Case 1: Progressive vomiting in a three-week-old infant

A 20-day-old female infant was transferred from a peripheral hospital with progressive vomiting and weight loss.

The infant was born to a 31-year-old primiparous mother at 37 weeks' gestation by spontaneous vaginal delivery. The pregnancy was uncomplicated, apart from a positive screen for group B streptococcus, which was adequately treated during labour. The infant's birth weight was approximately 3 kg.

Vomiting began at seven days of age, when nystatin was started for treatment of oral thrush. The vomiting progressively became more frequent and projectile in nature. By the time of admission, at three weeks of age, the infant had projectile nonbilious vomiting that occurred 1 h to 2 h after every attempted feeding. She appeared hungry immediately after vomiting. The infant had been offered two different formulas (Enfamil [Mead Johnson Nutritionals, Ottawa, Ontario] and Goodstart [Nestlé Canada]), and minimal expressed breastmilk by bottle since birth. The formula changes did not result in symptomatic improvement. She was offered approximately 60 mL of feed every 2 h to 3 h. Her bowel movements were normal, apart from a few loose, nonbloody stools on the day of admission. Her parents reported that there had been four to five wet diapers per day before admission. The infant was otherwise healthy, with no fever, rash or systemic symptoms.

Both parents were healthy and of Italian descent. Family history was not contributory.

The infant's admission weight was 2180 g (25% less than her birth weight), with the clinical appearance of significant dehydration and malnutrition (little subcutaneous fat and muscle wasting). She was afebrile, with stable vital signs for her age, including a pulse rate of 120 beats/min after initial fluid resuscitation of 20 mL/kg of 0.9% saline followed by isotonic fluid at a maintenance rate. Her abdomen was soft, scaphoid and nontender, with no organomegaly. There were no palpable masses, including no palpable 'olive' when the baby was quiet. The remainder of the examination was normal, apart from slight oral thrush.

Initial laboratory investigations revealed severe metabolic alkalosis with venous pH 7.64, PCO_2 50 mmHg, bicarbonate 54 mmol/L and base excess +26 mmol/L. Electrolytes were abnormal with serum sodium 119 mmol/L, potassium 4.7 mmol/L, chloride lower than 50 mmol/L and glucose 10.9 mmol/L. Both urea and creatinine concentrations were significantly elevated (blood urea nitrogen 22.7 mmol/L and creatinine 261 µmol/L). The infant's complete blood count was normal, apart from thrombocytosis (767×10^9/L). Her urine pH was greater than 9.0 and specific gravity was 1.010 g/L; she had normal microscopy, except for 2+ protein. Her abdominal ultrasound revealed stomach contents passing through a nonhypertrophied pylorus that was seen to open and close normally. The infant's abdominal radiograph showed a small amount of gas in a single, mildly prominent structure in the mid-abdomen and a paucity of bowel gas in the remainder of the abdomen.

An additional investigation revealed the diagnosis.

Case 2: Hyponatremia and hyperkalemia in a four-week-old boy

A four-week-old male infant presented to the emergency department with failure to thrive (360 g below his birth weight), and had a history of poor eating, increased sleeping and irritability over his first month of life. The infant's family history was significant for polycystic kidney disease in his mother and female relatives.

On presentation, his blood pressure was 102/74 mmHg, heart rate was 162 beats/min, respiratory rate was 52 breaths/min, oxygen saturation was 99% and rectal temperature was elevated at 39.4°C. A physical examination revealed a somewhat wasted, nondysmorphic, nontoxic baby with normal male genitalia. The rest of the physical examination was essentially normal. The infant's bloodwork showed a a sodium concentration of 121 mmol/L, and a potassium concentration of 7.1 mmol/L. (The tests were repeated and found to be accurate.) Capillary gases showed a pH of 7.32, bicarbonate of 13 mmol/L and PCO_2 of 26 mmHg. An electrocardiogram was performed, which did not show any abnormalities. His urine test was positive for blood and leukocytes, but negative for nitrites.

The initial management included a fluid bolus and initial empirical antibiotic therapy, with intravenous ampicillin and cefotaxime. Kayexalate (sanofi-aventis, Canada) was administered. Other therapies for hyperkalemia were held due to the normal electrocardiogram findings. A full-septic workup was performed, including a lumbar puncture. Fludrocortisone and hydrocortisone were given. The patient was subsequently admitted to the paediatric critical care unit, with a presumed diagnosis of congenital adrenal hyperplasia for correction of electrolyte and fluid balance.

Surprisingly, the endocrine workup for presumed congenital adrenal hyperplasia was negative. An ultrasound of the abdomen was performed, which together with one of the other test results helped to make the correct diagnosis.

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Figure 1) *Upper gastrointestinal contrast study showing dilated duodenum with tiny amount of contrast passing distally*

CASE 1 DIAGNOSIS: DUODENAL STENOSIS

An upper gastrointestinal contrast study demonstrated a dilated second portion of the duodenum, with nearly complete obstruction and stasis of contrast material (Figure 1). The duodenum was rounded and bulbous at the point of the obstruction, and only a tiny amount of contrast progressed after significant delay into the collapsed third and fourth portions of the duodenum. The duodenojejunal junction was in normal position.

Dehydration and hypochloremic alkalosis were corrected over the following 72 h, and the stomach was decompressed with a nasogastric tube. Laparotomy on the third day of admission revealed duodenal stenosis in the second portion of the duodenum, proximal to the ampulla of Vater. This was successfully repaired with a diamond-shaped duodenoduodenostomy, with uneventful postoperative recovery. The infant's vomiting was resolved, and she achieved appropriate weight gain in follow-up.

Congenital intestinal obstructions can be classified as intrinsic (atresia, stenosis and web) or extrinsic (malrotation, Ladd's bands, annular pancreas, duplications and, rarely, a preduodenal portal vein). Malrotation is potentially the most immediately life-threatening diagnosis, with the risk of midgut volvulus.

Partial or complete intrinsic congenital duodenal obstruction occurs in approximately one in 5000 to 10,000 live births, with duodenal atresia comprising the majority of these cases. Duodenal stenosis is relatively rare in comparison with complete obstruction of duodenal atresia. Finally, extrinsic obstruction from malrotation may also be associated with intrinsic duodenal stenosis.

The duodenum is derived from the caudal portion of the foregut and the cranial portion of the midgut, fusing just distal to the common bile duct opening at the ampulla of Vater. Failure of recanalization of the duodenal lumen during the eighth to 10th week of gestation, after temporary epithelial occlusion of the lumen in the fifth and sixth weeks of gestation results in duodenal atresia. Incomplete recanalization can lead to duodenal stenosis or the presence of a duodenal web.

Most duodenal atresias and stenoses occur distal to the ampulla of Vater, leading to bilious emesis. In a minority of cases (approximately 20%), the obstruction occurs proximal to the ampulla and the emesis is not bile-stained.

Duodenal atresia is diagnosed antenatally in up to 50% of cases, with polyhydramnios, dilation of the stomach and proximal duodenum visible on the third trimester ultrasound. After birth, complete high-intestinal obstructions usually present within the first 24 h of life, with persistent vomiting that may be bile-stained or nonbilious.

Incomplete duodenal obstructions have a more varied and often delayed presentation, making diagnosis and early intervention more challenging. These conditions can be easily mistaken for the much more common pyloric stenosis, infantile gastroesophageal reflux, metabolic abnormalities or intracranial pathology initially due to the recurrent, progressive nature of the vomiting.

A clinical scenario of antenatal polyhydramnios with suction of greater than 20 mL to 30 mL from the stomach at birth (normal is less than 5 mL) should raise suspicion of a high-intestinal obstruction. Infants with duodenal stenosis can present with early progressive vomiting, leading to clinically significant dehydration and failure to thrive, as in the present case. Normal passage of meconium and subsequent stools may be present in incomplete obstruction. There are reports of cases of duodenal stenosis presenting with recurrent aspiration and chest infections, or gastroesophageal reflux, peptic ulceration and, rarely, obstruction proximal to the stenosis with a bezoar, as late as adulthood.

Infants with intrinsic duodenal obstructions may present with other associated significant congenital anomalies. These are most classically described with duodenal atresia, occurring in 38% to 55% of cases, and less clearly delineated for later presentations of incomplete obstruction. Associated anomalies include Down's syndrome (in 30% of duodenal atresia), isolated cardiac defects (in 23% to 34% of duodenal atresia), esophageal atresia with or without tracheoesophageal fistula (in 7% to 12% of duodenal atresia) and, less commonly, malrotation, anterior portal vein, anorectal anomalies, other intestinal atresias or renal tract anomalies. Prematurity and intrauterine growth restriction are more prevalent among infants with intrinsic intestinal obstructions, particularly duodenal atresia.

Abdominal radiography in duodenal stenosis may reveal dilation of the stomach and upper duodenum, with variable gas pattern distally. Ultrasonography of the abdomen is helpful in excluding pyloric stenosis with dynamic monitoring of gastric emptying, and may exclude extrinsic compression

from an annular pancreas. An oral or nasogastric water-soluble contrast study is usually necessary with incomplete obstruction to demonstrate duodenal orientation, highlight the level of obstruction and, most importantly, rule out malrotation and volvulus. If duodenal atresia is diagnosed, echocardiography, renal ultrasound and karyotype are suggested. Children with duodenal obstruction and Down's syndrome are also at increased risk for Hirschsprung's disease; thus, a contrast enema and rectal biopsy can be considered if there is delayed passage of meconium or symptoms of distal colonic obstruction.

The initial management of any form of intestinal obstruction must include gastric decompression, fluid resuscitation and correction of electrolyte abnormalities, most commonly hypochloremic metabolic alkalosis. This should be performed slowly, initially with normal saline solution. Additional potassium will likely be required once urine output is established. The serum chloride concentration should be above 90 mmol/L to 100 mmol/L, the serum potassium concentration should be above 3 mmol/L and the serum bicarbonate concentration should be normal before surgery.

Surgical exploration and repair may be safely deferred to allow gradual correction of markedly abnormal electrolytes as in our case, as long as there is no concern of possible midgut volvulus. The preferred surgical repair of the primary anomaly is a diamond-shaped (proximal transverse to distal longitudinal) anastomosis. If there is a duodenal web, it may be excised through a duodenotomy, taking great care to avoid injury to the ampulla.

In the absence of other serious anomalies or prematurity, the overall survival for duodenal stenosis or atresia is nearly 100%, representing a significant improvement in the past few decades from improved respiratory support, paediatric anaesthesia and more refined surgical techniques. Major postoperative complications are uncommon. However, long-term follow-up is recommended.

CLINICAL PEARLS

- Incomplete duodenal obstruction may present with nonbilious progressive vomiting and hypochloremic metabolic alkalosis, mimicking the much more common presentation of infantile hypertrophic pyloric stenosis.
- The most emergent and potential life-threatening cause of incomplete upper gastrointestinal obstruction is malrotation with midgut volvulus, which usually presents with bilious vomiting and should be ruled out by an upper gastrointestinal contrast study.
- Severe dehydration and electrolyte abnormalities must be corrected slowly before undertaking surgery for duodenal stenosis.

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CASE 2 DIAGNOSIS: PSEUDOHYPOALDOSTERONISM SECONDARY TO URINARY TRACT INFECTION

The infant's ultrasound showed slightly enlarged kidneys (5.1 cm and 5.2 cm in length) and mild bilateral hydronephrosis. Voiding cystourethrogram showed bilateral grade 5 reflux, with no evidence of posterior urethral valves. A urology referral was obtained. The patient was managed in the paediatric critical care unit with conservative therapy, along with frequent monitoring of electrolytes. The empirical steroid therapy started because of presumed congenital adrenal hyperplasia (CAH) was discontinued following the ultrasound results and a negative 17-OH progesterone test. His urine culture was positive for *Escherichia coli* on initial catheter specimen. Over the course of admission, the patient's bloodwork abnormalities resolved, including his blood urea nitrogen (from 14.2 mmol/L to 1.4 mmol/L) and creatinine (from 96 µmol/L to 52 µmol/L). His weight improved to the 25th percentile for age, and he was discharged home after completing 14 days of antibiotic therapy on trimethoprim and sulfamethoxazole prophylaxis.

Pseudohypoaldosteronism (PHA) is a recognized, although rare, complication of multiple disease states and medical treatments. Our patient had PHA secondary to a urinary tract infection (UTI). A literature search for PHA caused by vesicoureteric reflux with pyelonephritis revealed a few reported cases in the urological literature, and only one case in the emergency literature (1-11). The mechanism is poorly understood, but it is speculated that it is due to aldosterone resistance secondary to endotoxin damage of the aldosterone receptors. This results in a lack of aldosterone response in the distal tubule.

Aldosterone exerts its effect on the distal tubule resulting in an increased uptake of sodium and increased excretion of potassium. Its production is regulated by the renin-angiotensin system. Aldosterone deficit results in hyponatremia and hypovolemia, accompanied by hyperkalemia and metabolic acidosis.

The finding of a combination of hyperkalemia and hyponatremia is relatively rare. It usually signifies hypoaldosteronism or PHA. The main cause of hypoaldosteronism is acute adrenal insufficiency (Waterhouse-Friedrichsen syndrome, Addison's disease and septic shock) or chronic adrenal insufficiency (Addison's disease and CAH).

PHA refers to a diffuse group of disorders with renal tubular resistance to aldosterone. PHA is characterized by hyperkalemia, metabolic acidosis and a normal glomerular filtration rate. PHA can be broken down into primary or secondary causes. Primary PHA was first described in 1958, and represents a diverse group of genetic defects causing decreased number or absence of mineralocorticoid receptors. These described syndromes include 'classic' PHA-1, multiple target organ defects, early childhood hyperkalemia, renal tubular acidosis type IV subtype 5 and PHA-II (chloride shunt syndrome).

Secondary PHA can be caused by UTIs, obstructive uropathies, renal vein thrombosis and medications (cyclooxygenase inhibitors [nonsteroidal anti-inflammatory drugs], beta-adrenergic antagonists, angiotensin-converting enzyme inhibitors, trimethoprim, heparin, calcineurin inhibitors [cyclosporine and tacrolimus] and potassium-sparing diuretics).

Our patient had a clinical presentation that could be consistent with the more common condition of CAH, making the diagnosis of PHA difficult. CAH is an autosomal recessive condition that results in excessive androgen production and a cortisol deficit due to the lack of a specific enzyme activity. Currently, most jurisdictions in the United States and Canada do not have an active screening program. However, many areas are currently in the process of introducing screening programs. These programs screen for the most common enzyme defect, 21-hydroxylase deficiency, and should, therefore, diagnose up to 90% of these infants before complications, and should reduce the number of infants presenting with salt wasting. As these programs become more widespread, the diagnosis of PHA will become an increasingly important diagnosis to consider in infants presenting with hyponatremia and hyperkalemia.

A recent review by Watanabe (12) of 60 cases of secondary PHA previously reported in the literature revealed some interesting points. All patients were less than seven months of age, 80% suffered from a urinary tract malformation and UTI. Twelve per cent had a urinary tract malformation in the absence of infection, and 8% had a UTI without an underlying malformation. Therefore, one can postulate that either the UTI or the malformation alone can cause secondary PHA, and that age may be a risk factor for its development.

When faced with electrolyte abnormalities such as hyperkalemia and hyponatremia, one must consider not only hypoaldosteronism (as in CAH), but also aldosterone resistance. Because this was a four-week-old infant, the initial management did not differ significantly. Management priorities in this case were centred around treatment of sepsis despite well appearance, correction of dehydration, and correction and monitoring of electrolyte abnormalities. In this case of secondary PHA due to a UTI and bilateral grade 5 reflux, the initiation of antibiotics was very important.

CLINICAL PEARLS

- Secondary PHA produces electrolyte abnormalities (hyponatremia and hyperkalemia) that can easily be confused with CAH.
- Secondary PHA can be caused by UTIs, obstructive uropathies, renal vein thrombosis and medications.

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