Psychotic depression due to primary hyperparathyroidism

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Neuropsychiatric symptoms in primary hyperparathyroidism are varied and can be easily missed, particularly in elderly population. It is believed that psychopathology emerges after a prolonged period of subclinical hypercalcaemia. This case highlights the importance of baseline tests when assessing patients presenting with mental health symptoms, and the presence of high serum calcium should prompt psychiatrists to consider testing for levels of parathyroid hormone and vitamin D levels.

Primary hyperparathyroidism, a primary abnormality of one or more of the parathyroid glands located in the neck, leads to inappropriate excess secretion of parathyroid hormone. This results in excessive renal calcium reabsorption, phosphaturia and increased bone resorption. Primary hyperparathyroidism is characterised by urolithiasis (‘stones’); osteopenia and osteoporosis (‘bones’); abdominal cramping, nausea and peptic ulceration (‘moans’); and depression, anxiety, cognitive dysfunction, insomnia, confusion and personality changes (‘psychiatric overtones’).1-3

The pathogenesis of psychiatric symptoms in primary hyperparathyroidism is unclear. It is proposed that the elevated calcium levels act through multiple mechanisms on various regions of the brain to produce a spectrum of psychiatric symptoms.4 Several studies have found a significant association between primary hyperparathyroidism with hypercalcaemia and psychiatric disturbances.5 6 Neuropsychiatric symptoms in primary hyperparathyroidism are varied and can be easily missed, particularly in the elderly population.7 It is believed that psychopathology emerges after a prolonged period of subclinical hypercalcaemia with mild-to-moderate hypercalcaemia presenting as depression, apathy, irritability, lack of initiative and severe hypercalcaemia presenting as delirium with psychosis, catatonia or lethargy and possibly coma.7-8

Presentation

We describe a case of 69-year-old woman who presented to mental health services for the first time with anxiety and irritability following a minor surgical procedure (removal of a non-malignant vaginal growth) from the gynaecology ward. This was an urgent psychiatry referral as her main carer, her husband, was struggling to cope with her increased anxiety and agitation. He was concerned about the sudden deterioration in her mental health. She presented as extremely anxious, irritable and depressed. Initial differential diagnosis included generalised anxiety disorder and moderate depression and she was treated with an antidepressant (venlafaxine 37.5mg OD), pregabalin (75mg BD for generalised anxiety disorder) and a benzodiazepine (lorazepam 0.5mg to 1mg) as required. She was reluctant to accept tablets and continued to refuse medications. Over the next few days her presentation changed with symptoms such as attempting to suffocate herself with a plastic bag placed over her head. She was offered informal admission again, which she declined. She was deemed not detainable under the Mental Health Act and she was discharged from A&E with mental health team follow up.

The following week her husband contacted mental health services in desperation to report further deterioration in her symptoms with increasing anxiousness, restlessness and disturbed sleep. A community psychiatric nurse agreed to visit the patient’s house urgently. At assessment she was anxious and agitated, through parts of the conversation she was inconsolable and on more than one occasion she put a cushion on her face and stated she wanted to die. She appeared impulsive and due to concerns around self-harm she was offered informal admission to a mental health unit, which she accepted.

On admission to the psychiatric unit the patient was highly anxious and needed a lot of reassurance. Her speech was rapid and she would repeat her thoughts. She presented with depressive cognitions with ‘free floating’ anxiety. Initial differential diagnosis included generalised anxiety disorder and moderate depression and she was treated with an antidepressant (venlafaxine 37.5mg OD), pregabalin (75mg BD for generalised anxiety disorder) and a benzodiazepine (lorazepam 0.5mg to 1mg) as required. She was reluctant to accept tablets and continued to refuse medications. Over the next few days her presentation changed with symptoms such as...
delusional mood and delusional perception. She often voiced concerns that her husband lay dead at home due to his physical comorbidities, despite reassurances that he was fine. She was hesitant to take medications and required a lot of reassurance from nursing and medical staff.

Baseline investigations revealed her calcium levels were high (3.06mmol/L) and her phosphate levels were low (0.79mmol/L). The normal range for calcium is 2.20–2.60 mmol/L and 0.8–1.50mmol/L for phosphate.

She then began stating that everyone was talking about her and on one occasion she telephoned her husband at 7am worried that he would be arrested by the police. Her speech became rapid with a low tone and there was a lack of eye contact during conversations; she also began pacing up and down the corridor, which she had not previously done. The dose of pregabalin was increased. The differential diagnosis was reviewed to include psychotic depression and she was commenced on antipsychotic medication (olanzapine) and the dose of antidepressant was gradually titrated. Repeat calcium level was high (3.24mmol/L) and she was transferred to A&E for intravenous fluids. While in A&E the patient remained paranoid and believed that everyone was talking and whispering about her. At the request of A&E one-to-one support from the mental health staff was offered to manage her agitation. After fluid therapy, her calcium returned to within the normal range and she was started on cinacalcet 30mg BD, which decreased the level of calcium and phosphate in the blood by lowering parathyroid hormone. She was diagnosed with primary hyperparathyroidism; her parathyroid hormone was 20.3pmol/L (normal range 1.6–6.9pmol/L). Due to her psychiatric symptoms she could not be managed on a physical health ward and was transferred back to the psychiatric unit.

She became increasingly delusional, hypervigilant and began to develop visual and auditory hallucinations. While on the psychiatric unit it was noted by the nursing staff that she had become increasingly paranoid. Her speech was of a low volume and repetitive. She would fail to maintain eye contact and looked at the floor during conversations; she also disregarded the importance of personal space. She had become fixated on another patient and she would follow her around the ward. She had taken hold of the wheelchair while her peer was still in it and began to tip it backwards. On one occasion she sat in the bathtub, tearful, ferociously scrubbing her skin muttering ‘disgusting’. On another occasion she became very agitated and unsteady on her feet and started to crawl on the floor on her hands and feet.

Her calcium levels were checked; again they were found to be high – 3.07mmol/L. She was admitted to the endocrinology ward and began to improve following hydration with iv fluids. She was given pamidronate, a biphosphonate, and her calcium levels were back within normal range – 2.51mmol/L. On the endocrinology ward staff from the psychiatric unit continued to provide one-to-one support due to agitation and she was continued on the same combination of pregabalin, olanzapine, venlafaxine and lorazepam. Ultrasound neck suggested the presence of parathyroid adenoma. Following correction of hypercalcaemia the patient’s presentation improved over the next few days and she was noted to be polite, relaxed and calm, communicating well with staff and peers. Her speech was coherent and there were no further delusions expressed.

There was complete resolution of her psychotic symptoms and both the patient and her husband believed that she was back to her baseline. She was treated with combination of olanzapine 7.5mg daily, and pregabalin 150mg daily and venlafaxine 150mg daily. In addition she was continued on cinacalcet 30mg twice daily as per advice from endocrinologist.

In summary, this elderly woman with no past history of psychosis or depression presented with generalised anxiety and psychotic depression, and was diagnosed to have primary hyperparathyroidism. There was marked decline in her presentation requiring intensive psychiatric input in an inpatient setting, which appeared to be directly related to high calcium levels in her blood with dramatic improvement following treatment of hypercalcaemia.

Discussion
Primary hyperparathyroidism often occurs in women over the age of 50 years and can present with neuropsychiatric symptoms, including general apathy, anxiety, sleep disorders, personality change and cognitive impairment.9–11 In samples of patients undergoing parathyroidectomy for primary hyperparathyroidism, these disturbances have been identified at a rate of 43.1%–53% for anxiety, 33%–62.1% for depression, 22% for thoughts of death or suicide, 51.9% for anger and irritability, 5%–20% for hallucinations and delusions, and 37.3%–46.5% for impaired cognition.1,8,12–15 Our patient presented with most of the symptoms described above, including anxiety, depression, suicidal thoughts, delusions, hallucinations and irritability.
Management of primary hyperparathyroidism has evolved with the changing presentation of the disease. Various treatment options have been recommended, including medical and surgical treatments. Medical treatment to reduce serum calcium such as forced saline hydration, forced diuresis, intravenous bisphosphonate (pamidronate)\textsuperscript{16} and cinacalcet, a calcium-lowering medication, can lead to improved psychiatric symptoms. Several studies have highlighted that parathyroidectomy leads to the definitive resolution of psychotic symptoms caused by hypercalcemia related to hyperparathyroidism,\textsuperscript{16–20} and can improve health-related quality of life.\textsuperscript{21}

This case study highlights complex neuropsychiatric phenomena seen with hypercalcemia, which, if promptly identified and treated, can lead to resolution of symptoms and improved quality of life. Neuropsychiatric symptoms in this age group can lead to disturbance in quality of life contributing to late-life disability. Our patient with psychotic depression was treated with antianxiety, antipsychotic and antidepressant medication. However, initially she presented a challenge to services due to her reluctance to engage in assessment and treatment. Options such as depot antipsychotic medication and ECT were initially considered. Joint working between endocrinology and psychiatry with active treatment of both the psychiatric symptoms and hypercalcemia appeared to be beneficial for the outcome in this case, which is a consistent finding even in previous studies.\textsuperscript{22} There is a possible risk that hypercalcemia can be missed in this age group, particularly in patients who have mild or asymptomatic hypercalcemia\textsuperscript{2} and may be given a high dose of antipsychotic medication, without correcting underlying hypercalcemia. There is a possibility that neuropsychiatric symptoms due to hypercalcemia can recur, hence this patient will need regular monitoring. Some patient groups might need consideration for further treatment options such as parathyroidectomy for primary hyperparathyroidism where benefits of surgical procedure outweigh the possible risks.\textsuperscript{8} This case highlights the importance of baseline tests when assessing patients presenting with mental health symptoms. The presence of high serum calcium should prompt psychiatrists to consider testing for levels of parathyroid hormone and vitamin D. A timely multidisciplinary approach involving endocrinologists and endocrine surgeons can contribute to better patient outcome.

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**Declaration of interest**

No conflicts of interest were declared.

**References**