

Added Value of Geriatric Consultation on the Emergency Department to Detect Primary Hyperparathyroidism in the Elderly Presenting as Frail Phenotype: Review of the Literature and A Case Report

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Abstract

A geriatric syndrome manifests itself as a group of signs and symptoms such as functional decline or cognitive problems leading to a vulnerable or frail phenotype. Here we present the case of an older woman with primary hyperparathyroidism masked by a frail phenotype detected during the geriatric consultation at the emergency department.

A 75-year-old woman with a history of hypertension, hypercholesterolemia, diabetes mellitus type 2, morbid obesity, non-alcoholic fatty liver disease, and secondary hyperparathyroidism due to vitamin D deficiency, presented at the emergency department with progressive fatigue, weakness, confusion, and cognitive decline over the last weeks. Previous consultation at the emergency department of another hospital a week earlier had not yielded a clear diagnosis.

Geriatric assessment revealed severe frailty, functional dependence and neurocognitive decline. Blood tests revealed severe hypercalcemia (3.71 mmol/L), hypophosphatemia (0.35 mmol/L), and elevated PTH (492 ng/L). Parathyroid 4D scintigraphy and CT scan showed a possible parathyroid adenoma and multiple thyroid nodules.

The patient underwent parathyroidectomy and subtotal thyroidectomy. Pathology revealed a parathyroid adenoma confirming the diagnosis of primary hyperparathyroidism, and papillary thyroid carcinoma. She was discharged after 22 days, and full functional and neurocognitive recovery was confirmed after 12 months.

Geriatric consultation on the emergency ward is of key importance. Clinical decisions in older people are indeed complex and require multidisciplinary input where experience of geriatricians provides important added value.

Keywords: Hyperparathyroidism, elderly, parathyroidectomy, geriatric syndrome, thyroid carcinoma

Introduction

Geriatric syndrome is a term used to indicate common health conditions in older adults that do not fit into specific organ-based disease categories. Atypical symptoms can be caused

by different underlying conditions. The etiology is often multifactorial, and symptoms can manifest acutely, as in delirium or syncope, or be of more chronic nature, such as functional decline, frailty, frequent falls, malnutrition or cognitive decline (1). The atypical character of geriatric syndromes

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harbors the danger of potentially masking other diagnoses, for example the hyperparathyroidism in the case we present here. Evaluation by a geriatrician of patients presenting to the emergency ward with what seems a geriatric syndrome is of key importance to avoid missing these underlying disorders presenting with atypical symptoms in the elderly (2-4).

Hyperparathyroidism is characterized by elevated parathyroid hormone (PTH) levels and activity. Primary hyperparathyroidism typically manifests itself with the symptom triad of bone loss, kidney stones and neuromuscular pain. Biochemically, it is characterized by hypercalcemia due to elevated PTH levels, as PTH, the central calcium regulating hormone, stimulates intestinal calcium absorption, calcium release from the bones, and renal calcium reabsorption (5).

The incidence of primary hyperparathyroidism increases with age and is three to four times higher in women (6,7). Its prevalence in those over 80 years of age can reach up to 7%. Many patients with hyperparathyroidism do not exhibit the classical symptoms, and although elderly patients often have clear biochemical hyperparathyroidism (6), symptoms such as cognitive impairment, muscular weakness, diffuse neuropsychiatric symptoms, and pain are often mistaken as age-related symptoms (8,9).

Here we describe the case of a 75-year-old female presenting with a geriatric syndrome, consisting of rapidly increased frailty and cognitive decline masking primary hyperparathyroidism. During further diagnostic workup, a papillary thyroid carcinoma was discovered as an incidental finding. The patient made a full recovery after surgical intervention.

Case Report

Patient Information

A 75-year-old Caucasian woman with a history of hypertension, hypercholesterolemia, diabetes mellitus type 2, morbid obesity, non-alcoholic fatty liver disease, total hysterectomy and secondary hyperparathyroidism due to vitamin D deficiency, was referred to the emergency department (ED) of the Antwerp University Hospital (UZA) by her general practitioner because of general deterioration with confusion, cognitive decline, fatigue, muscle weakness with recurrent falls, anorexia, dysphagia, polyuria.

She had visited the ED of another hospital the week before, where a routine diagnostic work-up [consisting of routine blood tests, urinalysis, electrocardiogram (ECG), thorax X-ray and computed tomography (CT) of the brain] did not lead to a definite diagnosis. She was sent home after reassurance without specific treatment. Calcium, phosphorus and vitamin D were not analyzed at that time, although mild hypercalcemia,

low vitamin D levels and secondary hyperparathyroidism had been diagnosed half a year before.

The patient presented to our ED in a somewhat confused state, with slow speech, but still adequately responsive during anamnesis. She reported a gradual decline in general health over the last 10 months, with serious deterioration over the last week.

She felt somnolent, unsteady and prone to falling due to muscle weakness in the legs. She had been unable to sleep in her upstairs bedroom for a while and required extensive help with daily activities such as hygiene, cooking, groceries, cleaning, becoming totally dependent upon her husband. She lost her taste and appetite and as a result lost 6.5 kg in weight over the last 3 to 4 weeks. There was no nausea or vomiting, she reported dysphagia with difficulty swallowing even small pills. She was known with urine-incontinence, but lately also complained of polyuria and nocturia. Her partner entirely confirmed her rapid and functional decline in cognitive functioning described by the patient.

At admission, the patient's medication consisted of a bisoprolol + hydrochlorothiazide 10 mg/6.25 mg combination, losartan 100 mg and simvastatin 40 mg for hypertension and hypercholesterolemia. Her diabetes was treated with metformin 850 mg/d, but semaglutide once a week was recently stopped by her general practitioner because of general deterioration including rapid weight loss. She had received vitamin D supplementation for six months, up to 3 months previously. There was no (history) of tobacco, alcohol or drug abuse.

Clinical Findings

Physical examination revealed no abnormalities besides dry mucosa, obesity and slightly reduced limb strength. Her blood pressure was in the hypertensive range (163/77 mm Hg). Body temperature was 37.2 °C, pulse 85/min, oxygen saturation was 95%, respiratory rate was 21/min.

A comprehensive geriatric assessment was performed, yielding a 7-8 score on the clinical frailty scale [(CFS), severe to very severe frailty], STRATIFY fall risk score of 2, 3/8 on the shortened mini mental state examination (Mini-MMSE), IADL 27/27, ADL 19/24, score C_D on the Belgian Katz index of independence (10), a score of 0 on the functional ambulation categories scale (FAC), and a pain score of 0 on the numeric rating scale (NRS), delirium observation scale (DOS) score of 9 indicative of delirium, neuropsychiatric inventory questionnaire (NPI-Q) score of 71/96. Clock drawing test could not be performed at this time (Table 1).

Diagnostic Assessment

Lab results showed calcium level of 3.71 mmol/L (normal range 2.18-2.60 mmol/L) and a phosphate level of 0.35 mmol/L (normal range 0.78-1.65 mmol/L). C-reactive protein was 17.3

mg/L. PTH was highly elevated (492 ng/L, normal range 18.5-88.0 ng/L). Vitamin D was 20 ng/mL (normal range 30-100 ng/mL). The pronounced hypercalcemia and hypophosphatemia explained the patient's malaise, weight loss, dysphagia, polyuria, obstipation, confusional mental state and muscle weakness.

Albumin (37 g/L), thyroid-stimulating hormone (1.03 mU/L) and T4 (19.1 pmol/L) values as well as ionogram and liver tests were normal. HbA1c was 5.3% (normal range 4.8-6.0%), eGFR=estimated glomerular filtration rate was 67 mL/min/1.73 mm². Bone mineral density on DEXA scan was completely normal.

ECG showed sinus rhythm with T wave inversion and normal QT and QTC intervals. On transthoracic echocardiography ejection fraction was 72% and a grade I left ventricular diastolic dysfunction without indications of volume overload or valve dysfunction was observed. Echography of the neck showed a thyroid imaging reporting and data system (TIRADS) III nodule (17x12x7 mm) in the right lobe and a TIRADS IV nodule (10x9x7 mm) in the left lobe of the thyroid gland. A parathyroid 4D scintigraphy and CT scan showed a possible parathyroid adenoma behind the left lower part of the thyroid gland (14x9x44 mm).

Therapeutic Intervention

The patient was treated with NaCl 0.9% IV 1 L/8h +30 meq KPO₄, alternating with NaCl 0.9% IV 1 L/8h +20 meq KCl and 2 g of magnesium, pamidronate 60 mg IV, and cinacalcet 4 IE/kg twice daily subcutaneously. The bisoprolol + hydrochlorothiazide combination was stopped because thiazide diuretics reduce urinary calcium excretion, it was replaced by furosemide 20 mg twice daily to induce diuresis and calciuresis and amlodipine

5 mg to control hypertension. Physiotherapy for mobilization and fall prevention was started.

A surgical intervention comprising subtotal bilateral thyroidectomy and upper left parathyroidectomy was performed after normalization of calcium and phosphate levels. The pathology evaluation diagnosed left parathyroid adenoma and multifocal right invasive papillary thyroid carcinoma with RET fusion. The resection margins were diagnosed as not entirely free of tumor, but it was decided not to re-operate in view of the patient's age and comorbidities.

Follow-up and Outcome

The patient's symptoms quickly improved postoperatively, with CFS score decreasing from 7 to 5 (mild frailty). She was discharged after 22 days, with levothyroxine 75 µg/d and calcium and vitamin D supplementation added to her original medication scheme.

After 12 months, the patient had made a nearly full functional recovery [CFS 3 (self-reliant), STRATIFY score 0, Katz category 0, FAC 5, NRS 0, ADL 6/24, IADL 12/27, NPI-Q 0/96, DOS 0], with a full restoration of cognitive function (MMSE score 30/30) (Table 1). PTH was in the normal range: 28 ng/L, echography of the thyroid region revealed no suspicious thyroid masses or lymph nodes.

Discussion

Geriatric consultation on the emergency ward is of key importance, as older people often present with a geriatric syndrome that may mask other diagnoses. Evaluation by a geriatric emergency medicine team reduces the length of the

Table 1. Results of the comprehensive geriatric assessment of the patient discussed in this case report at presentation and at follow-up 12 months later

Outcome	Assessment tool	Result	
		At presentation	At follow-up
Frailty	CFS	7-8 (severe to very severe frailty)	3 (self-reliant)
Neurocognitive functioning	Mini-MMSE	3/8	-
	MMSE	-	30/30
	DOS	9	0
	NPI-Q	71/96	0/96
	Clock drawing test	-	A
Pain	NRS	0	0
Fall risk	STRATIFY	2	0
Functional status	ADL	19/24	6/24
	IADL	27/27	12/27
	Katz index	C_D	0
	FAC	0	5

CFS: Clinical frailty scale, MMSE: Mini-mental state examination, DOS: Delirium observation screening, NPI-Q: Neuropsychiatric inventory-questionnaire, GDS-4: Four-item geriatric depression scale, NRS: Numerical rating scale, ADL: Activities of daily living, IADL: Instrumental activities of daily living, FAC: Functional ambulation categories

hospital stay (11) and geriatric assessment tools can predict revisit and readmission to the hospital (2). If geriatric assessment reveals fast functional (based on e.g., ADL, IADL scores), or neurocognitive deterioration (based on e.g., DOS, MMSE, NPI-Q scores), this is suggestive of underlying somatic disorders and needs to be investigated further.

The case we presented here demonstrates that fatigue, muscle weakness and neurocognitive symptoms which are often present in primary hyperparathyroidism, can be mistaken for manifestations of frailty and old age, especially in the absence of more typical manifestations such as renal stones, osteoporosis or fractures. The prevalence of primary hyperparathyroidism is estimated to be 0.5 to 34 per 1000, with highest prevalence between 40 and 70 years of age, and women affected 2-3 times more often. A Scottish population study reported 29.3% and 18.8% of identified primary hyperparathyroidism patients in the 70-79 years of age and >80 years of age groups, respectively (12).

A thorough evaluation needs to take into account the history of the patient (known hypercalcemia and hypovitaminosis D), must comprise a complete ionogram that includes measurement of calcium level, and a medication review. Our patient presented with hypercalcemia, that was diagnosed previously, and was on a thiazide diuretic, which can exacerbate hypercalcemia by reducing urinary calcium excretion. Her general practitioner discontinued semaglutide shortly before her visit to our hospital. Semaglutide causes weight loss and can cause fatigue, but none of our patient's other symptoms can be attributed to the effects of semaglutide.

Although the 2022 guidelines on the evaluation and management of primary hyperparathyroidism do not recommend surgery to improve neurocognitive function because of insufficient and inconclusive evidence (13), several prospective studies have reported improvement in neurocognitive parameters after parathyroidectomy (14-17). Replinger et al. (18) observed neurocognitive symptoms in 51.4% of patients presenting with primary hyperparathyroidism and found neurocognitive symptoms in patients with hyperparathyroidism to be predictive for parathyroid hyperplasia. The full functional and neurocognitive recovery of our patient is in line with these findings. Parathyroidectomy in the elderly has been shown to be effective and safe, with no increased incidence of complications (19).

Papavramidis et al. (20) reported decreased frailty index and improved quality of life after parathyroidectomy in older patients with primary hyperparathyroidism. Although surgical treatment is recommended for patients with calcium levels >1 mg/dL (0.25 mmol/L) above the upper limit of normal, nonoperative treatment with calcimimetics can be used as an alternative in older patients with contraindications for surgery (13). Normalization of calcium levels with calcimimetics

moreover predicts the cognitive response to parathyroid surgery in the elderly (9).

Thyroid cancer is relatively rare, although the incidence of papillary carcinoma, the most common type of thyroid cancer has been on the rise since the 1970s, mainly due to increased diagnosis (21). While the incident finding of a papillary thyroid carcinoma in our patient with primary hyperparathyroidism would seem a rare coincidence, the concomitant diagnosis of papillary thyroid carcinoma in patients with hyperparathyroidism has been reported previously: In a retrospective study, of 140 patients who underwent parathyroidectomy for primary hyperparathyroidism, 75 had concomitant thyroid surgery, and in those 19 papillary carcinomas were diagnosed (22).

The case presented here prompted the UZA, a tertiary training hospital, to routinely organize three daily multidisciplinary briefings in which all patients with a geriatric profile or geriatric syndrome are discussed by a multidisciplinary team consisting of a geriatrician, geriatric nurse, emergency physician and an ED nurse. Geriatric evaluation in the ED has been shown to facilitate decision making and improve service and patient outcomes (23,24).

Patient Perspective

At the time of presentation, the patient was convinced that she had lost her mind and had nearly reached the end of her lifetime. She was confused and entirely dependent on her husband for basic and instrumental daily activities.

When she was seen in a follow-up visit about a year after the surgery, the patient indicated that she was very happy to have undergone this surgery, which gave her "a new lease on life". She regained her independence in performing daily activities, is back to run her household normally, and recently went on a holiday by plane. She does not report any remaining systemic symptoms at this point.

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Ethics

Informed Consent: The patient provided consent for the publication of this case report to enable more swift diagnosis and treatment for others in a similar situation in the future.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: V.M., L.V.B., C.D.B., K.D.G., Concept: V.M., L.V.B., Data Collection or Processing: V.M., L.V.B., K.D.G., Analysis or Interpretation: V.M., L.V.B., C.D.B., M.V., G.H., S.P., G.M., Literature Search: V.M., L.V.B., C.D.B., M.V., Writing: V.M., L.V.B.

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