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CASE REPORT

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Parathyroid adenoma causing severe hypercalcaemia presenting as acute psychosis; not to be overlooked

Premasiri DGAL[1]*, Senadeera Y[1], Perera NM[1] , Pinto D[2], Hapuarachchi E[2]

Abstract

Neuropsychiatric manifestations due to hypercalcaemia is a known entity and rarely it can be the first manifestation of the disease. It can be challenging to diagnose acute psychotic symptoms associated with hypercalcaemia in individuals with existing psychological disorders particularly if organic causes are not properly evaluated. Therefore, it's important to consider hypercalcaemia as a potential cause in these patients. Mild cases may manifest as depression and cognitive changes, while severe cases can result in confusion, agitation, delusions, hallucinations and even coma.We present a case of a 68-year-old man with a previous history of diabetes mellitus, hypertension, dyslipidaemia and recently diagnosed moderate depression who presented to psychiatry services with psychomotor agitation, loss of short-term memory, disorientation, auditory hallucinations and delusions with a history of severe constipation. The patient showed poor response to psychotic medications and during the evaluation for organic causes, the patient was found to have severe hypercalcaemia with high parathyroid hormone levels. Ultrasound scan of the neck showed a heterogeneous hyperechoic lesion adjacent to the thyroid isthmus and 4D CT (parathyroid protocol) showed parathyroid adenoma in the right tracheoesophageal groove. Hypercalcaemia was initially managed with hydration and intravenous zoledronic acid. The patient's symptoms rapidly improved following the correction of hypercalcaemia and successful surgical resection of parathyroid adenoma without any post-surgical complications.

Keywords: hypercalcaemia, psychosis, parathyroid adenoma, primary hyperparathyroidism

Introduction

Primary hyperparathyroidism (PHPT) is the third most common endocrine disease, which can cause hypercalcaemia secondary to excessive parathyroid hormone secretion. In rare cases, it can initially present as acute psychosis. It is imperative to rule out organic causes before labeling it as primarily psychological. In patients with underlying psychiatric history, this is a diagnostic challenge.(13) Most patients are clinically asymptomatic but may experience signs or symptoms related to hypercalcaemia including polyuria, polydipsia, weakness, irritability, abdominal discomfort and nausea, skeletal complications/overt bone disease, nephrolithiasis, and occasionally acute pancreatitis. It is also known to cause neuropsychiatric manifestations including mood and cognitive changes. Rarely it also causes acute psychosis with aggression, delusions and hallucinations.(1-3)

Ultrasonography and Tc 99m-sestamibi scan and parathyroid four-dimensional CT are standard modalities for imaging parathyroid lesions. In overtly hypercalcaemic hyperparathyroidism, the decision to treat with parathyroidectomy is straightforward. Neuropsychiatric symptoms seen in patients with primary hyperparathyroidism often improve after parathyroidectomy.(4)

*Correspondence:

Premasiri DGAL
Colombo North Teaching Hospital, Ragama
E-mail: lankapremasiri15@gmail.com
Phone; +94714082309

Full list of author information is available at the end of the article

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Case presentation

A 68-year-old man with a previous history of diabetes mellitus, hypertension, dyslipidaemia and recently diagnosed moderate depression presented to psychiatry services with confusion, psychomotor agitation, loss of short-term memory, irritability, hallucinations and delusions for a week. He also had a history of severe constipation, depression and generalised weakness for 3 months. He had been evaluated by a psychiatrist previously and started on psychotherapy which had proven ineffective.

He was afebrile. Examination revealed a blood pressure of 130/70 mmHg and tachycardia at 92 beats per minute with clear lung fields. No organomegaly and focal neurological signs were observed. Psychiatric evaluation revealed psychomotor restlessness, lack of orientation in time and place, second person auditory hallucinations, paranoid delusions, and his mini-mental state score was 18.

Baseline investigations including full blood count, inflammatory markers, renal and liver function tests were initially normal with a calcium level of > 3.5 mmol/L. ECG showed a short QT interval. Myeloma screening was negative (table 1).

Skeletal survey showed features of hypercalcaemia including salt and pepper appearance on the skull X-ray and subperiosteal bone resorption along the radial aspects of the phalanges (figure 1). Supine X-ray abdomen showed impacted stools without air-fluid levels, which supported hypercalcaemia (figure 2).

Table 1 - Laboratory investigations of the patient

Investigation	Reference Range	Day 1	Day 3	Day 6
WBC (/udL)	4 -10	8.7	7.7	7.84
CBS (mg/dL)		185.3	154.2	126
ESR (mm/1st hour)	15 - 20	15		18
CRP (mg/L)	0 - 5	< 0.5	1.6	< 0.5
Serum creatinine (umol/L)	70 - 115	107.8	118.4	112.3
Serum sodium (mmol/L)	137 - 145	139	143	140
Serum potassium (mmol/L)	3.5 - 5.1	4.2	3.8	4.1
Serum calcium (mmol/L)	2.15 - 2.5	> 3.5	3.1	2.5
Serum magnesium (mmol/L)	0.7 - 0.9	0.5	0.3	0.5
Serum phosphate (mmol/L)	0.8 - 1.45	0.7	0.7	0.5
AST (U/L)	0 - 35	27	24	22
ALT (U/L)	0 - 40	24	21	28
PTH (pg/mL)	10 - 65		670.4	
TSH (mIU/L)	0.46 - 4.68		2.43	
UFR		Negative		
Urine calcium (mmol/L)	>0.6		6.4	3.6
Urine creatinine			5492	2510
Vit D level (ng/dL)	30 - 50		31	

WBC: white blood cells, CBS: capillary blood sugar, CRP: C reactive protein, ESR: erythrocyte sedimentation rate, AST: aspartate aminotransferase, ALT: alanine aminotransferase, PTH: Parathyroid hormone, TSH: Thyroid stimulating hormone, UFR: urine full report

Figure 1 - The skeletal survey showed features of hypercalcaemia including a salt and pepper appearance on X-ray skull and subperiosteal bone resorption along the radial aspects of the phalanges

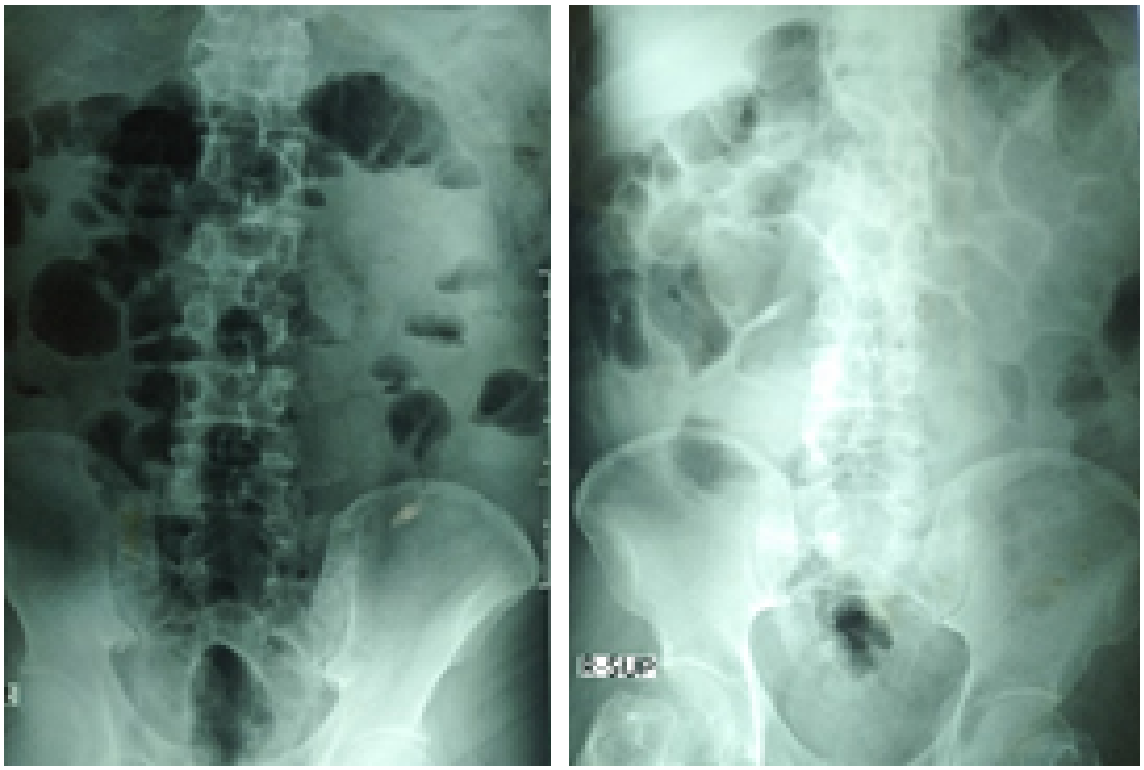

Figure 2 - Supine X-ray of the abdomen showing impacted stools without air-fluid levels supportive of hypercalcaemia

On the fourth day of admission, the intact parathyroid hormone level (PTH) was 670 pg/mL (10 – 65), thus confirming the clinical suspicion of primary hyperparathyroidism (pHPT). An ultrasound scan of the neck and abdomen revealed a well-circumscribed, rounded, hypoechogenic nodule of 0.9 x1.6 cm^2 in size adjacent to the thyroid isthmus, most likely a parathyroid adenoma with a left-side thyroid nodule, but no adrenal tumours were present.

4D CT parathyroid revealed a right trachea-oesophageal groove lesion suggestive of parathyroid adenoma.

The NCCT brain was normal and the MRI brain showed no haemorrhages/ infarctions or space-occupying lesions. There was no evidence to suggest vascular dementia. Neurological causes for changes in behaviour were excluded.

Primary hyperparathyroidism was considered the cause of severe hypercalcaemia and the reason for neuropsychiatric symptoms. Psychotropic medications were discontinued. The patient was hydrated with a continuous infusion of normal saline (4.5 L/day), and intravenous furosemide (80 mg/day).

Over the next 3 days, conservative therapy for the hypercalcaemia was continued with a mild decrease in calcium levels to 3.1 mmol/L. Daily Kleen enemas and laxatives were given for constipation. On day 3 of admission, according to the endocrine opinion, the patient was started on IV zoledronic acid 4 mg stat along with vitamin D3+ K2 supplementation.

On day 6, although the patient showed a good biochemical response to medical therapy, he had persistent lethargy, loss of short-term memory and disorientation. A surgical opinion was taken and the patient underwent right parathyroidectomy (figure 3). The histological diagnosis of the surgical sample was chief cell adenoma of the right parathyroid gland.

After removal of the parathyroid tumour, the serum calcium level dropped rapidly, returning to the normal range. Psychiatric symptoms improved with the disappearance of mental confusion and disorientation without any post-surgical complications.

Acute paranoid psychosis is not a frequent feature of primary hyperparathyroidism. It therefore requires early recognition to avoid unnecessary treatment with psychotropic drugs. Psychiatric symptoms often arise after a prolonged period of subclinical hypercalcaemia. However, their severity is poorly related to the degree of hypercalcaemia.

Our patient had gastrointestinal, skeletal, and neuropsychiatric manifestations of hypercalcaemia with acute psychosis which improved remarkably following combined medical and surgical treatment. One month later on follow-up, the patient remains in general good health, free of psychotic symptoms.

Discussion

The four parathyroid glands, located posterior to the thyroid gland, produce parathyroid hormone (PTH) which is an important regulator of calcium metabolism. Parathyroid adenomas, typically

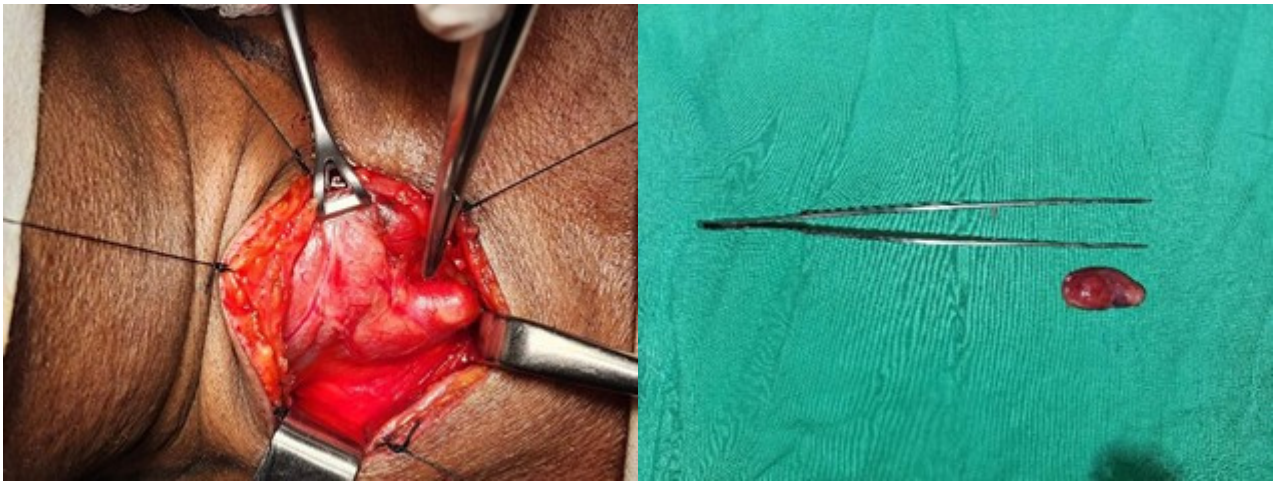

Figure 3 - Surgically resected right parathyroid adenoma

weighing less than 1g are the primary cause of hyperparathyroidism and hypercalcaemia, occurring at a rate of 20 - 22 per 100 000. About 80- 90% of cases are due to single parathyroid adenoma with other causes including hyperplasia of the gland (6%), double adenoma (4%) and parathyroid carcinoma (<1%). It can be a part of hereditary syndromes such as multiple endocrine neoplasia types 1 and 2A. Parathyroid adenoma, usually sporadic and benign, is more common in women than men (3:1) and can occur at any age, although it predominantly affects individuals between 50 - 60 years of age.(1-8)

Giant parathyroid adenomas weigh more than 3.5 g and have a diameter of >2cm. It is a distinct entity with clinical and biochemical features different from regular pituitary adenomas since these are usually clinically symptomatic and have many features overlapping with parathyroid carcinomas.(1 -2, 9)

The main pathophysiology of hyperparathyroidism is the excessive secretion of parathyroid hormone, which results in the release of calcium from bone cells through the inhibition of osteoblasts and promotion of osteoclast activity. PTH stimulates calcium resorption and inhibits the reabsorption of phosphate in the kidneys. Additionally, PTH enhances the absorption of calcium from the gut through active vitamin D by promoting the conversion of 25-hydroxyvitamin D to 1,25-hydroxyvitamin D.(10)

Hypercalcaemia is a known organic cause that can result in neuropsychiatric manifestations. In mild cases, patients may exhibit anxiety, depression and cognitive changes, while altered mental status, psychosis, confusion and coma are hallmarks of severe hypercalcaemia. Sudden alteration in mental status accompanied by auditory hallucinations, paranoia and persecutory delusions are rare manifestations with an incidence of about 4.2%. Although the exact mechanism underlying hypercalcaemia-induced psychosis is yet unknown, alterations in monoamine levels in the central nervous system and glutamate-mediated excitotoxicity may provide some insight. The severity of symptoms correlates with the weight of the adenoma and PTH level.(1, 2, 10)

High calcium levels can be a catalyst for neuronal demise, possibly as a result of glutaminergic excitotoxicity as well as dysfunction in the dopaminergic and serotonergic systems. Reduced levels of dopamine, serotonin and norepinephrine levels have been found in cerebrospinal fluid in hypercalcaemia-induced psychosis caused by parathyroid adenoma. Restoration of normal calcium levels or removal of the parathyroid adenoma has been shown to rapidly resolve neuropsychiatric symptoms.(3)

Ultrasonography and Tc 99m-sestamibi scan, parathyroid four-dimensional CT are standard modalities for imaging parathyroid lesions. Management includes hydration with intravenous fluids and reducing calcium levels using bisphosphonates (zoledronic acid, pamidronate). Definitive management with surgical resection of the adenoma usually correlates with clinical improvement, particularly affective symptoms.(3,8)

Conclusion

Before initiating treatment with psychotropic drugs, it is crucial to first rule out potential reversible organic factors such as hypercalcaemia in a patient presenting with acute paranoid psychosis. This case emphasises the significance of excluding correctable organic causes before beginning psychotropic drug therapy.

Primary hyperparathyroidism due to parathyroid adenoma is the commonest cause of hypercalcaemia and prompt correction of hypercalcaemia with intravenous fluids and bisphosphonates is the effective therapy. It may require surgical resection of adenoma as well.

Declarations

Author contributions
History taking, examination, necessary investigations arrangement, management under supervision, daily monitoring of the patient, and writing of the manuscript were done by Premasiri DGAL under the supervision of Senadeera Y, Perera NM. Surgical management of the patient was carried out by Pinto D, Hapuarachchi E, Professorial surgical unit, CNTH.

Conflicts of interest
The authors declare that they have no conflicts of interest

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Author details
[1]General Medical Unit, Colombo North Teaching Hospital, Ragama
[2]Professorial surgical unit, Colombo North Teaching Hospital, Ragama

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