder outline could be obtained because of the leakage through the suprapubic fistula. No changes were noted in a similar study made on May 17, 1943 (Fig. 1). Roentgenograms of the gastro-intestinal tract, taken May 20th, showed no intrinsic organic disease. An electrocardiogram showed a tendency to right axis deviation. Blood chemistry findings remained at the same levels throughout his hospital stay. His blood on April 19th showed 69 per cent Hb. and R. B. C. 3,300,000.

Pathologic Examination.—The specimen was a large mass of firm rubbery consistency, measuring 12 x 11 x 9 cm., and weighing 579 Gm. It was of a grayish-yellow color and apparently well encapsulated. The surface showed fibrous bands which constricted portions of the mass and gave it a somewhat nodular appearance. On section, the tumor was smooth, fibrous and generally homogeneous in appearance, with two apparently fresh hemorrhages (Fig. 2).

A diagnosis of granular cell myoblastoma was made after microscopic examination. Details of the histopathology are recorded at the end of the autopsy report.

Subsequent Course.—Slight leakage through a pinpoint suprapubic fistula persisted until August 13, 1943 (103 days following operation) after which the cicatrix was firmly healed. Cystoscopy 89 days after operation showed a bladder capacity of 90 cc.,

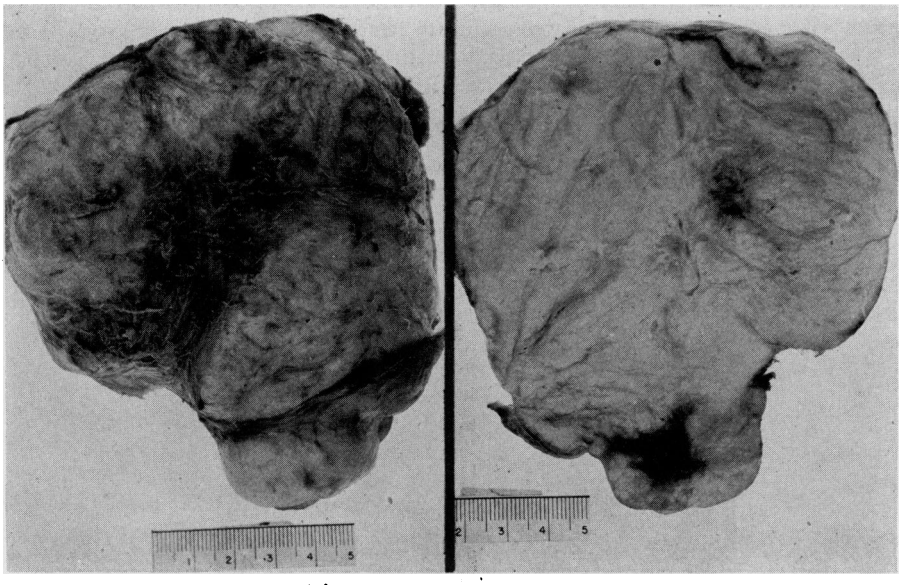

FIG. 2.—Photographs of surface and sagittal section of tumor removed at operation April 1, 1943.

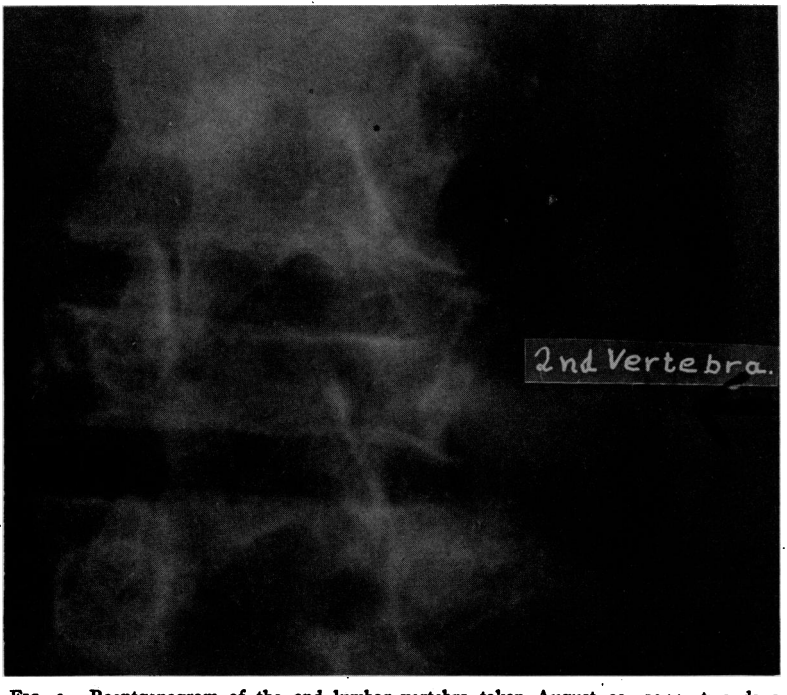

FIG. 3.—Roentgenogram of the 2nd lumbar vertebra taken August 29, 1944—two days before death, showing advanced destruction.

moderate general cystitis, considerable degree of trabeculation and congestion of the left ureteric orifice; the right ureteric orifice was not visualized. Cloudy urine and frequency continued at 104 days, but he felt well enough to return to his arduous work as pressman.

On November 24, 237 days after operation, there was slight rectal bleeding, apparently from small internal hemorrhoids. Rectal palpation at this time revealed slight thickening and fullness on the right side of the pelvis for the first time since operation. Roentgenograms and an intravenous pyelogram showed no dye and no kidney outline

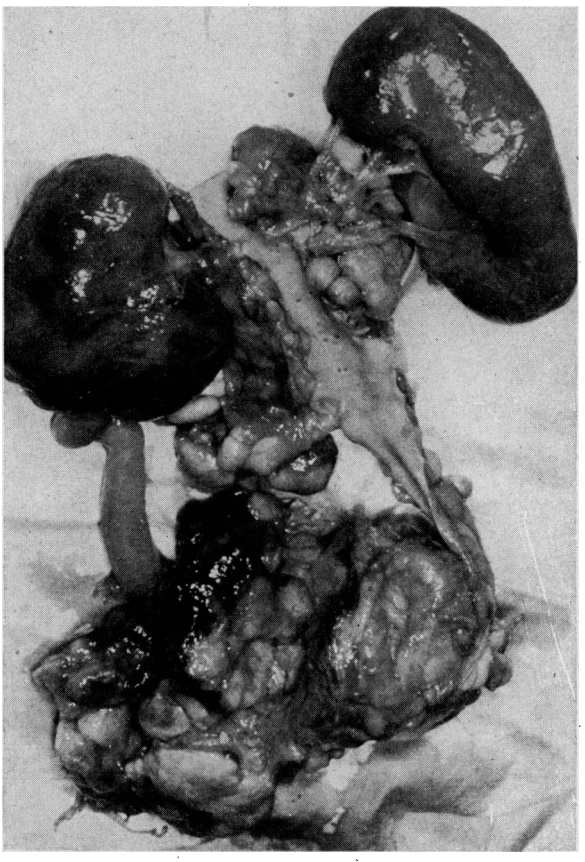

FIG. 4.—Photograph of the entire urinary tract, aorta, retroperitoneal lymph nodes and recurrent tumor which formed one mass with the bladder and prostate. The right kidney is distended. The markedly dilated right ureter plunges into the pelvic tumor mass below.

on the right side, but a normal left kidney. Left kidney function was good, with slight hydronephrosis, but a fairly normal left ureter. The bladder was seen on the left side of the pelvis. No masses were palpable suprapubically. Forty-seven days later, on January 10, 1944, an indefinite mass could be felt through the rectum extending above and confluent with the right side of the prostate. He had no subjective symptoms at this time, but on February 4th he complained of slight pain in the lower abdomen. The mass felt through the rectum on the right side was larger and abdominal palpation revealed a small indefinite mass in the left iliac fossa. Palliative roentgenotherapy was given by Dr. Asa B. Friedman from February 12 to April 17, 1944: 10 x 15 cm. left suprapubic and left sacral ports were used. The factors were: 200 K. V.; 50 cm.

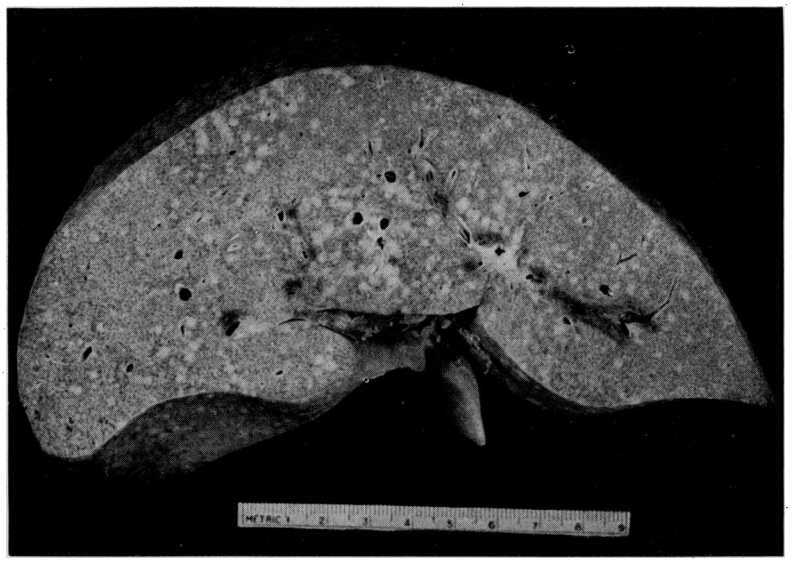

FIG. 5.—Photograph of the liver riddled with metastases.

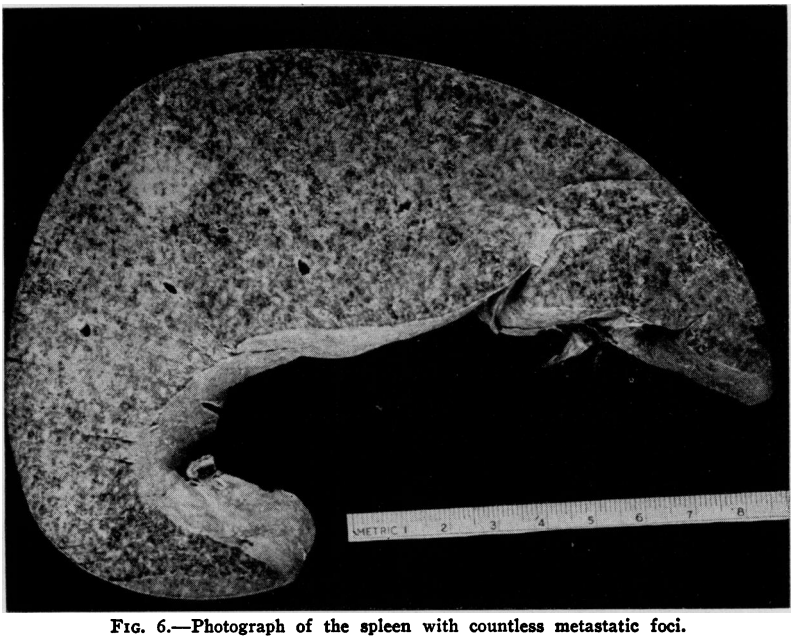

FIG. 6.—Photograph of the spleen with countless metastatic foci.

skin distance; filter 0.5 Mm. Cu. plus 1 Mm. Al. 2500 r. were given through each port delivering a tumor dose of 3000 r. This produced symptomatic improvement, with disappearance of the pain. On March 30th the rectal mass felt larger and the abdominal mass slightly smaller.

By May 5th, however, the pain returned in the left flank and grew increasingly severe. He was readmitted to the Adelphi Hospital, June 17, 1944, with the idea of removing the recurrent pelvic tumor, which at this time seemed more prominent in the left iliac region than on the right side. Two days later, a roentgenogram of the spine

showed some destruction of the 2nd lumbar vertebra, which was interpreted by Dr. Friedman as a metastatic lesion. Because of this finding, any further operative procedure in the pelvis was deemed futile. The vertebral destruction became progressively greater until the end (Fig. 3).

Although his general condition was quite good at this time, he soon began a gradual decline. Pain was kept fairly well under control by roentgenotherapy of the vertebra, cobra venom and later various narcotics. His inguinal nodes became enlarged and, on July 25th, two of them were removed and showed metastases. Toward the end, emaciation and cachexia became extreme and he finally died August 31, 1944, 17 months after the first operation.

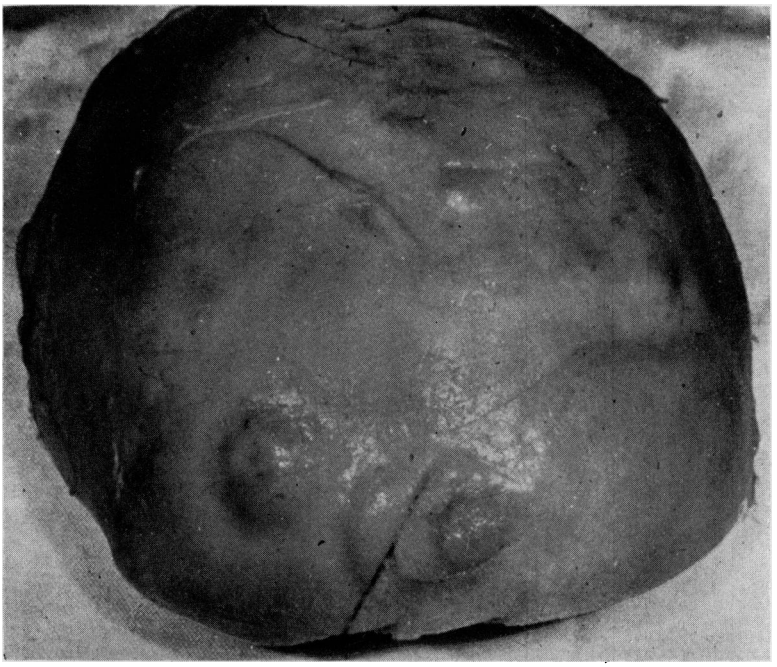

FIG. 7.—Photograph of the dome of the skull with metastases in the frontal area.

AUTOPSY.—Dr. D. M. Grayzel: The following pertinent findings are taken from his report.

There was a large recurrent tumor mass in the pelvis which extended upward to the second lumbar vertebral body posteriorly and to within 5 cm. of the umbilicus anteriorly. It encased the urinary bladder which had only a small cavity and the bladder wall seemed to be composed of tumor tissue. Both ureters plunged into the tumor mass and were lost within its substance. The sigmoid was displaced by the tumor but apparently was not involved by it. The right kidney was purple-brown, cystic, and its pelvis was distended. The right ureter was dilated up to a diameter of 3 cm. and kinked in several places. The left kidney was reddish-brown and did not show gross evidences of disease. The retroperitoneal chain of lymph nodes were enlarged by tumor all the way up to the diaphragm (Fig. 4). Above it the esophageal and tracheobronchial nodes and the nodes on the superior surface of the pericardium also seemed involved. The enlarged iliac nodes were continuous with much enlarged inguinal nodes on both sides. The liver weighed 1250 Gm., and extended 4 cm. below the xiphoid process. It was studded throughout with nodules averaging 3 Mm. in diameter, some of which were confluent (Fig. 5). The spleen weighed 720 grams and was

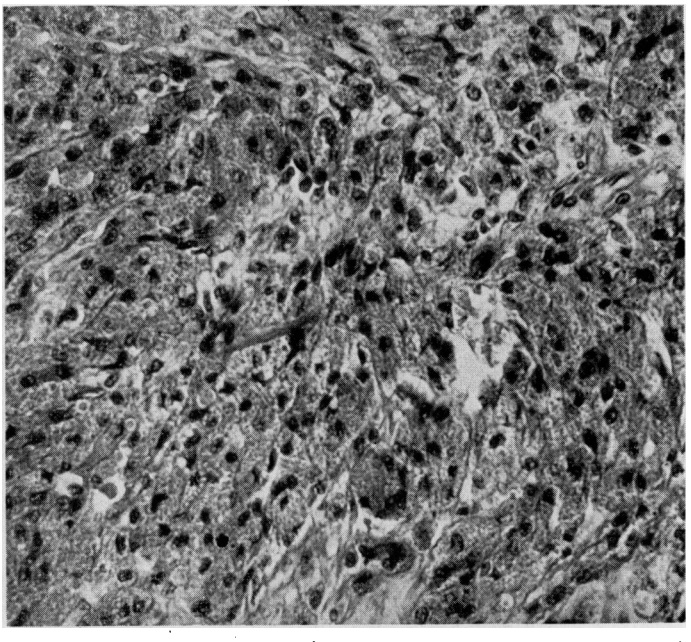

FIG. 8.—Photomicrograph of the primary tumor showing the arrangement of the cells and their relative shape and size.

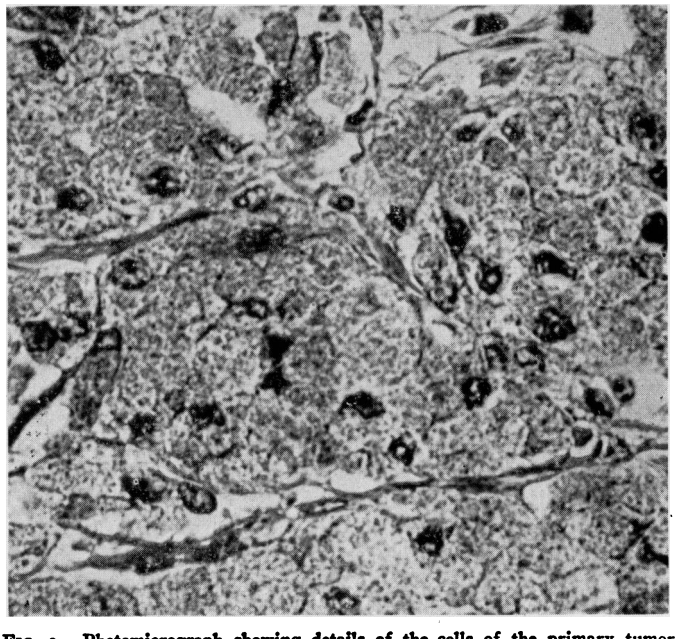

FIG. 9.—Photomicrograph showing details of the cells of the primary tumor and the characteristic granular cytoplasm. (× 600)

speckled throughout with fine yellow nodules, confluent in some areas (Fig. 6). The left lung weighed 190 Gm. and the right 250 Gm. At the base of the right lung was a 9-Mm. tumor nodule just beneath the pleura. The body of the second lumbar vertebra was soft and yellow-gray, and the tumor was adherent to it. Metastatic tumor in the frontal bones formed bony nodules, up to 3 cm. in diameter, which could be seen and felt beneath the scalp (Fig. 7). The rest of the viscera including the brain showed no evidence of metastases.

Anatomic Diagnoses: Tumor of urinary bladder (granular myoblastoma?) involving prostate gland, liver, spleen, lymph nodes, right lung, pericardium, skull, vertebra, peritoneum and pelvic tissues; right hydronephrosis and hydroureter, bilateral hydrothorax, hydropericardium; emaciation, decubitus ulcers and deformity of left foot.

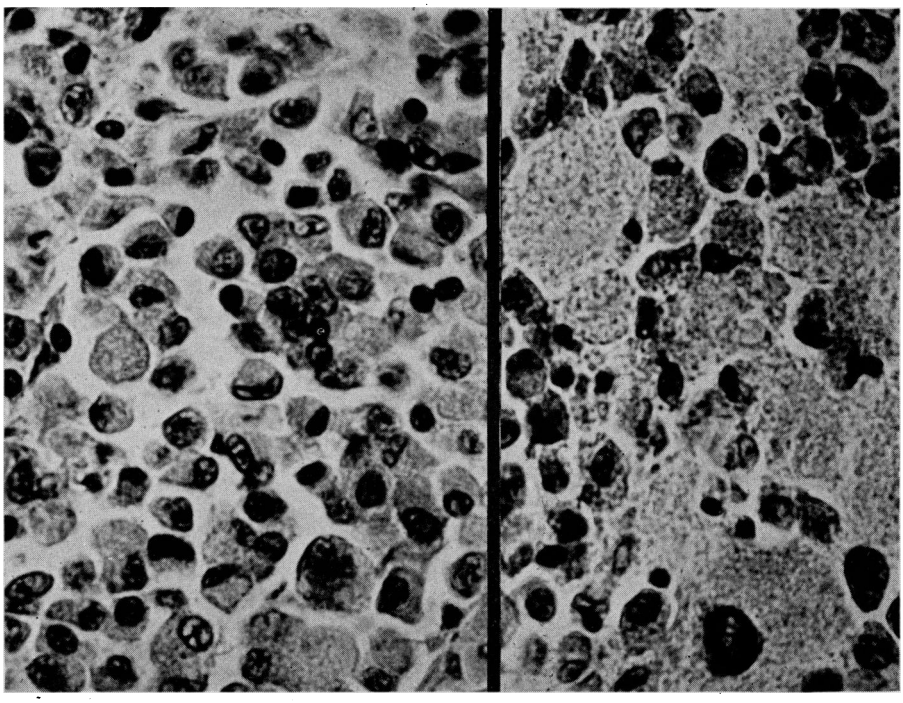

FIG. 10.—Photomicrograph of the tumor at autopsy. At the right a detail from the recurrent mass showing large granular cells like those in the primary tumor mingled with much smaller cells. At the left, small cells characteristic of the final malignant phase of the tumor. They show lack of cohesion and a tendency in some to form chondriosomes. (× 600)

Microscopic Examination: This, in general, confirmed the provisional diagnoses: The bladder wall was completely replaced by tumor up to the mucosa. Metastases were present in the second lumbar vertebra and frontal bone, the liver, spleen and all lymph nodes sectioned. Not only was the nodule in the right lung composed of tumor cells but all sections made from the lungs contained tiny foci.

The *primary tumor* is made up of cords of large, irregularly rounded and plump elongated cells with relatively small nuclei and voluminous cell bodies filled with fine acidophilic granules. No longitudinal or cross striations are observed. No mitoses are found but some of the larger cells have more than one nucleus and there is some variation in the relative size of the nuclei. The cords of cells are separated by slender strands of connective tissue (Figs. 8 and 9).

Recurrent Tumor and Metastases: In a few places, notably in the local recurrent tumor mass and the lung metastases, cells resembling those in the primary tumor are

encountered (Fig. 10) but for the most part the tumor cells have a different appearance. The majority are very much smaller, more definitely rounded, and they appear as distinct units instead of being in cohesive cords. The nuclei are relatively much larger, more hyperchromatic and the cytoplasm proportionately greatly reduced in amount. No mitoses are found. In most of the cells the granular habit of the cytoplasm is maintained but occasionally there seems to be some chondriosome formation (Fig. 10). In none of the many sections prepared were any definite cross striations or longitudinal fibers seen. It must be remarked, however, that the tissue was fixed in formalin and no reliable preparations with Haidenhain's hematoxylin or phosphotungstic acid could be made.

COMMENT.—There was some question in our minds as to the exact site of origin of this tumor because at the first operation the major portion of the growth was outside of the bladder. However, its only intimate attachment was to the bladder wall and it would seem more probable that its origin was from this structure than from the retroperitoneal tissues outside of it.

The histologic features of the primary tumor compel us to classify it as an example of Abrikossoff's third group of myoblastic myomas or granular cell myoblastomas, as we prefer to call them. We have been unable to find any reports of this tumor form arising either in the bladder or in the retroperitoneal tissues. These granular cell myoblastomas are almost certainly of rhabdomyoblastic origin, as was originally pointed out by Abrikossoff on histologic grounds and confirmed by the, as yet unpublished, observations on tissue cultures by Dr. Margaret Murray, of the Laboratory of Surgical Pathology of Columbia University. The suggestion of chondriosome formation in some of the metastatic tumor cells may also be regarded as confirmatory evidence.

It need not be any cause for surprise that an embryonal striated muscle cell tumor should arise in the bladder for there are a number of cases of rhabdomyoma and rhabdomyosarcoma of that organ on record. Montpellier, in 1929, found records of 12 cases. Ten years later, Uhlmann, Grossman and Calvin found seven more, and we have found at least seven other cases not included in those two groups (Janū and Stolz, 1932; Bailey, 1934; Planque, 1937; Hirsch and Brown, 1938; Vermooten, 1939; and Hunt, 1943, two cases). All of these tumors were composed of more or less differentiated rhabdomyoblasts usually with cross striations and none had the granular cells characterizing this tumor. Most of them occurred in children and displayed their malignancy by rapid infiltrative local growth. Metastases were very uncommon.

But perhaps the most important observation here recorded is the fact that one of these granular cell myoblastomas has behaved like a malignant tumor and metastasized. So far as our information goes, this is the first proved case to have exhibited this phenomenon among 50 cases recorded in the Laboratory of Surgical Pathology of Columbia University, and nearly 100 other reported cases. It will, therefore, no longer be possible to regard the granular cell myoblastoma with equanimity as an entirely benign neoplasm which never metastasizes. On the other hand, such an event must be extremely uncommon so that usually it need not be anticipated.

SUMMARY

A malignant granular cell myoblastoma is reported which arose probably in the urinary bladder, recurred following excision, and caused death with metastases 17 months after operation. The primary growth is identified as an example of Abrikossoff's third group of myoblastic myomas. As such, it is believed to be the first example of its kind to have developed in the bladder and also the first record of such a tumor to metastasize and cause death.

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