



Paediatric VIPoma: A Jamboree of Electrolytes

Pediatric VIPoma: Elektrolit Karmaşası

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Cite this article as: Rastogi A, Priya V, Haldar R, Riaz R. Paediatric VIPoma: A Jamboree of Electrolytes. Turk J Anaesthesiol Reanim 2018; 46: 158-60.

Vasoactive intestinal peptide secreting tumour (VIPoma) is a rare type of neuroendocrine tumour (NET), primarily located in the tail of pancreas. This type of tumour presents with myriad of metabolic and electrolyte imbalances in the preoperative period, mainly due to increased vasoactive intestinal peptide (VIP) levels. Perioperative management of patients with VIPoma is challenging, especially when dealing with paediatric patients. The anaesthetic management of a two-year-old girl who was selected for VIPoma resection is hereby presented.

Keywords: Diarrhoea, dyselectrolytemia, hypokalaemia

Vazoaktif intestinal peptid salgılayan tümör (VIPoma) primer yerleşim yeri pankreas kuyruğu olan nadir bir nöroendokrin tümör (NET) türüdür. Bu tümör preoperatif dönemde, genelde artmış vazoaktif intestinal peptid (VIP) düzeyinden dolayı, çok sayıda metabolik ve elektrolit dengesizliği ile seyredir. VIPoma olan hastaların perioperatif yönetimi özellikle pediatrik hastalarda zordur. Burada VIPoma rezeksiyonu için seçilen iki yaşındaki bir kız çocuğunun anestezi yönetimi sunulmaktadır.

Anahtar Kelimeler: Diyare, diselektrolitemi, hipokalemi

Introduction

Neuroendocrine tumours (NET) are a heterogeneous group of neoplasms. Vasoactive intestinal polypeptide secreting tumour (VIPoma) is an extremely rare NET, causing the syndrome of watery diarrhoea, hypokalaemia, and achlorhydria (WDHA syndrome), or the Verner-Morrison syndrome, named after its discoverers.

Vasoactive intestinal polypeptide (VIP) is a hormone that, in addition to its various roles, stimulates intestinal production of adenosine 3',5'-cyclic phosphate (cAMP). An excessive VIP secretion in VIPoma results in increased cAMP levels, thereby causing profuse diarrhoea and an extensive water and electrolyte loss (pancreatic cholera) (1).

VIPomas in adults are primarily pancreatic tumours, with the tail of pancreas being the most common site of origin (2). However, in paediatric patients, VIPomas commonly occurs in adrenal glands and sympathetic ganglia. We present the perioperative management of a 2-year-old child with VIPoma, selected for tumour resection.

Case Presentation

A two-year-old girl (body weight 6 kg) presented to emergency department with chief complaints of diarrhoea, failure to thrive, severe weight loss and extreme weakness.

Diarrhoea was watery and chronic (10-15 episodes/day). Stools were not blood stained, and they were neither foul smelling nor associated with cramps or fever. There was no history of travel. A detailed history revealed that the child was asymptomatic 1 year back when she had the first bout of diarrhoea with initial stool frequency at 7-8 per day, which later worsened to 10-15 per day. She required frequent hospitalisation and did not show any response to antibiotics or gluten-free diet.

At the time of emergency admission, the child was severely dehydrated and was resuscitated with Ringer's lactate solution. Relevant clinical findings were normal, except for severe hypokalaemia ($K^+ < 2$ mEq L⁻¹).

For potassium supplementation and guided fluid therapy, central venous access was established in the right internal jugular vein. Potassium replacement was accomplished via potassium chloride infusion. Arterial Blood Gases (ABG) showed a mild metabolic acidosis, secondary to bicarbonate loss (pH 7.30, HCO_3^- -15.6 mEq L^{-1}).

An abdominal ultrasonography (USG) showed a large left suprarenal hypoechoic lesion, which was confirmed on a triple-phase CT scan (Figure 1; see arrow). Because neuroendocrine tumours were suspected, serum VIP levels were done by radioimmunoassay. Elevated VIP levels, approximately 8 times the normal value (2030 pmol L^{-1}) were found and, along with other related clinical features, confirmed the diagnosis of VIPoma. The somatostatin receptor-positive octreoscan scintigraphy and bone scan revealed no metastasis.

Patient was started on intravenous octreotide therapy (5 μg kg^{-1} twice a day). She showed a significant symptomatic improvement with reduced frequency and changes in stools consistency. Subsequent to volume resuscitation and correction of electrolyte deficit, the child was selected for exploratory laprotomy for VIPoma resection.

In addition to routine monitoring, neuro-muscular and invasive blood pressure monitoring was planned. Following in-

halational induction with sevoflurane, fentanyl injection 2 μg kg^{-1} and vecuronium injection 0.1 mg kg^{-1} were administered, and anaesthesia was maintained with sevoflurane, air and oxygen. Intra-operatively, the ABG revealed severe hypokalaemia and non-anion gap acidosis. Potassium replacement was started intra-operatively using potassium chloride infusion at the rate of 5-8 mEq hour^{-1} . Fluid therapy was central venous pressure-guided, and Ringer's lactate and colloid were used intraoperatively.

After normal arterial blood gas analysis and normal serum electrolytes levels and adequate train-of-four (TOF) ratio, the child was extubated and transferred to post-operative Intensive Care Unit.

Following tumour resection, VIP levels returned to normal. Oral potassium supplementation and subcutaneous octreotide were tapered gradually. The patient was discharged from hospital on 10th post-op day. Informed consent was obtained from the child's father regarding mentioning the case details in this report.

Discussion

Vasoactive intestinal polypeptide, a 28-amino acid polypeptide hormone, structurally similar to secretin, functions exclusively as a neurotransmitter. Apart from being present in

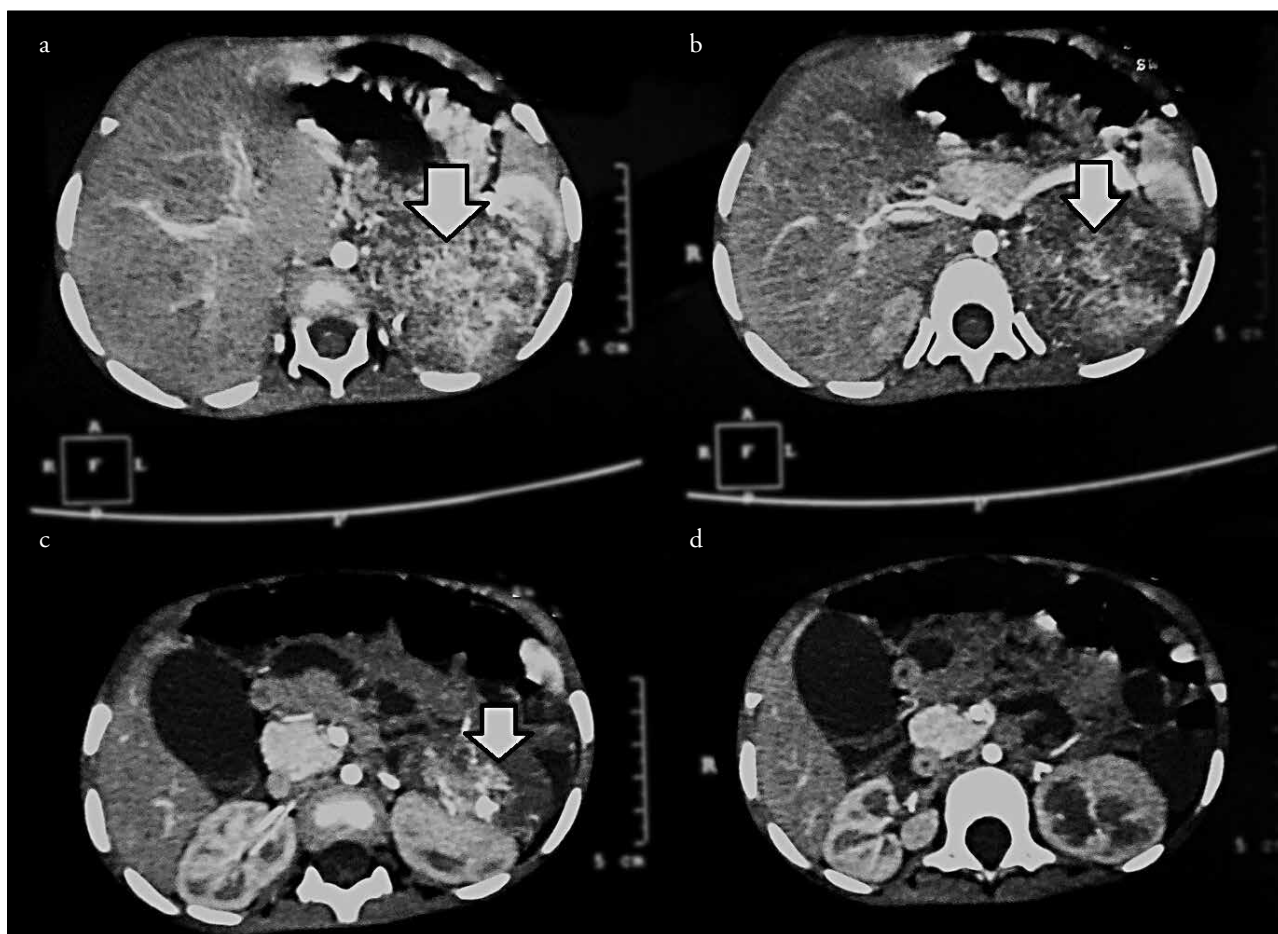


Figure 1. a-d. Triple-contrast computed tomography abdomen scan showing a mass measuring 3 cm×4 cm, arising from the left adrenal gland

enteric neurons, VIP is also present in neurons of the brain, spinal cord, lungs, urogenital system, and other endocrine organs. VIP functions include stimulation of enteric smooth muscle, stimulation of pancreatic exocrine and intestinal secretion, inhibition of gastric acid secretion, and modification of immune function and gastrointestinal blood flow.

Plasma levels of VIP in normal individuals are quite low and are not affected by food ingestion. The majority of VIPoma's are sporadic. The VIP level is elevated in almost all VIPoma cases, but it can also be normal between episodes of diarrhoea. Non-specific signs and symptoms make prompt diagnosis of VIPoma difficult.

VIPomas usually present as chronic watery diarrhoea, refractory to conservative management. The diarrhoea of neuroendocrine etiology, such as VIPoma, is unaffected by 48 to 72 hrs of fasting, and is marked by faecal stool volumes exceeding 3 L day⁻¹ (in adults). Stools characteristically resemble dilute tea in appearance and are rich in electrolytes, particularly potassium with an average secretion of 300 mmol day⁻¹ (3).

In the initial stages, the predominant symptom, diarrhoea, is episodic and intermittent as it was in our case. As VIPoma enlarges, the diarrhoea worsens, and the ensuing electrolyte abnormalities become life-threatening.

Elevated serum levels of VIP result in all segments of the intestine secreting of Na⁺, K⁺, Cl⁻, and HCO₃⁻³ and hence watery diarrhoea, thereby leading to dehydration, hypokalaemia and acidosis. Other effects of excessive VIP levels include inhibition of gastric acid secretion, bone resorption, glycogenolysis and vasodilation. These effects lead, respectively, to the hypochlorhydria, hypercalcemia, hyperglycaemia, and flushing often seen with these tumours.

Hypomagnesemia resulting in tetany and refractory hypokalaemia can also be seen in these patients (2).

VIPoma and gastrinoma in MEN1, both can present as diarrhoea, thereby making preoperative investigations aimed at diagnosing and localising them an imperative. Symptoms of dyselectrolytemia, which include cardiac arrhythmias, neuromuscular deficits, profound shock and cardiovascular collapse are coexistent and need correction before surgery (4). The fluid of choice is an isotonic electrolyte solution containing adequate sodium, potassium and base.

Simultaneous octreotide therapy for remission of symptoms is recommended.

Preoperative octreotide therapy (somatostatin analogue) is the cornerstone of management of VIPoma patients (5). Octreotide in a dose of 250-450 µg day⁻¹ has been observed to bring about a 60% symptomatic, 70% biochemical and 5%-10% tumour response. However, prolonged treatment with octreotide may result in tachyphylaxis, which makes the treatment with agents such as interferon-α imperative.

Octreotide acetate exerts pharmacological actions similar to the natural hormone, somatostatin. However, octreotide has important side effects, such as QT prolongation, bradycardia, conduction defects, abdominal cramps, nausea, and vomiting. Preoperative preparation must include H₂-receptor-blocking drugs to prevent rebound gastric acid hypersecretion after the tumour resection. Informed consent was obtained from the father of the patient.

Conclusion

Before any curative or palliative therapy is started, the patient's potentially life-threatening electrolyte and volume status abnormalities must be corrected. However due caution must be exercised in the event of hemodynamic instability during tumour resection, as concomitant fluid loss, especially bleeding, is primarily responsible for intra-operative instability, rather than hormone excess, which is rare. Thus, fluid resuscitation may be the answer rather than further octreotide therapy.

Informed Consent: Written informed consent was obtained from patients' parents who participated in this case.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - A.R., V.P.; Design - A.R., V.P.; Supervision - R.H., R.R.; Literature Search - V.P., R.H.; Writing Manuscript - A.R., V.P.; Critical Review - R.H., R.R.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

Hasta Onamı: Yazılı hasta onamı bu olguya katılan hastanın ebeveynlerinden alınmıştır.

Hakem Değerlendirmesi: Dış bağımsız.

Yazar Katkıları: Fikir - A.R., V.P.; Tasarım - A.R., V.P.; Denetleme - R.H., R.R.; Literatür Taraması - V.P., R.H.; Yazıyı Yazan - A.R., V.P.; Eleştirel İnceleme - R.H., R.R.

Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

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