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CASE REPORT

A case of hyponatraemia secondary to vitamin D deficiency

LS Greenstein[a,b*], **R Daya**[c,d], **D Jacob**[e,f] and **Z Bayat**[c,d]

[a]*Division of Geriatric Medicine, Department of Internal Medicine, Helen Joseph Hospital, Johannesburg, South Africa*
[b]*Division of Geriatric Medicine, Department of Internal Medicine, School of Clinical Medicine, University of the Witwatersrand, Johannesburg, South Africa*
[c]*Division of Endocrinology and Metabolism, Department of Internal Medicine, Helen Joseph Hospital, Johannesburg, South Africa*
[d]*Division of Endocrinology and Metabolism, Department of Internal Medicine, School of Clinical Medicine, University of the Witwatersrand, Johannesburg, South Africa*
[e]*Department of Chemical Pathology, National Health Laboratory Services, Helen Joseph Hospital, Johannesburg, South Africa*
[f]*Department of Chemical Pathology, School of Pathology, University of the Witwatersrand, Johannesburg, South Africa*
**Correspondence: greensteinlara@gmail.com*

Hyponatraemia and Vitamin D deficiency are common conditions in older adults. Both conditions cause bone fragility and gait abnormalities, which are risk factors for falls and poor health outcomes in older adults. Vitamin D deficiency is a risk factor for osteoporosis and increases the risk for fragility fractures. Hyponatraemia, the commonest electrolyte abnormality, causes bone resorption and contributes to falls by impairing cognition and by causing gait abnormalities. Sodium homeostasis is complex and the syndrome of inappropriate antidiuretic hormone secretion (SIADH), a diagnosis of exclusion, is one of the most common causes of hyponatraemia. Instability is a feared geriatric syndrome, as falls can have devastating consequences for the older adult, leading to significant morbidity and mortality. Previous studies have shown that patients with hyponatraemia had a higher rate of vitamin D deficiency and, conversely, those with vitamin D deficiency had a higher rate of hyponatraemia. The exact pathophysiological mechanism behind this correlation is unclear but may involve bone derived hormone fibroblast growth factor 23 and the renin–angiotensin–aldosterone system. A case of an 83-year-old Asian female, who presented with an osteoporotic intertrochanteric femoral fracture following a fall, is presented. She was found to have chronic hyponatraemia and was subsequently diagnosed with SIADH due to vitamin D deficiency.

Keywords: falls, hyponatraemia, osteoporosis, SIADH, vitamin D deficiency

Introduction

Osteoporosis results in bone fragility, which is a risk factor for fragility fractures.[1] These low-impact fractures are often the initial presentation of osteoporosis in older adults and have a devastating impact on both morbidity and mortality. Consequences of osteoporotic fractures include impaired mobility, increased use of healthcare resources and institutionalisation.[2] Geriatric syndromes are a group of conditions resulting from impairments of multiple systems leading to a decline in physical and cognitive functioning, which render an older person vulnerable to poor outcomes from even minor insults.[3] Falling and osteoporosis are two such syndromes.

Figure 1: Radiograph showing intertrochanteric fracture of left femur with profound bone loss of the femoral neck and head of femur.

Hyponatraemia, defined as a sodium level of <135 mmol/l, is the most common electrolyte abnormality, affecting up to 35% of hospitalised patients.[4] The prevalence of hyponatraemia is highest in frail hospitalised patients older than 65 years of age.[5] Chronic hyponatraemia is associated with many adverse events including poor bone quality, falls, gait abnormalities, fatigue and cognitive impairment, which have detrimental effects on quality of life and mortality.[6] Hyponatraemia itself is a risk factor for fractures, independent of bone mineral density. The two mechanisms include cognitive impairment leading to gait abnormalities and falls, and increasing bone resorption.[7] A study looking at hyponatraemia in elderly patients with fragility fractures reported a prevalence rate of 26%. The causes of hyponatraemia in this study were dehydration and medication use.[8] Hyponatraemia therefore increases the risk of many geriatric syndromes including immobility, instability, cognitive impairment and frailty.

Sodium homeostasis is maintained by complex physiological mechanisms.[8] The syndrome of inappropriate antidiuretic hormone (SIADH) is one of the most common causes of hyponatraemia, accounting for approximately 50% of cases.[7,9] This syndrome is characterised by hypotonic, euvolaemic hyponatraemia associated with urine hyperosmolarity, which results from inappropriate antidiuretic hormone (ADH) release. Older

Table 1: Biochemical investigations

		Date					
Parameter	**Normal reference range**	**2/4/2019**	**10/3/2022**	**14/3/2022**	**16/3/2022**	**18/3/2022**	**8/4/2022**
Sodium	136–145 mmol/l	132	122	125		127	139
Corrected calcium	2.20–2.55 mmol/l		2.24				
Thyroid stimulating hormone	0.35–5.50 mIU/l			3.51			
Serum osmolality	275–295 mmol/kg			262			
Serum protein electrophoresis					Negative		
Total 25-OH vitamin D	> 50 nmol/l				17.39		
Alkaline phosphatase	42–98 U/l			190			
Parathyroid hormone	1.6–6.0 pmol/l				4.5		
8 am serum cortisol	nmol/l			980			
Urine protein electrophoresis						Negative	
Urine osmolality	50–1200 mmol/kg					406	
Urine sodium	< 40 mmol/l					96	

people have an increased concentration of ADH as well as age-related changes in sodium and water handling by the kidneys.[10] SIADH is a diagnosis of exclusion and all other causes of hyponatraemia must first be excluded.[6]

Vitamin D deficiency, defined as a level < 30 nmol/l, is common even in countries with adequate sun exposure, with prevalence depending on a number of factors including gender, vitamin D intake and activity level.[11] There is no consensus regarding the level at which vitamin D is regarded as deficient. The National Health Laboratory Service (NHLS), our laboratory, uses the revised South African clinical guideline for the diagnosis and management of osteoporosis, where deficiency is defined as < 30 nmol/l and vitamin D insufficiency is defined as a 30–50 nmol/l. The Institute of Medicine (IOM) concludes that a vitamin D level below 50 nmol/l is considered insufficient.[12] Vitamin D deficiency has been linked to type 2 diabetes mellitus, obesity, cardiovascular disease and poor bone and muscle health.[11] Vitamin D is necessary for the mineralisation of bone and is particularly important for bone health in that it decreases the rate of bone turnover and therefore decreases fractures. Vitamin D supplementation does not decrease fracture risk in those people who are not deficient and who do not have osteoporosis.[13,14]

Hyponatraemia and vitamin D deficiency are both common in older adults. Both conditions are risk factors for falls and osteoporosis. A study conducted in Italy showed that patients with vitamin D deficiency had lower sodium levels than those who were vitamin D replete.[15] A similar result was found in a study conducted in India, showing a significant correlation between the serum levels of sodium and total vitamin D in a group of outpatients.[16]

Vitamin D deficiency is treated by replacement in the diet and with supplements. SIADH is not as easy to treat, as the underlying cause needs to be identified and rectified.

Herein, we report a case highlighting SIADH caused by vitamin D deficiency in an elderly patient with an osteoporotic neck of femur fracture.

Case

An 83-year-old Asian female was brought to hospital by her son, with a history of a fall from a standing height three days previously with a subsequent inability to walk. She had pain and swelling of her left hip and leg. She had no chronic medical conditions and had no history of any medication use, including thiazide diuretics, spironolactone, angiotensin converting enzyme inhibitors and angiotensin receptor blockers. Prior to the fall, she was able to perform both basic and instrumental activities of daily living independently. She did not have any headache, dizziness or disturbance of consciousness. She had a poor diet and, although she was mobile, spent her time almost exclusively indoors, living a reclusive lifestyle. This was her first fall.

Physical examination revealed a lean female, with a body mass index of 19 kg/m^2 and normal vital signs. She was clinically normovolaemic, with no signs of fluid retention. There was tenderness in the left greater trochanteric region and inability to actively raise the left lower limb, as well as reduced range of motion. Mild swelling was present in the left intertrochanteric region with some ecchymoses. There was no radiating pain or numbness present, but the patient was not able to walk or bear weight due to pain. She also had a haemarthrosis of her left knee secondary to her fall. The rest of her examination was unremarkable.

A radiograph of the pelvis showed an intertrochanteric fracture of her left femur (Figure 1). She was admitted to the orthopaedic ward for further management.

Baseline investigations revealed a low haemoglobin and high mean cell volume in keeping with acute blood loss from her hip fracture (Table 1). Her renal function showed a sodium of 122 mmol/l (136–145 mmol/l), with a serum creatinine of 49 umol/l (49–90 umol/l) and a corrected calcium of 2.1 mmol/l (2.20–2.55 mmol/l). Hepatic and renal functions were normal. She was subsequently referred to the geriatric unit to assist with further investigations and management.

As fractures occurring in a setting of low-level or low-energy trauma (falling from standing height or less), are usually considered as osteoporotic, a diagnosis of osteoporosis was made in this patient. An incidental biochemical diagnosis of hyponatraemia was made. She was then worked up for both these conditions.

An algorithm was followed to work up the hyponatraemia.[4] Pseudohyponatraemia was excluded and the patient was euglycaemic. Serum osmolality was low at 262 mosm/kg (275–

295 mmol/kg). As she was euvolaemic and not on any medication (thiazide diuretic) SIADH was considered to be the cause of the patient's hyponatremia. Workup of SIADH revealed a urine osmolality of 406 mmol/kg (50–1200 mmol/kg) and a urine sodium of 96 mmol/l (< 40 mmol/l). Thyroid and adrenal function were both normal. Her 8 am cortisol was high at 980 nmol/l. This confirmed the diagnosis of SIADH. Results from 2 years prior to admission also showed a low sodium level, albeit not as low as during this current admission.

A contrasted computed tomography (CT) scan of her brain, as well as her chest radiograph and the electrocardiogram (ECG), was normal.

Investigations for causes of secondary osteoporosis were carried out, where the only abnormality found was a vitamin D deficiency with a total 25-OH vitamin D level of 17.39 nmol/l (>50 nmol/l). The rest of the workup was normal. As she was in traction and had not yet received surgery, a dual-energy X-ray absorptiometry (DEXA) scan could not be done.

Treatment during the admission included analgesia and thrombosis prophylaxis. Sodium chloride was given intravenously at a rate of 150 ml/hour for 3 days with no improvement in the sodium level. Once the vitamin D result was available (1 week post admission), vitamin D replacement (calciferol 50000 IU once a week) was given. Two weeks later the sodium level had improved to 139 mmol/l. Urine and serum osmolality normalised to 126 and 290 mmol/kg respectively. In view of finding no other cause for the persistent hyponatraemia, which corrected upon replacement of vitamin D, a diagnosis of vitamin D deficiency resulting in SIADH was made. Reduced sunlight exposure and poor diet were likely the cause of the vitamin D deficiency.

Surgery was initially delayed due to the electrolyte abnormalities, and thereafter the patient declined surgery. She received intensive physiotherapy and was able to mobilise to a wheelchair prior to discharge. Unfortunately, she was not able to live independently and had to be placed in a care facility.

Discussion

Osteoporotic fractures are more common in older persons. South Africa has a rising population of those aged over 60 years. Unfortunately, osteoporotic fractures in South Africa are not seen as a healthcare priority for a number of reasons, including the burden of communicable and non-communicable diseases, as well as the lack of dual X-ray absorptiometry equipment.[17] The main risk factors for the development of osteoporosis are genetic predisposition, female gender, older age, low body mass index, poor dietary calcium and vitamin D intake, a sedentary lifestyle, the use of certain bone toxic medications, poor socioeconomic factors and a high fall risk.[17]

Vitamin D deficiency is known to impair mineralisation of bone, thereby hampering bone remodelling. A systematic review, published in the *Lancet*, showed that the prevalence of low vitamin D status was 17.31% using a serum 25(OH)D concentration of less than 30 nmol/l.[18] As with osteoporosis, predictors for vitamin D deficiency include older age, female gender and lower socioeconomic status.

Hyponatraemia is the commonest electrolyte abnormality in older adults. Age itself is a risk factor for hyponatraemia due to a decreased glomerular filtration rate (GFR) leading to impaired water excretion capacity. Other factors include reduced intrarenal prostaglandins and the age-related decrease in total body water. Despite all these factors, hyponatraemia usually only develops in the face of an additional precipitating factor such as medication use.[6]

Symptomatic chronic hyponatraemia presents with fatigue, cognitive impairment and gait imbalance, which in turn predispose to a high fall risk. Hyponatraemia has a direct effect on bone quality, which, together with an increased fall risk, predisposes to fragility fractures.[6]

A study conducted in Italy showed that those patients with vitamin D deficiency had a statistically significant higher rate of hyponatraemia and, conversely, hyponatraemic patients had a higher rate of vitamin D deficiency.[15]

The exact pathophysiology behind the observed association between these two biochemical impairments is still unclear. However, the increased prevalence of hyponatraemia, particularly in elderly patients presenting with fractures, has been previously described.[19] A study by Kruse *et al*. found an association between serum sodium and bone mineral content and density, suggesting a higher risk of osteoporosis in hyponatraemic patients.[20,21] Vitamin D deficiency is also a well-recognized cause of osteoporosis.[13] Hyponatraemia can increase resorptive activity by stimulating osteoclast formation. Research done in mice shows that ADH downregulates osteoblasts and stimulates osteoclastic activity.[22] A link between endogenous vitamin D synthesis and circulating sodium concentrations may be possible, but has not been identified as yet.[23] One suggested mechanism involves the bone derived hormone fibroblast growth factor 23 (FGF23). 1,25 (OH)2 vitamin D (calcitriol) acts as a regulator of FGF23 production and disrupted calcitriol pathways reduce concentrations of circulating FGF23. Experimental studies have shown FGF23 causes an increase in sodium chloride cotransporter membrane expression in the distal convoluted tubule, allowing increased sodium reabsorption.[24] This likely extrapolates that with low vitamin D stores compromising calcitriol synthesis, FGF23 concentration may also be low resulting in lower sodium reabsorption. This theory requires more robust investigation. Studies suggest vitamin D status may have an influence on the renin–angiotensin–aldosterone system (RAAS), but this relationship is thought to be reciprocal in nature and does not explain the hyponatraemia noted in the setting of vitamin D deficiency seen in this case.[15]

Our patient had a comprehensive workup for her hyponatraemia. SIADH was found to be the cause. Her sodium level normalised after receiving vitamin D replacement, and as such a diagnosis of vitamin D deficiency induced SIADH was made.

Conclusion

Both hyponatraemia and vitamin D deficiency are common in older adults and are contributory factors to gait instability and falls. Vitamin D deficiency is a rare cause of hyponatraemia and does not form part of the workup for hyponatraemia. This case highlights the need to identify and evaluate geriatric syndromes in older patients and to understand the complicated interplay between different syndromes. Since both hyponatraemia and vitamin D deficiency are common, testing for both conditions should be included in the workup for any older person presenting with gait disturbances, instability, falls and osteoporosis.

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ORCID

LS Greenstein http://orcid.org/0000-0002-2945-1193
R Daya http://orcid.org/0000-0003-2395-2613
D Jacob http://orcid.org/0000-0003-2835-7303
Z Bayat http://orcid.org/0000-0002-0946-5934

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