Retroperitoneal Ganglioneuroma: A case report and review of literature

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Ganglioneuroma, a tumor of neural crest origin, is a rare neoplasm; to encounter it in an adult over 50 years of age is very rare. This report describes the case of a 56-year-old man who was seen at Henry Ford Hospital with an abdominal mass confirmed as ganglioneuroma on histopathology. Experience at Henry Ford Hospital and the available literature on the subject are reviewed.

Introduction

Ganglioneuromas are relatively rare, benign tumors which arise from the sympathetic ganglia and thus eventually originate in the neural crest. They are usually found along the distribution of the sympathetic chain and have been commonly reported in the neck, mediastinum, and retroperitoneum. The histological course of a malignant neuroblastoma maturing into a benign ganglioneuroma has been well established in the literature, with most cases occurring in children and young adults. A review of available English literature reveals that only 20 cases of ganglioneuromas have been reported in adults over 50. This article reports the case of a 56-year-old man who presented with a retroperitoneal mass confirmed histologically as a ganglioneuroma. Experience at Henry Ford Hospital with this neoplasm is also reviewed.

Case Report

A 56-year-old black man was first seen in March, 1976 with increasing epigastric discomfort of one month's duration. In 1960, he had been treated elsewhere for a duodenal ulcer marked by upper gastrointestinal bleeding. Since then, he had been using antacids with satisfactory, temporary relief. During the past month, the exacerbation of his symptoms prompted him to come to our Gastroenterology Clinic.

Physical examination showed a nontender, ballotable mass in the upper right quadrant of the abdomen lying posteriorly and measuring approximately 20 x 15 cms. Examination of cardiovascular, respiratory, and central nervous systems was unremarkable. The patient's blood counts, blood chemistry (SMAC), urinalysis, alphafetoprotein, hepatitis antigen, and serum immunoglobulins were all within normal limits. VDRL was negative. Plain x-rays of the abdomen showed increased tissue opacity in right upper quadrant of abdomen with obliteration of psoas shadow. Intravenous pyelogram showed an extrarenal mass on the superior and lateral aspect of the right kidney pushing it medially and anteriorly. Abdominal echogram showed a solid mass closely related to the inferior surface of the right lobe of the liver but definitely separate from the right kidney and with a slightly different echographic character from that of the liver. Oral cholecystogram, upper gastrointestinal
and small bowel series, and barium enema x-rays were all normal except for the extrinsic mass effect pushing the right colon anteriorly.

On April 5, 1976, an exploratory laparotomy was done through a right subcostal incision. A firm, well-encapsulated mass, 20 x 15 x 7 cm, was found in the right retroperitoneal region below the liver, displacing the right kidney medially and right colon anteriorly. The right adrenal gland was normal and intact. The mass was grayish-white and attached to the underlying muscles with loose areolar tissue. Its blood supply was circumferential coming from the underlying muscles. No attachment was noted either with the spine or the sympathetic chain. The mass was excised intact. The specimen weighed 700 gms, and cut section revealed variable consistency and uneven surface with glassy appearance (Figure 1). Histologic examination confirmed the diagnosis of ganglioneuroma (Figure 2). The patient's postoperative course was uneventful, and he was discharged one week later.

**Analysis of Case Records**

Fifteen, histologically-documented cases of ganglioneuromas were recorded at Henry Ford Hospital from 1965 to 1976. Eight of these were diagnosed by surgical excision and seven were detected at autopsy. The site and age distribution of these cases are given in Table 1.

**Incidence**

In 1846 Knoefallanch reported the first case of ganglioneuroma, and in 1870 Loretz reported another one in the mediastinum. In 1947, when Stout reviewed the world literature, he cited only 243 instances of ganglioneuromas in all age groups. Carpenter et al described only 21 cases in 44 years' experience at the Mayo Clinic, while Hamilton and Koop reported 17 cases which had been treated and followed at Childrens' Hospital in Philadelphia from three to 23 years. Thus, the relative rarity of this tumor is obvious from these reports and from our experience at Henry Ford Hospital.

Sixty percent of these tumors are found in persons under 20 years of age, with most under ten years. This was reflected clearly in the collective review of Stout as well as in the Mayo Clinic series and the Henry Ford Hospital experience (Table 2). Although there are six patients over 50 in our series, in five of them the tumors were incidental autopsy
findings. Three were found in the adrenal gland, one in the retroperitoneum, and one in the colon; all were small. Our reported case, the sixth in the series, is the only patient over 50 in whom a large retroperitoneal ganglioneuroma was excised surgically.

A female-to-male ratio of three to two has been reported universally. However, the preponderance of tumors found on the left side, as reported by Coenen and quoted in Stout's review, was not substantiated in other reports. Our cases show equal distribution for sex and side of body.

TABLE I
Ganglioneuromas: Henry Ford Hospital Experience, 1965-1976
Distribution of Location, Age, and Mode of Detection

<table>
<thead>
<tr>
<th>Location of Tumors</th>
<th>Autopsy Cases</th>
<th>Surgical Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Age Distribution</td>
</tr>
<tr>
<td>Adrenal</td>
<td>4</td>
<td>4, 69, 73, 82 yrs</td>
</tr>
<tr>
<td>Mediastinal</td>
<td>0</td>
<td>3, 60 yrs</td>
</tr>
<tr>
<td>Retroperitoneal</td>
<td>2</td>
<td>55 yrs</td>
</tr>
<tr>
<td>Colonic</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Orbital</td>
<td>0</td>
<td>7 yrs</td>
</tr>
<tr>
<td>Sacral</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>7</strong></td>
<td><strong>8</strong></td>
</tr>
</tbody>
</table>

*This case is reported in detail.*
Most of these tumors are located along the sympathetic chain with an average distribution of 48% in the abdomen, 43% in the thorax, and 9% in the neck. However, small sympathetic ganglia can also give rise to such tumors, and dumbbell extensions of them in the spinal canal have been described. One of our patients, a 17-year-old woman, presented with spinal cord compression which required laminectomy and partial excision of the retroperitoneal growth before abdominal exploration to remove the remainder.

Although several reports in the literature describe these tumors in the alimentary tract, we had only one such case. In this patient, who had Von Recklinghausen’s disease and died of congestive heart failure, autopsy showed three firm, nodular, intramural lesions in the ascending and transverse colon. Histological examination demonstrated ganglioneuroma in all of these lesions, the largest of which was 3 cm in diameter. Alimentary tract ganglioneuromatosis has also been reported as a major component of the syndrome of multiple endocrine neoplasia, type 2B.

Occasional cases have been reported in the nasopharynx, maxilla, tongue, breast, peripheral joints, mesentery, peritoneum, kidney, bladder, uterus, and vas deferens.

In our series, we found an orbital ganglioneuroma, 2.5 x 1.5 x 1.0 cm, in a seven-year-old girl who had an inoperable neuroblastoma of the left adrenal gland. This orbital tumor was excised with excellent preservation of eye function, and the patient remains free of tumor recurrence at the age of fifteen. Stout’s review of 243 cases included only four instances of orbital and eyelid ganglioneuromas.

Pathology

Grossly, these tumors are moderately firm, rounded or lobulated, usually well encapsulated, and of any size. The two largest in Stout’s review were those described by Peters and Zagarese. In 1913 Peters reported a 6 kg tumor measuring 20 x 40 cm; in 1933 Zagarese reported a retroperitoneal tumor weighing 6.25 kg and measuring 54 x 42 cm. The largest tumor removed in the Mayo Clinic series weighed 5,200 gm. In our reported patient, the tumor weighed 700 gm and measured 20 x 15 x 7 cm.

To understand the origin of these tumors, the following scheme, modified from Gale et al., is helpful (Figure 3).

### TABLE II

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>0-9</td>
<td>69</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>10-19</td>
<td>43</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>20-29</td>
<td>30</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>30-39</td>
<td>20</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>40-49</td>
<td>5</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Above 50</td>
<td>20</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Total No. of Cases</td>
<td>187</td>
<td>21</td>
<td>15</td>
</tr>
</tbody>
</table>
Ganglioneuroblastomas, the in-between group, show various degrees of malignant potential. Maturation of a malignant neuroblastoma into a benign ganglioneuroma, which occurs in about 2% of the cases, has been well documented in several clinical and tissue culture reports. Sitarz et al., in a 1975 report which documented the stages of complete maturation of a neuroblastoma even with bone metastasis, have reported five cases of neuroblastoma out of 170 that matured to ganglioneuroma.

In his collective report, Stout concludes that ganglioneuromas in general do not seem to show any hormonal activity, although according to Hamilton and Koop, the tumor in one of their patients gave adrenergic symptoms. Histologically, ganglioneuromas are composed of Schwann cells, which are arranged in coarse, interlacing fascicles, and mature ganglion cells, which lie in compact clusters or in an irregular fashion. It has been conclusively shown by various reports that fully differentiated ganglioneuromas do not metastasize. If a metastasis occurs, a diagnosis of ganglioneuroblastoma should be considered.

Clinical manifestations and investigations
Ganglioneuromas are usually asymptomatic and found accidentally at routine physical examination or at autopsy, as we have seen in seven of our 15 cases. Sometimes, these may show symptoms due to local pressure effect, such as ureteric obstruction, spinal cord compression, or bowel obstruction. Occasionally, the patient himself may notice a mass. Hamilton et al. have reported a few cases which were hormonally active and presented with adrenergic symptoms like severe diarrhea, episodic hypertension, sweating, and flushing of the skin.

X-rays and urinary chemistry are most important in preoperative diagnosis. Plain x-rays may demonstrate some soft tissue swelling, as well as deformities of adjacent bone due to erosion and displacement of neighboring organs. Sometimes calcification may be seen. According to some investigators, intratumoral calcification indicates immaturity and, consequently, malignancy in the tumor, although Hamilton and Koop believe that it has no significance in differentiating malignant from benign tumors. According to them, calcification represents the end stage of a mass which has outgrown its blood supply, resulting in necrosis and calcification. Selective arteriograms, venograms, and myelograms have been helpful, as have contrast studies of the gastrointestinal and urinary tracts, which are useful only for localization and delineation of anatomic extent.

Twenty-four hour urinary vanil mandelic acid and homovanillic acid determinations have been reported to be helpful both in the diagnosis and follow-up of some patients. Hamilton and Koop, Greenberg and Gardner, Smillie, and Kogur have shown that hormonally active, benign ganglioneuromas do occur and can be accompanied by elevated vanil mandelic acid levels. Since malignant neuroblastomas show elevation of homovanillic acid rather than vanil mandelic acid, Bettes and his associates have recommended these determinations to distinguish between malignant neuroblastomas and benign ganglioneuromas. Postoperative elevation of urinary vanil mandelic acid may suggest probable recurrence of the tumor, although no such instances have been reported.

Management
Wherever possible, complete excision of the tumor is desirable in order to alleviate the symptoms from pressure effects, as well as to obviate the difficulty of definitive diagnosis on frozen sections between a more malignant neuroblastoma and a benign ganglioneuroma. Sometimes, due to the larger size of the tumor involving or encircling vital structures, it may not be technically possible to remove all of it. In such cases, as much should be removed as possible without jeopardizing vital structures. Long-term follow-up of such partially excised tumors has shown no further symptoms. Radiotherapy and chemotherapy have not been used for ganglioneuromas.

References