Perioperative Management of an Infant for Resection of a Neuroblastoma Symptomatic from Massive Catecholamine Secretion.

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Introduction: Neuroblastoma is the most common solid tumor of infancy. Neuroblastoma has the potential for catecholamine secretion, but even so, symptomatic presentation from catecholamine release is very rare in infancy. We describe the previously unreported perioperative management of an infant symptomatic from a catecholamine secreting neuroblastoma.

Case Report: A four month old (6 kg), baby girl was found to have an abdominal mass on exam by her pediatrician. She was also tachycardic and hypertensive, and she had been noted to become diaphoretic with feeding since five weeks of age. Prior workup had included a cardiac echocardiogram which was normal. A computed tomography scan was obtained, and demonstrated an isolated left paraspinal (3.5mm) mass. An MIBG (metaiodobenzylguanidine) scan was negative for metastases. Her free normetanephrine level was 14.9 nmol/l (normal < 0.9), urine vanillylmandelic acid and homovanillic acid were 115 mg/g creatinine (normal for age 0-2yrs: 0 – 27) and 257.5 mg/g creatinine (normal for age 0-2 yrs: 0-42), her serum norepinephrine level 8330 pg/ml (normal 270 – 1120), and her serum dopamine level was 931 pg/ml (normal 0 – 20). Free metanephrine and epinephrine levels were within the normal range. The patient was suspected to have stage I neuroblastoma and was scheduled for surgical resection.

Because of her history of diaphoresis, her tachycardia and hypertension, it was decided to pretreat her, and she was admitted to the ICU for initiation of alpha adrenergic receptor blockade. Phenoxybenzamine was started at 0.2 mg/kg twice daily (0.4 mg/kg/day) while administering intravenous maintenance fluids in addition to oral intake ad libidum. Blood pressure remained high and phenoxybenzamine was gradually increased to eventually 0.35 mg/kg four times a day (1.4 mg/kg/day) over 5 days. The last dose was administered on the morning of surgery. With initiation of alpha adrenergic blockade, her heart rate increased with resting heart rates at times greater than 200 / min. Labetalol 1 mg/kg was therefore added every six hours starting on the third day of treatment. Blood pressure and heart rate were in the normal range at the time of her surgery.

On the morning of surgery, the patient received midazolam intravenously for separation from her parents, anesthesia was induced with propofol and she was intubated following muscle relaxation with cisatracurium. Anesthesia was maintained with isoflurane in oxygen and air, supplemented by fentanyl. A thoracic epidural catheter was placed and following loading with 0.5 ml/kg bupivacaine 0.25%, a continuous infusion of bupivacaine 0.1% with fentanyl 2 mCg/ml was started at 0.3 ml/kg/h and maintained into the postoperative period. In addition to standard non-invasive monitors, an arterial and a central venous catheter were placed. A single dose of 50 mg/kg magnesium sulfate was administered. The intraoperative course was stable until manipulation of the tumor started, at which time blood pressure and heart rate increased but were easily controlled with sodium nitroprusside at a rate of up to 0.25 µg kg⁻¹ min⁻¹ and esmolol up to 50 µg kg⁻¹ min⁻¹. As expected, after tumor resection the blood pressure dropped, and dopamine up to 5 µg kg⁻¹ min⁻¹ as well as phenylephrine up to 0.5 µg kg⁻¹ min⁻¹ were required initially, but weaned off by the time of the end of surgery. The patient received a transfusion of 20 ml/kg packed red blood cells for an estimated blood loss of 110 ml and approximately 150 ml/kg crystalloid fluid. Surgical open resection of her left retroperitoneal mass was uneventful. She was extubated at the end of the surgery and transferred back to the ICU for postoperative monitoring.

The postoperative course was uncomplicated and the patient required no further hemodynamically active medication. Pain control was achieved via her epidural catheter using bupivacaine 0.1% with
fentanyl 2 mCg/ml and clonidine 0.4 mCg/ml at 0.3 ml/kg/h. She was discharged home on postoperative day five. Her final diagnosis was stage I neuroblastoma. She has remained asymptomatic, normotensive without diaphoresis, and without evidence of recurrence.

**Discussion:** Tumors of neural crest origin have the potential to secrete catecholamines. Catecholamine secretion by neuroblastomas is rarely symptomatic in infants. There are many confounding factors that make it difficult to attribute symptoms such as tachycardia, hypertension, and diaphoresis to tumor related catecholamine excess. Infants are often uncooperative with physical exams, and tachycardia and hypertension may be reflective of discontent rather than pathology. Pulmonary overcirculation and other cardiac phenomena as possible etiologies for diaphoresis and difficulties with feeding may lead to cardiac evaluation prior to entertaining the possibility of a catecholamine secreting tumor. Once the diagnosis is made, perioperative control of catecholamine surges becomes paramount. There is good experience with using both alpha and beta blockade for older patients with catecholamine secreting neuroendocrine tumors. However there is a paucity of experience in using these agents and strategies in infants. Our patient was therefore treated in the ICU, to allow better monitoring of preoperative interventions meant to control catecholamine surges.

**Conclusion:** Infants with neuroblastoma must be evaluated for catecholamine release and alpha blockade, hydration, and subsequent beta blockade upon tachycardia must be offered if the patients are symptomatic.