Catecholamine-secreting extra-adrenal pelvic ganglioneuroma in a child presenting with diaphoresis: A case report and review of literature

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Sweating, in normal physiologic conditions, is mediated both by cholinergic and adrenergic stimulation. Excessive sweating, or diaphoresis, may be caused by the beta-adrenergic effects of circulating ectopic catecholamines, produced by functional tumors, of which pheochromocytoma and paraganglioma are the most common. Diaphoresis as a clinical indicator of an underlying disease has been infrequently reported in pediatric age group, especially the very young, and might be overlooked by pediatric healthcare providers.

Ganglioneuromas (GNs) are benign tumors that originate from neural crest cells, which form the sympathetic nervous system. They are composed mainly of mature ganglion cells. The International Neuroblastoma Pathology Committee (INPC) define GNs as a schwannian stroma-dominant tumor, predominantly composed of ganglioneuromatous stroma, with a minor component of scattered collections of differentiating neuroblasts, and/or maturing or mature ganglion cells [1].

GNs can either develop de-novo, or as a result of spontaneous or chemotherapy induced maturation of a less mature neuroblastic tumor, such as neuroblastoma or ganglioneuroblastoma [2]. GNs may develop anywhere along the sympathetic nerve chain, most common locations in descending order of frequency are posterior mediastinum, retroperitoneum, adrenal gland, neck, and pelvis. Functional GNs are relatively rare in children.

1. Case report

4 year, 2 month old, otherwise healthy boy, presented to our care because of a history of copious sweating of 2 years duration over his entire body. His mother noted a significant increase in the severity of sweating, over the past 3–4 months, occurring mostly at night. History was negative for seizures, fever, diarrhea, loose stools, flushing, chest pain, tremors, abdominal pain, headaches, or visual changes. On physical exam, no abnormalities were detected. Blood pressure and heart rate readings, for the last three clinic visits were reviewed, and were always in the normal range. Initial laboratory evaluation was unremarkable.

The child was referred to pediatric endocrinology clinic. Thyroid function tests and serum electrolytes were all in the normal range. However, plasma dopamine and norepinephrine levels were found to be elevated. Urinary normetanephrine to creatinine,
norepinephrine to creatinine, and dopamine to creatinine ratios were also elevated. Table 1 summarizes the pre-operative and post-operative (48 days after surgery) catecholamine values, in plasma and urine.

Surgical consultation was obtained and a computerized tomography scan of the chest, abdomen and pelvis, with intravenous and oral contrast, was performed (Fig. 1). The study demonstrated a pelvic soft tissue mass measuring $31 \times 39 \times 51$ mm. It was rounded, with some irregular enhancing areas, and multiple speckled calcifications were present, with no evidence of bony erosion, or invasion. The adrenal glands and kidneys appeared normal, with no evidence of metastatic disease. Metaiodobenzylguanidine (MIBG) scan was done and interestingly showed no uptake in the pelvic mass.

The child was pretreated with an alpha-blocking agent, Phenoxybenzamine 10 mg, given daily orally. The drug was provided initially as an inpatient and subsequently at home, to complete one week of treatment prior to surgery. A beta blocking agent, atenolol 1 mg/kg given daily orally, was added for 48 h before surgery. Both drugs were well tolerated, with no recorded hypotension or bradycardia. Laparoscopic resection of the pelvic tumor was then performed. The mass was situated at the aortic bifurcation deriving most of its blood supply from the sacral artery and branches of the internal iliac artery. The dissection plane was developed on the adventitia of the aorta, common iliac arteries and internal iliac arteries. The iliac veins were also intimately associated with the mass. However the adventitial plane remained free of tumor. Normal and stable vital signs were maintained with tumor manipulation, and blood pressure support was not required intra-operatively. The mass was extracted through a slightly enlarged umbilical incision. After surgery, patient had an uneventful recovery, started a regular diet on the first day after surgery. Pain was well controlled. He received intravenous morphine for one day (two doses of 0.05 mg/kg), and oral acetaminophen (15 mg/kg every 6 h) for three days. He was discharged home on the third post-operative day. His symptoms of sweating resolved completely after surgery. Pathological evaluation of the surgical specimen showed maturing ganglionoma with no evidence of malignancy (Fig. 2). The boy remains asymptomatic, without evidence of recurrent disease.

### 2. Discussion

Functional adrenergic tumors in general are uncommon in the pediatric population. Adrenergic tumors presenting with diaphoresis are reported infrequently, possibly because complaints of excessive sweating may be difficult to elicit from young children. To our knowledge, this is the first report of a child presenting with diaphoresis resulting from a functional GN. In another reported case, a 4 month old girl with 3.5 cm right paraspinal neuroblastoma, who initially presented with an abdominal mass and resting tachycardia and hypertension, was retrospectively discovered to have had a history of excessive sweating with feeding [3].

GNs are most commonly clinically silent, and are often discovered incidentally on imaging studies [4]. Because they may not produce symptoms, GNs may not be discovered until they are very large and compress nearby structures. In contrast, patients with GNs that secrete catecholamines or their metabolites may present with labile hypertension, diarrhea, flushing, diaphoresis, or palpitation [5]. The proportion of patients with GNs, that secrete catecholamines, and are symptomatic, is not known.

Diagnosis may be suspected when excessive levels of catecholamines and their metabolites are detected in serum, or urine of patients. Axial and functional imaging such as computerized tomography (CT) scan, magnetic resonance imaging (MRI), and

### Table 1

Pre-operative and post-operative (48 days after surgery) catecholamine values, in plasma and urine.

<table>
<thead>
<tr>
<th>Catecholamine</th>
<th>Normal range</th>
<th>Pre-operative value</th>
<th>Post-operative value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dopamine, plasma (pg/mL)</td>
<td>0–20</td>
<td>724</td>
<td>47</td>
</tr>
<tr>
<td>Norepinephrine plasma (pg/mL)</td>
<td>85–1250</td>
<td>3096</td>
<td>499</td>
</tr>
<tr>
<td>Metanephrine/Creatinine ratio, urine</td>
<td>0–500</td>
<td>239</td>
<td>191</td>
</tr>
<tr>
<td>Normetanephrine/Creatinine ratio, urine</td>
<td>0–610</td>
<td>5043</td>
<td>336</td>
</tr>
<tr>
<td>Norepinephrine/Creainine ratio, urine</td>
<td>27–110</td>
<td>1817</td>
<td>81</td>
</tr>
<tr>
<td>Dopamine/Creatinine ratio, urine</td>
<td>220–720</td>
<td>1417</td>
<td>595</td>
</tr>
<tr>
<td>Vanilmandelic acid/Creatinine ratio, urine (mg/gCR)</td>
<td>0–13</td>
<td>6</td>
<td>–</td>
</tr>
<tr>
<td>Homovanillic acid/Creatinine ratio, urine (mg/gCR)</td>
<td>0–22</td>
<td>11</td>
<td>–</td>
</tr>
</tbody>
</table>

Fig. 1. a) Axial contrast enhanced computed tomography of lower pelvis. b) Sagittal contrast enhanced computed tomography. Presacral soft tissue mass measuring $31 \times 39 \times 51$ mm, with irregularly enhancing areas, and multiple speckled calcifications.
Laparoscopic resection of pelvic and abdominal retroperitoneal tumors is feasible and can be done safely, even when tumors secrete catecholamines, with low rate of significant blood loss, complications, and conversion [5].

There are currently no specific recommendations for preoperative alpha adrenergic blockade for GNs presenting with diaphoresis. In the Italian co-operative neuroblastoma group study, there was no report of any surgery complicated by hypertensive crisis [8]. Unlike pheochromocytoma, GNs are less likely to be metabolically active. However, in cases of catecholamines-secreting GNs, there is a potential that excess amounts of catecholamine might be released during the manipulation of the tumor, such an occurrence can result in catecholamine surge, leading to intra-operative hemodynamic instability. We feel that in patients with neurogenic tumors, which are shown to be catecholamine secreting, preoperative alpha-adrenergic blockade is necessary and may facilitate safer surgical excision. Hypertensive spells upon tumor manipulation have been reported during resection of metabolically active GNs [15]. We elected to proceed with alpha and beta adrenergic blockade in our patient. This was well tolerated well and we believe contributed to a smoother perioperative course.

3. Conclusion

GNs are rare, benign tumors, usually nonfunctional and asymptomatic, however a proportion of GNs might be hormonally active. Prolonged and unexplained diaphoresis in a child warrants screening urine and serum for catecholamine overproduction. The pre-operative utilization of alpha blockade is not recommended in non-functional GNs. However in symptomatic, hormonally active tumors, pre-operative alpha blockade might be indicated and can be safely performed.

Conflicts of interest

There are no conflicts of interest.

Acknowledgments

None.

References


