Multiple and highly malignant neurogenic sarcomata confined to the nerves of the retroperitoneal spaces and following the distribution of these nerves to the abdominal viscera are extremely rare. The patient whose record follows showed no cutaneous nodules, pigmentation, or other phenomena commonly associated with tumors of the von Recklinghausen type.

CASE REPORT

A white woman, fifty-seven years of age, a chambermaid, was admitted to St. Luke's Hospital, Oct. 18, 1934, complaining of loss of strength and weight, beginning about a year earlier. Her previous health had been good. Shortly after the onset of the initial symptoms anorexia developed, and the patient, too fatigued to prepare her meals, would often go to bed immediately upon returning from her work. Despite these symptoms she continued at her occupation until two weeks and a half before admission, when she was seized with severe pain in the right lower quadrant of the abdomen, which gradually spread to the upper right quadrant. The pain was very sharp and was aggravated by bending forward. It remained more or less constant during the ensuing four days, at which time the patient noticed that her abdomen had become considerably enlarged. A heavy, dragging sensation in the left lower quadrant forced her to sleep on the right side. Ten days prior to admission she was unable to retain any food other than fluids. No blood or coffee-ground material was observed in the vomitus, nor was there any gross blood in the stools.

On examination the patient was found to be somewhat emaciated, and obviously suffering severe pain. The skin and mucous membranes showed no abnormalities. There was some tortuosity of the retinal veins, but the discs were normal. There were no physical signs of changes in the lungs. The heart was not enlarged; the rate was somewhat rapid though regular, and a blowing systolic murmur was heard at the base. The blood pressure was 140/70. In the left lower abdomen was a firm, oval mass slightly tender on pressure and extending from the left parasternal line below the costal margin to the iliac crest.
Adjacent to the main mass was a less prominent tumor extending to the right of the midline to the brim of the pelvis. There was slight edema of the lower extremities. Neurologic examination revealed no abnormalities. The blood showed 35 per cent hemoglobin; red blood cells 2,600,000; white blood cells 17,900, with 92 per cent polymorphonuclear leukocytes and 8 per cent lymphocytes. The blood urea was 17.2 mg. per 100 c.c.; glucose 125 mg.; the bile index was 9. The Wassermann reaction was negative and no bone changes were demonstrable in the radiographs. The stool contained a normal amount of trypsin, but gave a positive blood test on three occasions. No ova or parasites could be discovered. The urine was negative.

Two blood transfusions were given and an exploratory laparotomy was performed. Following a thorough exploration of the abdominal cavity, the lesion was deemed inoperable and the wound was closed. The temperature remained between 100 to 102° for five days and the patient became progressively weaker and died. Autopsy (No. 3554) was performed seventeen and one-half hours after death.

![Fig. 2. Neurogenic Sarcoma of the Peritoneal Cavity. X 280](image)

No cutaneous pigmentary changes, nevi, tumors or nodules on the peripheral nerve trunks were found. There was no enlargement of the superficial nodes. The pupils were round, the right considerably smaller than the left. The sclerae were clear. On opening the abdomen, approximately one liter of thin bloody fluid was found in the peritoneal cavity. Beneath the operative incision was a large soft mass of fibrinous blood clot. The great omentum covered the upper portion of the retroperitoneal tumor, which was solid, oval, hard and white, extending across the vertebral bodies into the left flank (Fig. 1). It measured 23 × 17 × 14 cm. and weighed 3100 gm. The posterior surface was attached rather firmly to the retroperitoneal tissues and overlay both kidneys, the pancreas, and the duodenum. No connection between it and the lumbosacral plexus could be found. A portion of the jejunal mesentery was firmly attached to its medial surface. Numerous sessile and pedunculated nodules were present over the surface of the main mass, varying from 0.5 to 4 cm. in diameter. Their consistency was variable; some were soft, yellowish, and degenerated; others were hard; the cut surface was in general a dull white, except for the hard portions, which had a tendinous shiny appearance with a whorl-like structure. The main tumor was fibrous in consistency and dull white on cut section. Focal areas of necrosis
FIG. 3. SECTION FROM THE LARGE MASS IN THE PERITONEAL CAVITY, SHOWING PARALLEL AND INTERLACING BUNDLES OF CLOSELY PACKED ELONGATED FIBERS RESEMBLING NERVE FIBERS. × 225

FIG. 4. TUMOR TISSUE SHOWING AREA OF CONTACT BETWEEN LARGE AND SMALL CELL GROUPS. × 280
were present near the center of the growth, some of which were hemorrhagic. In the mesentery of the entire small intestine were many pedunculated nodules, tending to radiate from its root outward in linear fashion, and studding the parietal peritoneum, particularly about the brim of the pelvis and beneath the diaphragm. The omentum was completely infiltrated by these nodules. The stomach and esophagus showed no changes. No tumor masses projected into the lumen of the jejunum or ileum nor were any palpable within the muscle coats, though the mucosa was greatly congested. There were a few soft polypoid tumors attached to the epiploic appendages throughout the colon, but there was no invasion of the wall or lumen. The presence of blood in the gastro-intestinal tract, therefore, was not related directly to the tumor but to the passive congestion of the intestinal mucosa.

The liver weighed 2000 gm. Its capsule was smooth and glistening, and on section the organ had a uniform dark reddish-brown mottled color. It was studded with numerous, hard, round, apparently encapsulated tumors, measuring 3 to 5 cm. in diameter. These nodules could be shelled out from the surrounding liver parenchyma. On section they showed a dull white, whorl-like, interlacing structure similar to those found in the mesentery. The gallbladder and extrahepatic ducts showed nothing remarkable. The spleen weighed 275 gm. A few small, white tumor nodules were present on the diaphragmatic capsular surface. A small white infarct was observed in the lower pole beneath the capsule, but no tumor tissue was found in the organ. The pancreas and adrenals were normal. The right kidney weighed 125 gm., the left 150 gm. No tumor nodules were present in either kidney, and ureters and bladder showed nothing of interest. There were a few small, white, soft, polypoid tumor nodules on the posterior peritoneal surface of the uterus and on the broad ligament, resembling the mesenteric nodules on section. The tubes and ovaries were not involved.

A few hard, white, nodular tumors, 1 to 2 cm. in diameter, were seen under the pleural surface of the lower lobe of the right lung and extending into the lung parenchyma. In the lower lobe of the left lung were a few subpleural nodules, not exceeding 0.5 cm. in diameter. There was no involvement of the tracheobronchial or posterior mediastinal nodes. The heart showed only moderate sclerotic changes in the larger coronary branches. There was a moderate degree of atheroma involving both the thoracic and abdominal portions of the aorta. While there was a slight left lumbar scoliosis, there was no evidence of erosion of the vertebral bodies or transverse processes. The brain, spinal cord and peripheral nerves could not be examined because of autopsy restrictions.

Microscopic examination of the tumor showed the main mass to be composed of long spindle-shaped cells with elongated hyperchromatic nuclei, the whole arranged in interlacing whorls. Mitotic figures were fairly numerous, and interspersed throughout the tumor tissue were large polyhedral cells with deeply staining vesicular nuclei (Fig. 2). There was a moderate infiltration of lymphocytes and eosinophils throughout the tumor and large areas of necrosis were present. Silver stains with the Bielschowsky-Maresch technic showed the capsule to contain bundles of branching, interlacing neurofibrils which penetrated the substance of the tumor, forming a delicate reticulum about some of the cells. Silver impregnation, as with the Laidlaw stain, showed fine strands of connective tissue running parallel to the cell nuclei.

The mesenteric, peritoneal, omental, uterine, and other abdominal nodules showed essentially the same structure as the large tumor, though varying in cellularity, amount of intercellular tissue, and tendency to penetrate the surrounding capsule. A few of the small nodules in the omentum were composed almost entirely of closely packed, large, polyhedral cells with round and spindle-shaped hyperchromatic nuclei, but there remained a certain amount of zonal structures with interlacing bands of tissue. Occasionally very large tumor cells were seen, with polymorphous nuclei, and masses of these cells were sometimes contiguous with tumor areas composed of small cells with palisaded nuclei (Fig. 4).

Sections of the tumor involving the liver (Fig. 5) and the lung (Fig. 6) showed little difference in morphology from the main mass. The capsule was occasionally thick and well defined. A palisading of the nuclei and interlacing bundles of spindle cells were evident throughout. Neurofibrils were demonstrable with silver stains both in the capsule and throughout the tumor.
Discussion

The histogenesis of the so-called neurogenic sarcomata is a much discussed question. Virchow regarded them as false neuromata in that they did not contain multiplying nerve cells. Verocay thought the tumor cells of the neurinomata were proliferating sheath cells from the sheath of Schwann and therefore ectodermal in origin. The more modern French authors, Letulle, Charrier, Bertrand, and others, also adhere to this doctrine, classifying the growths as schwannomas. Hassin accepts the idea that the derivation is from the embryonic cells of the Schwann lemmoblasts. Penfield and others believe the tumors to be mesodermal derivatives arising from the epineural, perineural and endoneural connective-tissue sheaths, particularly the latter. Obviously even those that adhere to the schwannoma idea have to grant that mesodermal derivatives must enter the tumor with the vessels and nerve sheaths. Masson holds that they are neuro-ectodermal derivatives. Stout considers that the tumor, being derived from the sheath of the nerve, may properly be designated as a neurilemoma.

In the patient described the uniformity of the tumor architecture and the undoubted malignant character raise the question of a multicentric or unicentric origin. In their anatomical relations in the peritoneal tissues, along the course of the intestinal mesentery and omentum, and in their gross morphology, these tumors present a striking analogy to the multiple, cutaneous, pedunculated nodules of so-called von Recklinghausen's disease. In this case the tumor followed the abdominal sympathetic nerve distribution. The variation in cellularity, the amount of intercellular tissue, and the presence of a capsule also bespeak a primary origin from a neurofibromatous structure.
Fischer in 1927 collected a total of 466 cases of von Recklinghausen's disease reported in the literature and found evidence that a sarcomatous change had occurred in 13 per cent of them. These neurogenic sarcomas were observed most frequently in the nerve trunks of the lumbosacral and brachial plexuses. Garré differentiated between a primary sarcoma of nerves unassociated with von Recklinghausen's disease and the secondary sarcomas occurring in a pre-existing von Recklinghausen's disease. He found the former to be of greater malignancy and prone to earlier metastasis to internal organs, while the latter tended to remain encapsulated for a long time even if rapidly growing. Hosoi, however, found metastasis to occur in 22 per cent of 65 cases of von Recklinghausen's disease in which a sarcomatous change was noted. The lungs, pleura, diaphragm and liver are the sites of metastatic predilection. Bone metastases have been twice reported (Hume and Gray).

Primary multiple sarcomas arising in two or more neurofibromas in a case of von Recklinghausen's disease appear unusual, though cases have been reported by Plenge, Hulst, von Recklinghausen, and others. Also many observers have noted that, following extirpation of one sarcoma, a neurofibroma in another location may show rapid growth and a sarcomatous structure on removal (Habermann, Finotti, von Winiwarter, Hartmann). It is not unlikely in these cases that malignant changes were present in tumors which were assumed to be benign until growth was well advanced. Stewart's observations on sarcomatous change occurring in von Recklinghausen's disease would appear to substantiate this, contrary to the earlier observations of Garré. He found that there was a tendency toward multiple nerve trunk involvement and, what is more important from the point of view of treatment, that the disease often extended along a nerve trunk without being evident from any

**Fig. 6. Neurogenic Sarcoma. Metastasis in Lung. X 225**
increase in size. If, therefore, the tumor is removed surgically the nerve involved should be resected as far as possible, since numerous recurrences have been observed after such removal, frequently in the distal nerve segment.

Stewart in analyzing his material groups the tumors as Grades I, II, and III. Grade I includes relatively acellular fibrous tumors composed of spindle cells lying in dense hyaline fibrous material. In this group also belong tumors with very extensive mucinous degeneration and few cells. Grade II includes the more cellular tumors with interlacing whorls of hyperchromatic spindle cells and occasional giant cells. Grade III consists of very cellular tumors with small spindle or polyhedral, closely packed or large polyhedral and atypical giant cells, occasionally with telangiectatic features. For clinical analysis Stewart grouped his patients into those in which nerve connections were demonstrated by dissection and those in which the stigmata of von Recklinghausen's disease were present. The case just reported obviously falls into the former group and should certainly be considered as of Grade III because of the cellular, sarcoma-like areas and extensive metastases.

The clinical results when compared with the grading as shown in Stewart's paper are interesting. Among 16 patients with Grade I lesions from the Memorial Hospital material, there were 4 five-year cures. In Grade II there were 36 patients and only 2 five-year cures. In Grade III there were 21 patients and only one has remained well for over five years.

Stewart does not feel that trauma had anything to do with the appearance of the neoplasms, and our patient gave no history of injury.

Conclusions

1. A very unusual example of neurogenic sarcoma arising within the abdominal cavity and spreading intraperitoneally is reported. The rapid growth, the numerous metastases, and the morphology of the tumor all warrant its classification as a Grade III neoplasm.

2. Careful physical examination showed no associated cutaneous pigment spots, bone changes, skin neurofibromata, or other anomalies commonly seen in so-called von Recklinghausen's disease. No family history of von Recklinghausen's disease could be elicited from the patient.

3. The primary tumor, the multiple abdominal nodules, and the metastases in the liver and lungs could not be differentiated histologically. It is probable, therefore, that the disease began as a localized retroperitoneal tumor, possibly in some of the nerve trunks close to the origin from the spinal column, spreading laterally about the abdomen and into the mesentery, and forming extensive metastases elsewhere.

4. The case under consideration and the examples reported in the literature are sufficient evidence that the prognosis in the presence of a neurogenic sarcoma is always grave.