# MEDIASTINAL GANGLIONEUROMA

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Case.—Girl, aged seven and one-half years, was admitted to Roosevelt Hospital, November 1, 1930, with complaints of cough and fever, of one and a half years' duration. These symptoms occurred in attacks in which the patient coughed until breathless, raising a small amount of sputum. There was no vomiting, no night sweats, no loss of weight. The past history was negative. She had been immunized against diphtheria and vaccinated against small-pox. The present attack began two days before admission and

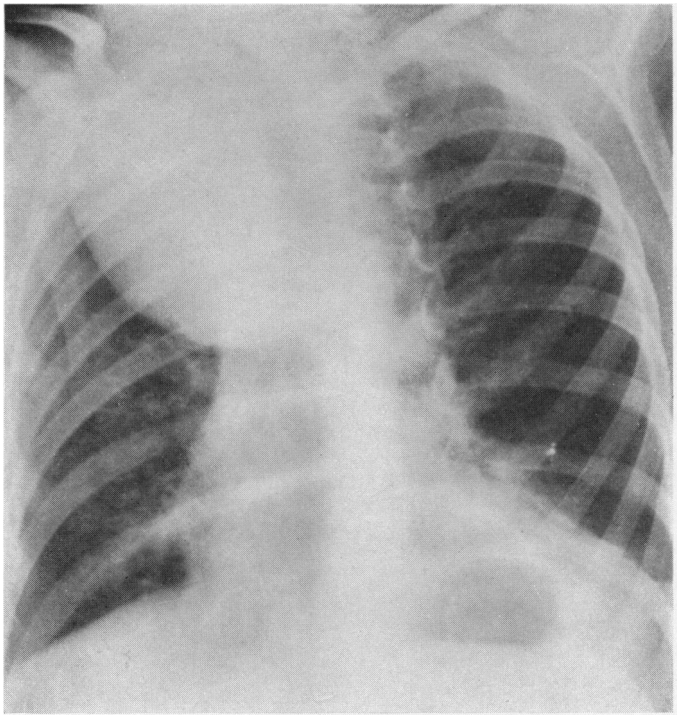

Fig. 1.—X-ray, November 3, a shadow with a sharp convex external margin is seen in the extreme upper portion of the right lung field. Trachea is displaced to the left.

was accompanied by fever, ranging from 99° to 104°. On examination the only positive findings were dry, squeaking râles over the entire chest. There was no evidence of consolidation.

X-ray of the chest taken November 3 demonstrated a circular shadow of increased density occupying the extreme upper portion of the right lung field. The trachea was displaced to the left. A lateral view showed an anteroposterior diameter greater than that found in the posterior-anterior film. (Fig. 1.)

Physical examination in this zone showed increased dullness and decreased breath

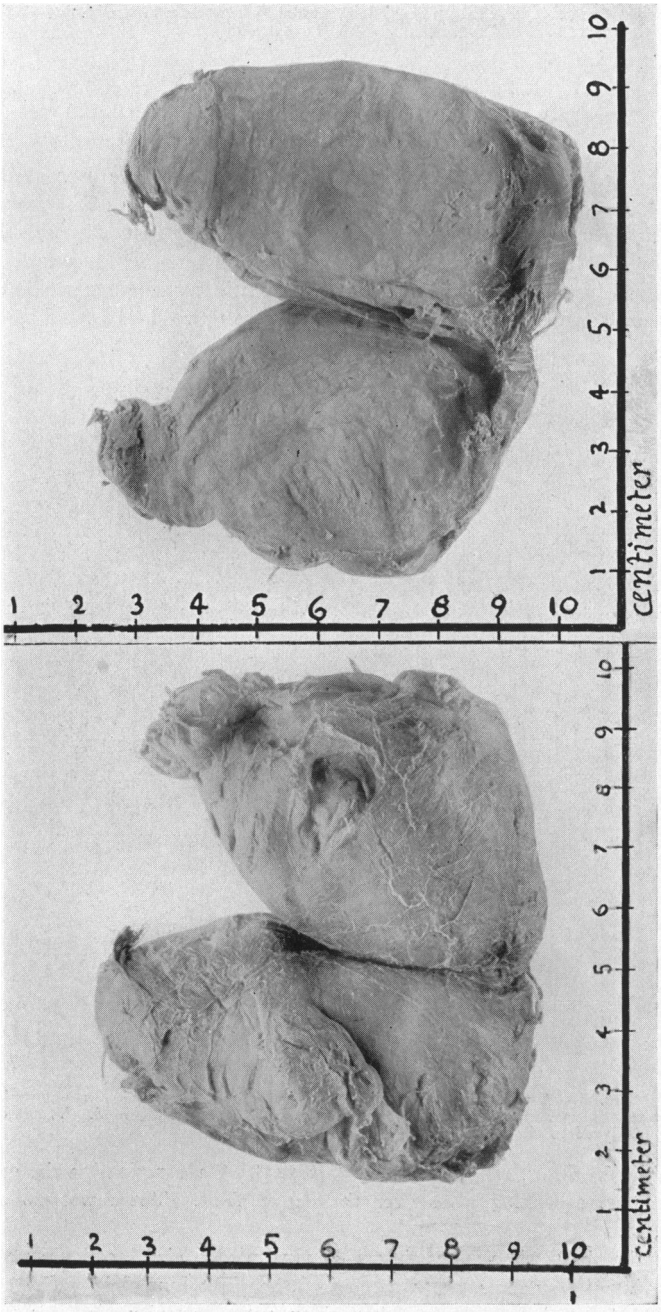


FIG. 2.—Gross specimen showing capsule with projecting tabs.

FIG. 3.—Cut surface showing distinct fibrous markings.

sounds, high on the posterior aspect of the right side of the chest, beginning one inch below the spine of the scapular and extending over the apex of the lung to the second interspace anteriorly.

Blood examination revealed red blood-cells 4,300,000; hæmoglobin 65 per cent.; white blood cells on several examinations varied between 6,300 and 16,700 of which, in the latter count, 81 per cent. were polynuclear neutrophils.

November 14, 1930, operation was undertaken under intratracheal anæsthesia by Dr. J. I. Russell. A large hypodermic needle was first introduced into the back over the estimated position of the tumor and an attempt was made to aspirate, in order to exclude the presence of a cyst. No material could be obtained except a small amount of blood. Following this, an incision was made obliquely from the first rib near the midline posteriorly, downward and outward across the third rib. The second, third and fourth

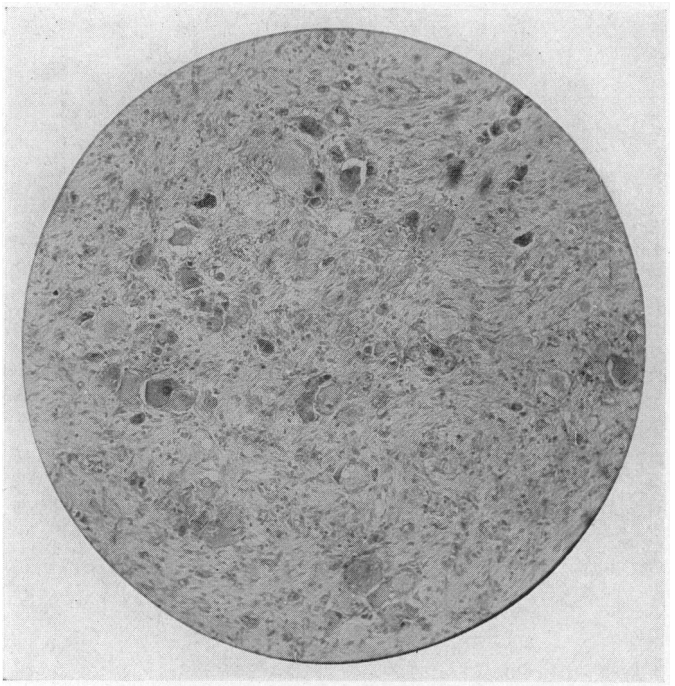

FIG. 4.—Microscopic (X-125), showing numerous ganglion cells of irregular form, some with multiple nuclei. The stroma is loose and fibrillary in some areas and densely fibrous in others.

ribs were exposed after separation of the trapezius and rhomboid muscles and the third rib was resected. The tumor was exposed and found to be extrapleural. On account of its size it was then found necessary to resect the second and fourth ribs. The incision was then enlarged, through the periosteum and subcutaneous tissue and the lung exposed. The tumor appeared to be about 3½ by 2 inches and encapsulated. By gradual finger dissection it was brought into the wound and raised from the mediastinal cavity. A small pedicle was found attaching it opposite the body of the second dorsal vertebra. This was divided. There was very slight bleeding. The pleura was torn at one point and immediately repaired. The lung did not collapse at any time, even when the positive pressure was withheld. The deep parts were closed with continuous catgut, the muscles with interrupted catgut and the skin with interrupted sutures of silk which were removed on the sixth day.

*Pathological Examination.*—The specimen (Fig. 2) was ovoid, weighed 150 Gm.

and measured 10 by 7 by 6 cm. The color was yellowish pink, and the capsule fibrous with a projection on one broad surface which came to a ragged point where an attachment had been cut. A rounded lobulation was noted on one surface. On section (Fig. 3) the cut surface was pinkish gray and showed fibrous markings, like a fibroma. The consistency was resilient and in the central portion occurred a small linear hæmorrhage (possibly caused by the needle puncture).

Microscopic examination (Fig. 4) revealed a stroma of small spindle cells scattered among a considerable amount of fibrillary substance. Very striking were the numerous large rounded and stellate cells which stained deeply with hematoxylin and presented rounded nuclei, frequently with one prominent nucleolus. These cells appeared sometimes grouped among delicate fibrillæ and surrounded by trabeculæ of denser supporting stroma.

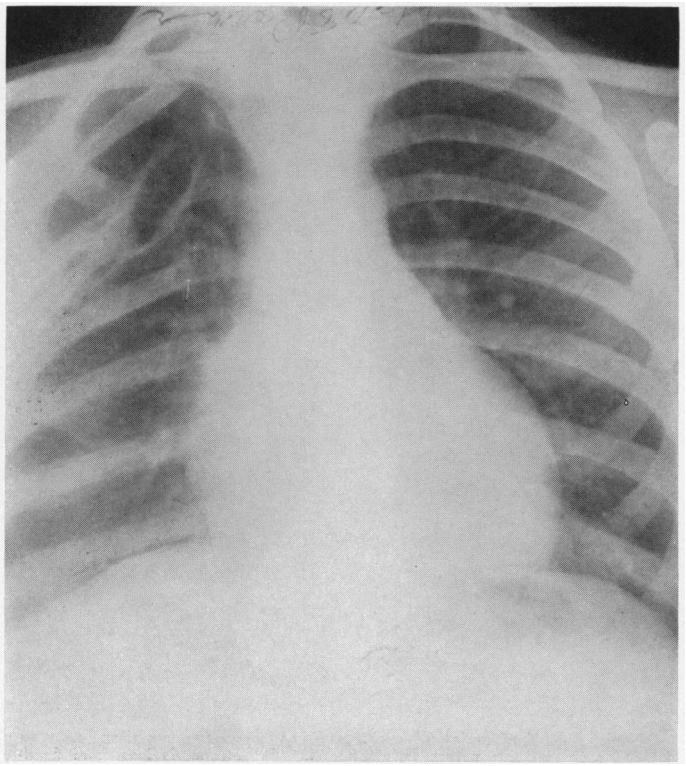

FIG. 5.—X-ray of chest on April 29, 1933, without evidence of recurrence.

Some foci consisted of non-nucleated rounded or tubular masses 20 to 30 micra in diameter staining with eosin. By the Weigart method these appeared to be myelin. There were also some foci of fat with necrosis, calcification and giant-cell formation of the foreign body type. In such zones could be seen clusters of lymphocytes. Diagnosis.—*Ganglioneuroma.*

*Post-operative Course.*—X-ray November 25 showed a definite fluid level in the cavity from which the tumor had been removed. The heart and trachea were in the midline. December 19, the shadow in the right upper lung field was considerably reduced and the fluid line was absent. The shadow assumed an irregular outline and diminished in size on subsequent examination January 3, 1931. The patient was discharged in excellent physical condition on this date. The postoperative course was smooth with fever diminishing after ten days and remaining normal. On subsequent examinations the physical condition was found excellent. X-ray April 29, 1933, showed no evidence of recurrence, the lung tissue filling in the right apex completely. (Fig. 5.)

COMMENT.—*Occurrence.* Ganglioneuroma has been observed in various portions of the central and peripheral nervous systems and in connection with outlying sympathetic ganglia, mainly in the adrenal gland, carotid body, coccygeal gland and Zuckerkandl's organ. A few cases have occurred in the cerebral hemispheres and a number have been subcutaneous.

The first reported case was that of Loretz in 1870, arising in a prevertebral ganglion. The number of known cases has increased rapidly during the past twenty years. In 1924 Brunner[1] could collect only fifty-one cases to which he added an operated mediastinal case of his own. In 1931 in reporting an additional case, McFarland[2] tabulated references to ninety-three reported cases, under the anatomical subdivision, central nervous system, cranial nerves and roots, neck, thorax, abdomen and peripheral nerves. The abdominal group includes alimentary, adrenal, retroperitoneal (the most numerous) and pelvic.

A recent review by Bigler and Hoyne[3] carried the total number to ninety-seven. Since then cases have been added by Haven and Weil[4], Jergesen[5] and by Schliefstein[6]. A majority of the reported cases have been accidentally discovered during the course of routine autopsy examinations.

The age distribution includes infancy and old age, but a striking number of cases below sixteen makes the condition of especial interest to the pediatrist. Of their ninety-seven, Bigler and Hoyne[3] found forty-one fell into this age group. A definite preponderance of females is also apparent.

*Histogenesis.*—Ganglioneuroma is the most adult variety of a series of tumors formed by primitive cells of the nervous system. The most primitive cell, the neuroblast, sympathicoblast or neurocyte, is an undifferentiated, round cell with little cytoplasm, resembling on casual examination a lymphocyte, but identified by the formation of neurofibrils and rosettes, and by an extremely active malignant growth potentiality. Some cells of this type may at times be found in a ganglioneuroma, and presumably account for the malignant varieties of this tumor. A remarkable example of the relationship between the sympathicoblastoma, the common malignant tumor of the adrenal medulla in infants, and the ganglioneuroma is that of Cushing and Wolbach[7]. They observed a malignant sympathicoblastoma of the paravertebral region in a one year old infant. A recurrence removed at the age of eleven years revealed a transformation of this tumor into a benign ganglioneuroma. This is perhaps another point in favor of regarding these tumors as embryonal rests or misplaced tissue with limited capacity for aberrant growth, the type of tumor called hamartoma by Allbrecht.

The mature ganglioneuroma presents a very striking histologic appearance well described by Wahl[9], Stout[8] and others. The stroma varies from delicate loose fibrils to firm collagenous fibrous tissue. The ganglion cells may be unipolar, bipolar or multipolar, may or may not contain tigroid granules and frequently have more than one nucleus. Unmyelinated nerve fibers are very numerous, but myelin also occurs. The ganglion cells are

usually grouped together. Evidence of necrosis is usually found in some foci. Occasionally, there are groups of neurocytes.

*Surgical Anatomy.*—Arising in and developing along the cranial nerves and the cervical, thoracic and retroperitoneal sympathetic trunks, the anatomic relationships of a ganglioneuroma are conditioned to a great degree by the pre-existing structures in which it arises. Thus Stout[8] points out that in the region of the superior cervical ganglion, a ganglioneuroma will reach up to the region of the tonsil, push aside the tongue and extend up to the submaxillary fossa behind the mandible. Similarly in the neck the tumor is usually between the carotid artery and the jugular vein and is always in front of the vagus nerve. In the thorax, ganglioneuroma extends from the bodies of the vertebræ forward and away from the midline, pushing the parietal pleura in front of it and not invading the lung. There is sometimes an extension through an intervertebral foramen and an invasion of the spinal canal with pressure on the spinal cord. The outline seen in the *x*-ray is usually ovoid with a flattened medial aspect facing the vertebral bodies and a sharply defined convex lateral border which may reach a greater or lesser distance toward the parietes. This outer border is usually very well defined. The density is homogeneous throughout.

*Degree of Malignancy.*—The great majority of ganglioneuromata appear to be completely benign neoplasms. The growth is usually slow. Riggs and Good's[11] case showed no change in size in *x*-rays taken over a course of over a year. Some cases have grown rather rapidly. McFarland's case attained a size of 4½ pounds in a year's clinical observation.

The capsule is usually incomplete and on this account the surgical removal may leave small portions of the tumor behind. Busse-Kredel (quoted by Brunner[1]) was obliged in his case to leave a small portion of tumor and on subsequent observation found that this was completely absorbed. In our case the projections from the capsule were transected and no clear-cut dissection was possible, yet the small portions left behind have showed no growth activity.

Malignant types of this tumor have been reported. Brunner[1] quotes a case reported by Beneke in 1901 occurring in a ten year old female, in which metastases developed. A similar malignant variety (degeneration would be an unjustified term, since the cell type is probably primarily either benign or malignant) was that of Berner[11] a four and one-half year old female with metastases of ganglion cells and neurofibroma stroma in the regional lymph nodes.

*Prognosis.*—In the collected cases of Bigler and Hoyne[3], there are thirty-nine operated cases. Of these, twenty-five were in children, with twenty reported as cured. Of the fourteen adult cases, all were cured. The mediastinal cases in the same series numbered ten, of which half were in children. Five of these cases were operated upon (four were children) and three were pronounced cured. Our case is therefore to be placed in this small group of cured mediastinal cases.

A variety of operative and postoperative complications and sequelæ are to be considered. In the neck, the occurrence of paralysis of the cervical sympathetic nerve is to be expected from its close anatomic connection with the tumor. This occurred in Lillienthal's[12] case and in one of Stout's[8], resulting in the development of Horner's syndrome. Brunner's[1] case required several reoperations and transpleural approach, and was complicated by gangrene of the lung. An extensive thoracoplasty was necessary. The deep-seated position of these tumors and their frequent proximity to large vessels make hæmorrhage another serious factor.

It should also be pointed out that a number of cases have showed the presence of multiple tumors, sometimes widely distributed. In one such case the removal of all the observed tumors was successful.[4]

A definite prognostic value exists in the recognition of this tumor, because of its benign course, as contrasted with the marked tendency to recurrence and malignant development of neurogenic fibroma, a tumor of similar gross and, when inadequately examined, microscopic appearance, occurring in similar anatomic structures.

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