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SEVERE HYPERCALCEMIA MIMICKING COGNITIVE DECLINE: A CASE REPORT OF PRIMARY HYPERPARATHYROIDISM

Medicine

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ABSTRACT

Primary hyperparathyroidism (PHPT) is a common cause of hypercalcemia, most frequently due to a solitary parathyroid adenoma. However, severe symptomatic hypercalcemia presenting predominantly with altered mental status, neuromuscular weakness, and gastrointestinal symptoms is uncommon and may lead to diagnostic confusion. We report a case of a 66-year-old male with longstanding diabetes mellitus, hypertension, and dyslipidemia who presented with progressive cognitive decline, proximal muscle weakness, and gastrointestinal dysfunction. The nonspecific and predominantly neurocognitive presentation initially suggested neurological or psychiatric etiologies, posing a diagnostic challenge and risk for mismanagement. Biochemical evaluation revealed marked hypercalcemia with elevated parathyroid hormone levels, and imaging demonstrated a MIBI-avid lesion in 99mTc-sestamibi single photon emission computed tomography consistent with a parathyroid adenoma. The patient underwent total thyroidectomy with right parathyroid excision, resulting in significant postoperative improvement and full recovery. This case underscores that severe hypercalcemia due to primary hyperparathyroidism may present as cognitive impairment, reinforcing the importance of evaluating metabolic and endocrine causes in older adults with unexplained neurocognitive decline to prevent delayed diagnosis and avoidable morbidity.

KEYWORDS

primary hyperparathyroidism, hypercalcemia, parathyroid adenoma, altered mental status, thyroidectomy

INTRODUCTION

Primary hyperparathyroidism(PHPT) is the most common outpatient cause of hypercalcemia and results primarily from a solitary parathyroid adenoma1-3. Clinical presentation varies widely, ranging from asymptomatic biochemical abnormalities to severe systemic manifestations including neurocognitive dysfunction, renal impairment, gastrointestinal symptoms, and cardiovascular or musculoskeletal involvement1,2. Hypercalcemic crisis is uncommon but represents a medical emergency requiring rapid identification and intervention 3,4. Although classic symptoms of hypercalcemia are well described, cases presenting predominantly with altered mental status or behavioral and cognitive changes can be diagnostically challenging, particularly in older adults where symptoms may be mistakenly attributed to dementia, psychiatric disease, or cerebrovascular pathology. Such atypical presentations increase the risk of delayed recognition, inappropriate diagnostic pathways, and symptomatic rather than curative management. This report describes a patient with severe symptomatic hypercalcemia presenting primarily with neuropsychiatric decline due to a parathyroid adenoma, highlighting the potential for misdiagnosis and underscoring the importance of considering metabolic causes in unexplained cognitive deterioration.

CASE PRESENTATION

A 66-year-old male with type 2 diabetes mellitus, hypertension, dyslipidemia, hyperuricemia, and osteoarthritis presented with progressive fatigue, poor oral intake, constipation, polyuria, altered mental status, irritability, and declining mobility over one month. He developed bilateral pedal edema, abdominal distension, and proximal muscle weakness. There was no history of seizures, renal calculi, malignancy, thyroid disease, or endocrine tumors.

On examination, he was disoriented, minimally interactive, and nearly bedridden. Vital signs were stable. Neurological examination revealed proximal muscle weakness and hypotonia.

DIAGNOSTIC ASSESSMENT

Serum calcium was markedly elevated at 14.7 mg/dL, with a corrected calcium of 13.6 mg/dL, and intact Parathyroid hormone (PTH) elevated to 275.5 pg/mL. Phosphate was low-normal (2.15 mg/dL) and serum magnesium was reduced (1.61 mg/dL). A 24-hour urinary calcium excretion of 261 mg/day supported hypercalciuria and effectively excluded familial hypocalciuric hypercalcemia. Vitamin D level was within the normal range. Electrocardiography showed normal sinus rhythm with a QTc of 400 ms, ST depression in lead II, and ST elevation in V4 and V6, consistent with repolarization abnormalities associated with hypercalcemia5,6.Echocardiography demonstrated a preserved left ventricular ejection fraction (61.5%) with concentric left ventricular hypertrophy. Further laboratory evaluation demonstrated preserved renal function with serum urea of 17.2 mg/dL and creatinine of 1.24 mg/dL. Although the urine albumin–creatinine ratio was moderately elevated (78 mg/g), this degree of albuminuria was insufficient to indicate chronic kidney disease capable of driving secondary hyperparathyroidism. Serum alkaline phosphatase was mildly elevated at 129 U/L, suggestive of increased bone turnover rather than renal osteodystrophy. Liver function showed a mild increase in total bilirubin (1.71 mg/dL) without cholestatic enzyme elevation. These findings, together with normal vitamin D status and preserved renal function, supported exclusion of secondary hyperparathyroidism.

Neck ultrasound demonstrated multinodular goiter. Sestamibi parathyroid scintigraphy with SPECT-CT demonstrated a focal persistent radiotracer uptake corresponding to a discrete nodular lesion inferior to the thyroid lobe, consistent with a hyperfunctioning parathyroid adenoma. No additional abnormal uptake was identified, supporting a solitary adenoma rather than multiglandular disease (Figure 1). Planar dual-phase 99mTc-sestamibi scintigraphy demonstrated a persistent focal area of radiotracer retention in the lower neck on delayed imaging, consistent with a hyperfunctioning parathyroid adenoma. Background thyroid activity washed out appropriately, and no additional abnormal uptake was seen to suggest multigland disease or ectopic parathyroid tissue. (Figure 2). A skull radiograph (AP and lateral views) showed no classical skeletal changes of hyperparathyroidism, such as a “salt-and-pepper” appearance or lytic lesions, indicating the absence of long-standing skeletal involvement (Figure 3).

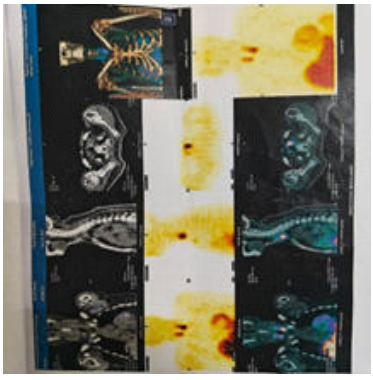

Figure 1. Sestamibi Parathyroid scintigraphy with SPECT-CT

Delayed-phase sestamibi scintigraphy demonstrating persistent focal radiotracer uptake at lower pole of the left thyroid lobe suggestive of hyperfunctioning parathyroid adenoma. No additional abnormal uptake was identified, supporting a solitary adenoma rather than multiglandular disease.

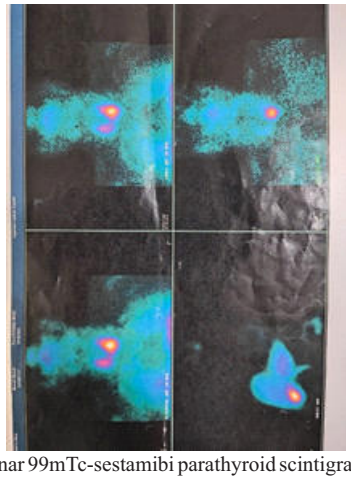

Figure 2. Planar 99mTc-sestamibi parathyroid scintigraphy

Dual-phase 99mTc-sestamibi planar scintigraphy showing a persistent focal radiotracer uptake in the inferior neck region on both early and delayed images (red focus), consistent with a parathyroid adenoma. Thyroid background activity demonstrates expected washout over time, supporting the parathyroid origin of the lesion.

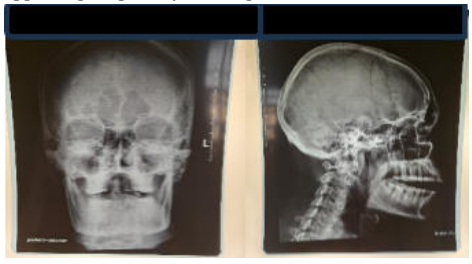

Figure 3 Skull radiographs

AP and lateral views of skull radiographs showing normal calvarial bone density and architecture with no evidence of salt-and-pepper appearance, cortical thinning, or lytic lesions. Findings suggest absence of long-standing skeletal involvement in primary hyperparathyroidism.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for severe hypercalcemia in this patient included both PTH-dependent and PTH-independent aetiologies. Primary hyperparathyroidism was strongly suspected early, given the markedly elevated serum calcium with inappropriately raised PTH, high urinary calcium excretion, and a MIBI-avid focal lesion consistent with a parathyroid adenoma, along with clinical symptoms such as neurocognitive decline, proximal muscle weakness, constipation, and polyuria. Parathyroid hyperplasia remained a consideration initially and was later identified as a secondary finding intraoperatively, while parathyroid carcinoma was unlikely due to the absence of extreme hypercalcemia, significantly elevated PTH, or a palpable neck mass. Secondary and tertiary hyperparathyroidism were excluded based on preserved renal function, normal vitamin D levels, and lack of chronic kidney disease. Among PTH-independent causes, malignancy-associated hypercalcemia was ruled out due to elevated rather than suppressed PTH, while vitamin D intoxication and granulomatous disease were excluded based on normal vitamin D status and biochemical pattern. Drug-related causes such as thiazide diuretics, as well as endocrine disorders including hyperthyroidism, adrenal insufficiency, and acromegaly, were excluded clinically and biochemically. Familial hypocalciuric hypercalcemia was ruled out by elevated 24-hour urinary calcium excretion, and although prolonged immobilization could contribute to hypercalcemia, it would not explain elevated PTH. Taken together, the biochemical profile, imaging, and intraoperative findings confirmed primary hyperparathyroidism due to a parathyroid adenoma as the definitive diagnosis.

TREATMENT AND OUTCOME

The patient received intravenous hydration, calcitonin, bisphosphonates, and magnesium replacement. Once stabilized, he underwent total thyroidectomy with excision of the right parathyroid adenoma via Kocher incision. Intraoperatively, a 1.5 × 1.5 cm parathyroid adenoma adjacent to the superior thyroid pole and multinodular goiter were confirmed. Histopathology demonstrated a parathyroid adenoma, parathyroid hyperplasia, and benign multinodular colloid goiter. Postoperatively, serial calcium monitoring demonstrated normalization (POD3: 9.4 mg/dL) (Figure 4). Calcium and calcitriol supplementation were initiated. Levothyroxine replacement was started with later dose adjustment. Neurological function, strength, and cognitive status improved gradually over six weeks.

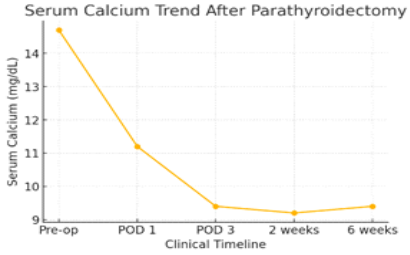

Figure 4. Serum Calcium Trend After Parathyroidectomy

Line graph demonstrating the decline in serum calcium levels from severe hypercalcemia prior to surgery to normalization over the postoperative period, reflecting successful biochemical response to parathyroidectomy.

DISCUSSION

Severe hypercalcemia secondary to primary hyperparathyroidism can present with multisystem involvement, including neurocognitive impairment, gastrointestinal symptoms, and musculoskeletal weakness1-3. Neuropsychiatric manifestations may closely mimic dementia, functional psychiatric illness, or cerebrovascular events, leading to diagnostic uncertainty and delayed intervention, particularly in older adults1,3. In this patient, markedly elevated serum calcium with inappropriately high PTH confirmed PTH-dependent hypercalcemia, distinguishing it from malignancy-associated or vitamin D–mediated etiologies1,2,4. Elevated urinary calcium excretion excluded familial hypocalciuric hypercalcemia4, and MIBI localization along with intraoperative findings confirmed a parathyroid adenoma as the underlying cause4,7. ECG abnormalities, including ST–T changes and a shortened QT interval, reflected known electrophysiologic effects of hypercalcemia[5,6].

As part of the skeletal assessment, a skull radiograph (anteroposterior and lateral views) was obtained. Although skull X-ray is rarely required in modern diagnostic pathways due to the availability of sensitive modalities such as Dual Energy X Ray Absorptiometry (DXA) scan and CT scan, it remains useful for detecting classical skeletal changes in long-standing disease—such as a "salt-and-pepper" skull pattern, cortical thinning, or lytic lesions consistent with osteitis fibrosa cystica. In this case, the skull X-ray demonstrated no such abnormalities, supporting early disease recognition before irreversible skeletal involvement and confirming the absence of advanced bony changes typically seen in chronic, untreated hyperparathyroidism.

Surgical excision remains the definitive treatment in symptomatic PHPT4,7, and postoperative surveillance is essential to detect complications such as hungry bone syndrome6. This case is clinically significant because the patient initially presented with progressive cognitive decline, behavioural changes, and functional deterioration—features often attributed to neurodegenerative conditions or psychiatric illness rather than an endocrine disorder. The absence of classic hypercalcemia symptoms further contributed to the diagnostic challenge and created potential for misdiagnosis and symptomatic rather than curative management. Mild albuminuria, musculoskeletal complaints, and age-related neuroimaging changes added complexity and could have suggested alternative diagnoses such as secondary hyperparathyroidism or age-related cognitive decline. Importantly, failure to identify hypercalcemia as a reversible aetiology may have resulted in delayed definitive therapy, prolonged morbidity, or unnecessary neurological or psychiatric intervention.

This case therefore underscores the importance of maintaining a high index of suspicion for metabolic and endocrine disorders when evaluating unexplained cognitive or functional decline in older adults, particularly when accompanied by subtle gastrointestinal, cardiovascular, or neuromuscular symptoms.

CONCLUSION

This case demonstrates severe symptomatic hypercalcemia secondary to a parathyroid adenoma presenting predominantly with neurocognitive decline. Prompt biochemical evaluation and definitive surgical management resulted in full clinical recovery. This highlights the importance of recognizing hypercalcemia as a reversible cause of delirium, particularly in older adults. Because severe hypercalcemia may mimic dementia, psychiatric illness, or other neurological disorders, timely identification of primary hyperparathyroidism is essential to prevent misdiagnosis, delayed treatment, and potentially avoidable morbidity.

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