Case report

Vomiting, constipation, and weight loss as presenting symptoms of primary hyperparathyroidism in a paediatric patient: a case report

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Abstract

A 15-year-old boy presented with vomiting, constipation and weight loss. Venous blood gas showed high ionised calcium. Serum calcium and parathormone were elevated. ECG showed signs consistent with hypercalcaemia. CT-scan of the parathyroid glands showed two nodules suspicious for adenoma. Symptomatic hypercalcaemia was treated with intravenous hyperhydration and bisphosphonates. Electrolyte imbalances were supplemented. Definitive treatment consisted of parathyroidectomy. There were no postoperative complications and calcium homeostasis was restored.

PHPT is uncommon in paediatric patients and can present with a diverse range of symptoms. Knowledge of its primary diagnosis and treatment is important for general paediatricians, especially in cases of hypercalcaemia.

Introduction

Primary hyperparathyroidism (PHPT) is a medical condition characterised by excessive production of parathormone (PTH), resulting in hypercalcemia (1, 2). It is an uncommon condition in children, with an incidence of 1 in 300,000. The aetiology includes a single parathyroid adenoma (60-92%), four-gland hyperplasia (0-40%), or rarely parathyroid carcinoma. PHPT can manifest with a broad spectrum of symptoms, including gastrointestinal, renal, psychiatric/neurological and bone manifestations. However, it can also present as an asymptomatic incidental biochemical finding or lead to end-organ damage. Given its rarity and diverse symptomatology, there is often a delay in the diagnosis of PHPT in children, who typically exhibit symptoms at the time of presentation (3). Although PHPT is infrequent in the paediatric population, the initial approach to diagnosis and the management of hypercalcemia in children remains crucial for general paediatricians. As cases of PHPT in children are scarce, the principles of care are mainly extrapolated from broader experience in adults.

Case presentation

Clinical presentation

A 15-year-old male patient with no relevant prior medical history presented at the emergency department with symptoms of persistent vomiting for two weeks and a total weight loss of eight kilograms (12% of his total body weight). He had a fever at the onset of the symptoms, which resolved spontaneously. He complained of vasovagal tendencies and constipation. There were no other complaints. He had recently travelled to Morocco but there were no other environmental risk factors. Metoclopramide, domperidone, paracetamol and ibuprofen were started by the family doctor without any effect. On referral, he showed signs of dehydration with a capillary refill of four seconds and abdominal pain in the right and left fossa.

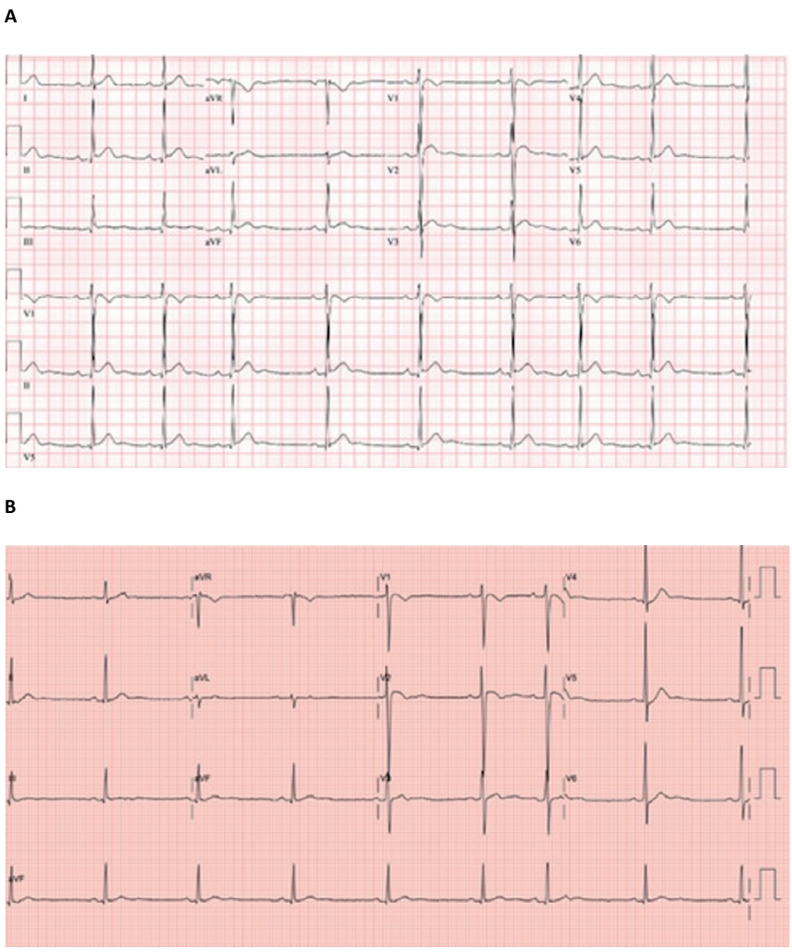
Diagnostic assessment

The venous blood gas was normal except for an ionised calcium of 2.34 mmol/L (1.20-1.32). Pending further laboratory results, a CT scan of the brain was performed, which showed no evidence of space-occupying lesions. Abdominal ultrasound visualised some enlarged lymph nodes in the right fossa and hyperechoic kidneys. Initial laboratory findings included a sedimentation rate of 20 mm/h (0-10), thrombocytosis of 457,000/µL (166,000-396,000), C-reactive protein 4.4 mg/L (<10); creatinine 1.26 mg/dL (0.60-1.10), urea 84 mg/dL (13-43), uric acid 9.8 mg/dL (2.4-7.9), with an estimated glomerular filtration rate of 48.2 mL/min/1.73m2 (>90) due to acute kidney injury caused by dehydration and hypovolemia. Calcium was 3.97 mmol/L (2.25-2.67), phosphorus 0.79 mmol/L (1.00-1.78), parathormone 374 ng/L (18.5-88.0), di-OH vitamin D 98.3 pg/mL (19.0-95.0). Lipase was 76 IU/L (12-53) with no other liver function tests abnormalities. Neuron specific enolase (NSE) was 33.1 µg/L (<16.3). Electrocardiogram at presentation showed ST elevation in V2 and V3 and a short QTc interval due to hypercalcaemia. CT scan of the parathyroids showed two nodules, one inferior to the left thyroid lobe and a smaller one posterior to the right thyroid lobe, suspicious for parathyroid adenoma.

Therapeutic intervention

In the emergency department, our patient received a bolus of normal saline after which a maintenance fluid infusion was started. Constipation was treated with a single enema and the initiation of macrogol. Because of the PHPT caused by multiple parathyroid adenomas and an increase in serum calcium, fluid administration was increased to hyperhydration at 3000 mL/m²/24h and pamidronate 1 mg/kg was given intravenously over a period of 4 hours. The evening after the second dose of pamidronate the patient developed a fever without clinical focus and with low inflammatory parameters. There was no need for antibiotic therapy. There was no

Figure 1: Electrocardiograms of our patient: A) ECG at presentation , B) ECG day two of hospitalisation.



recurrence of fever. It was most likely caused by the administration of bisphosphonate. Two days later serum calcium normalised, phosphate decreased, for which supplementation with sodium phosphate was started. However, he developed paraesthesia of the left arm and the face, for which supplementation was increased. Because of further decrease in calcium after pamidronate there was need for intravenous calcium supplementation. He also developed hypokalaemia and hypomagnesemia, which required supplementation. After two days of intravenous calcium supplementation, switch to oral therapy was possible. With this regimen, the electrolyte imbalances were restored. Al supplements were weaned over a period of fourteen days, after which they could all be stopped. A surgical resection, parathyroidectomy, was planned three weeks after initial presentation. By the time of re-admission for surgery, he had developed hypercalcaemia again for which hyperhydration was restarted, resulting in stable calcium levels. After parathyroidectomy there was no need for intravenous calcium supplementation because of the hypercalcaemia on admission. One day after surgery calcium carbonate was started, (1000 mg, three times a day). After surgery he developed hypophosphatemia which resolved without supplementation. Parathormone normalised rapidly after parathyroidectomy. After two days he was discharged from the hospital with only calcium carbonate and paracetamol.

Follow-up and outcomes

Calcium was checked weekly after discharge. Supplementation could be weaned and was stopped ten days after surgery. Due to low vitamin D, vitamin D and calcium supplementation was restarted and continued to date. Genetic testing for MEN1 and MEN2A/2B were negative, a spinal radiograph showed a sclerotic aspect of the endplates of the thoracic and lumbar vertebrae with early signs of Rugger jersey spine morphology as seen in parathyroidism. Abdominal MRI scan was normal and showed no evidence of an insulinoma.

Discussion

Although PHPT is rare in the paediatric population, it is important for general paediatricians to have a clear understanding of its diagnosis and management. Early recognition and appropriate management of hypercalcaemia are crucial for optimal patient outcomes.

Asymptomatic PHPT is common in adult patients (1). In paediatric patients, symptomatic presentation is more frequent. It is therefore important to be aware of the symptoms caused by hypercalcaemia. Our patient presented with predominantly gastrointestinal complaints. Non-specific symptoms such as vomiting, weight loss and constipation. Acknowledging the combination of hypercalcaemia and elevated PTH was essential in our case. This led to the diagnosis of PHPT. We also screened for malignancy, even though hypercalcaemia caused by malignancy usually shows suppressed PTH (1).

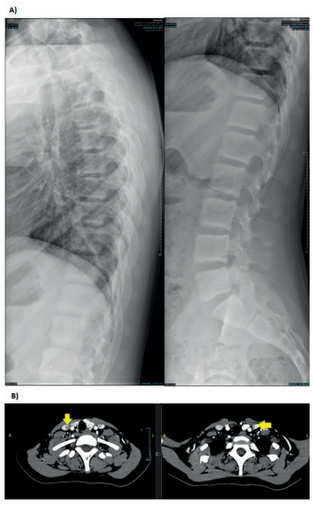
The initial assessment of hypercalcaemia should include a complete blood count, total and ionised calcium, PTH, phosphorus, renal function tests, 1,25-hydroxyvitamin D, 25-hydroxyvitamin D levels, bone density scan, and renal ultrasound (3). To distinguish PHPT from familial hypocalciuric hypercalcaemia (FHH) a urine calcium/creatinine ratio should be obtained. The UK guidelines also recommend genetic testing of all children with PHPT, including screening for CaSR and menin mutations (CASR and MEN1 genes). Additional tests should be performed if the former tests are normal, if there is a positive family history, or if anatomopathology shows an atypical adenoma, or carcinoma (3, 4).

The goal of medical management in paediatric patients with PHPT is to control the hypercalcaemia. The first step is hydration to restore euvolemia, this may include a bolus infusion followed by an infusion of three to four litres of normal saline over a period of 24-48 hours. Denosumab or bisphosphonates may be added to the treatment plan to inhibit bone resorption. Pamidronate 60-90 mg in 500 mL NaCl 0.9% over 2-4 hours can be given intravenously. Bisphosphonates can cause transient fever, flu-like symptoms, myalgias and transient hypocalcaemia and hypophosphatemia as seen in our patient. The result can be seen after four days and the effect can last from a few days to eight weeks. In addition, calcitonin can be used to achieve a more rapid fall in serum calcium. Loop diuretics can be associated tp induce calciuresis. Glucocorticoids should be considered for refractory hypercalcaemia. Ketoconazole should be considered in certain conditions. Calcimimetics can be given as adjuvant therapy when treating patients with bisphosphonates or denosumab. In case of severe refractory hypercalcaemia, dialysis should be started. Finally, mobilisation should be initiated as soon as possible (3-5).

The definitive treatment for PHPT is surgery: parathyroidectomy. Based on recommendations from the National Institutes of Health (NIH), all paediatric patients with PHPT should undergo surgery. The goal of this surgery is to remove the abnormal parathyroid glands and preserve the normal ones.

Figure 2:

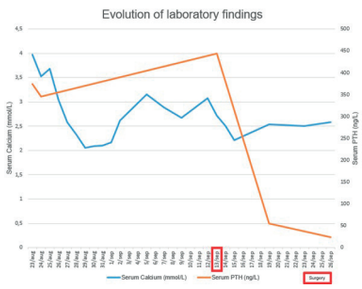
Medical imaging in the work-up of our patient with PHPT: A) Spinal radiography ; Rugger jersey spine describes the prominent endplate densities at multiple contiguous vertebral levels to produce an alternating sclerotic-lucent-sclerotic appearance, this mimics the horizontal stripes of a rugby jersey (6). B) CT-scan parathyroids ; nodule 1 (posterior to the right thyroid lobe, inferior part, 0.5x0.4x0.7 cm) and nodule 2 (inferior to the left thyroid lobe, 13x10x21 mm), shown with arrows.



Preoperative imaging is critical because of the aforementioned potential for abnormal localisation of the adenoma. Cervical ultrasound can be a first-choice investigation as it is easily accessible and non-invasive. A better investigation, especially for the detection of ectopic adenomas is a dual-phase technetium-99m-sestamibi scan with single-photon emission computed tomography/computed tomography (SPECT/CT) (2). In our case, this study was requested, but could not be performed because our patient had undergone a CT scan with contrast administration the day before. Therefore, ectopic adenomas could not be definitively excluded, although the CT scan did not show any mediastinal masses. CT has a sensitivity of 40-86% for detecting an adenoma. Another option would have been an MRI-scan with contrast, which has a sensitivity of 69-88%. This preoperative imaging will determine the surgical approach. If possible a minimally invasive procedure is the first choice because of its advantages: shorter operative time, lower hospital costs, shorter length of stay, and fewer episodes of postoperative hypocalcaemia (2).

Figure 3:

Evolution of laboratory findings in our patient. Serum calcium (in mmol/L), with normal values between 2.25 mmol/L and 2.67 mmol/L; and serum parathormone (in ng/L), with normal values between 18.5 ng/L and 88.0 ng/L. Both in function of time. Marked date (September 13th) is the date on which surgery, parathyroidectomy, was performed as definitive treatment for PHPT.



Our patient underwent a minimally invasive procedure, which resulted in a short hospital stay and no hypocalcaemia. The most common post-operative complication is hypocalcaemia (hungry bone syndrome), which requires supplementation. Follow-up of serum calcium is necessary to assess surgical outcome, as PTH levels may remain elevated despite normal calcium levels (2).

Conclusion

Primary hyperparathyroidism is a rare condition in the paediatric population and can present with a large variety of symptoms, from asymptomatic to end-organ damage. This case demonstrated that the presenting symptoms can be very non-specific and therefore a patient with these symptoms may present to any emergency department. Therefore, a general knowledge of the initial diagnosis and management of PHPT and hypercalcaemia is essential for all healthcare professionals.

Conflict of interest

The authors have no conflicts of interest in relation to the subject matter of this manuscript.

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