CASE REPORT

Case Report: Cervical chondrocalcinosis as a complication of Gitelman syndrome [version 1; referees: 3 approved]

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Abstract

Gitelman syndrome is an inherited tubulopathy leading to a hypokalaemic metabolic alkalosis with hypomagnesaemia and hypocalciuria. Most cases are due to mutations in *SLC12A3*, encoding the apical thiazide sensitive co-transporter in the distal convoluted tubule. Musculoskeletal effects of Gitelman syndrome are common, including muscle weakness, tetany and cramps. Chronic hypomagnesaemia can lead to chondrocalcinosis, which often affects knees but can affect other joints. Here we present a case of Gitelman syndrome complicated by cervical chondrocalcinosis leading to neck pain and numbness of the fingers. Treatments directed at correcting both hypokalaemia and hypomagnesaemia were initiated and allowed conservative non-surgical management of the neck pain. Recognition of chondrocalcinosis is important and treatments must be individualised to correct the underlying hypomagnesaemia.

Open Peer Review

Referee Status: ✓ ✓ ✓

	Invited Referees 1	2	3
version 1 published 12 May 2016	✓ report	✓ report	✓ report

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Background

Gitelman syndrome (GS) is an autosomal recessive tubulopathy due to mutations in *SLC12A3* encoding the thiazide sensitive sodium chloride co-transporter (NCC) in the distal convoluted tubule. The estimated prevalence is 1:40,000[1]. Biochemically the phenotype is similar to long-term thiazide diuretic treatment: hypokalemia, hypomagnesemia, a hypochloraemic metabolic alkalosis and reduced urinary calcium levels[2]. Although an inherited condition, the disease is usually diagnosed during adolescence or early adult life. However presentations late in life, often with chondrocalcinosis do occur[3,4].

Case report

A 55-year-old lady was referred to the renal unit with persistently low serum potassium and magnesium levels following an episode of acute cholecystitis. Urinary electrolytes confirmed potassium wasting and hypocalciuria. On admission, her serum electrolytes were deranged: potassium 2.5 mmol/L, magnesium 0.31 mmol/L, corrected calcium 2.04 mmol/L, sodium 134 mmol/L and creatinine 53 µmol/L. Additional biochemistry tests confirmed hyperreninaemic hyperaldosteronism (renin >14.4 pmol/ml/hr (NR 0.5–3.1) and aldosterone 2794 pmol/L (NR 100–800)). Random urine sodium was 97 mmol/l, urine potassium 33 mmol/l and urine osmolality 467 mosm/kg. Biochemically, the diagnosis was consistent with GS.

She previously had no other significant medical history but had required NSAIDs for longstanding back, hip and neck pain. She was commenced on oral potassium and magnesium supplements (magnesium oxide 16 mmol/day) together with spironolactone 100 mg daily as a long term treatment. Molecular genetic analysis confirmed GS with the identification of compound heterozygous mutations in *SLC12A3* (p.Arg209Gln and p.Ser615Leu)[5]. Despite oral supplementation, serum magnesium levels remained low (0.5–0.6 mmol/L).

At 60 years of age, she had a MRI spine examination for worsening neck pain and the onset of numbness in her fingers. The MRI spine revealed widespread chondrocalcinosis in the cervical spine and soft tissues, with a large ossified bony bar at the level of C3 and C4 compressing the spinal cord (Figure 1). In addition, there were multiple areas of chondrocalcinosis in the intra-vertebral discs, annulus fibrosus, ligamentum flavum and in the transverse ligament behind the odontoid process. Despite the fingertip numbness and severe chondrocalcinosis, physical examination demonstrated no apparent neurological loss, with normal, tone, power, reflexes and sensation. Neurosurgical advice was sought and a conservative approach was adopted. Oral magnesium supplementation was changed to magnaspartate and increased to 40 mmol/day in an attempt to normalise serum magnesium levels and prevent progression of the chondrocalcinosis and improve symptoms. From 60 to 62 years of age the serum magnesium has been maintained at near normal levels (0.6–0.75 mmol/L) with improvement of musculoskeletal symptoms and no progression of any functional deficit in hand movements. Neurology follow-up continues to adopt observational and conservative management.

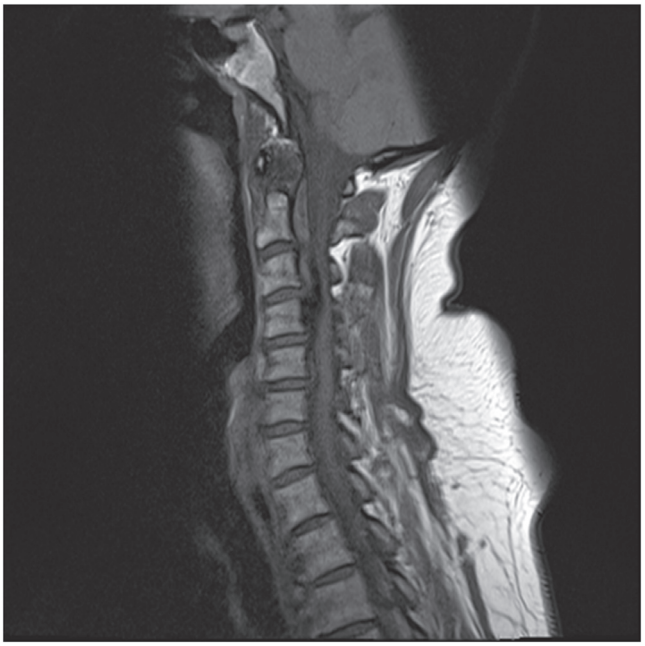

Figure 1. CT Cervical spine demonstrating a large ossified bony bar extending from the posterior surface of the C4 vertebral body up to the level of the upper surface of the C3 vertebral body. There are also multiple areas of calcification involving the intravertebral discs, annulus fibrosis, the ligmentum flavum and the transverse ligament behind the odontoid process.

Discussion

Chondrocalcinosis is the deposition of calcium pyrophosphate crystals in the articular cartilages throughout the body and has been associated with the longstanding hypomagnesaemia secondary to GS[6]. Chondrocalcinosis may cause swelling, heat and tenderness over the affected joints. As well as GS, chondrocalcinosis may also be seen in association with hyperparathyroidism, haemochromatosis and hypophosphatasia.

Chondrocalcinosis is a known complication of GS and can affect various joints, most typically knees[7]. Cervical spine chondrocalcinosis due to GS, however, is not often reported. Calcium pyrophosphate dehydrate deposits in the peri-odontoid soft tissues can lead to a condition called ‘crowned dens syndrome’ which causes acute neck pain and has been associated with GS[8]. Treatment relies on magnesium replacement and symptom control with non-steroidal anti-inflammatory drugs. Surgery is rarely performed.

Patients with GS can experience salt craving, tetany and cramps, fatigue and severe lethargy, often impacting greatly on their quality of life[5]. The chondrocalcinosis associated with it further adds to the musculoskeletal disease burden. It is therefore important to monitor patients and try to correct the potassium and magnesium disturbances to prevent acute exacerbations and progression[9]. Complete normalisation of serum magnesium is often difficult due

to diarrhoea associated with magnesium supplements. Various magnesium preparations are available, including magnesium oxide, magnesium glycerophosphate, magnaspartate, and magnesium lactate (Mag-Tab SR), which is slow release and is often better tolerated. Trial of various preparations and individual tailoring of dosing is required.

In summary we present a case of GS presenting with typical electrolyte disturbances (hypokalaemic metabolic alkalosis and hypomagnesaemia) complicated by severe chrondrocalcinosis of the cervical spine. Treatment directed at correcting these electrolyte disturbances has allowed an improvement of symptoms and avoidance of neurosurgery.

Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images and/or other details that could potentially reveal the patient's identity.

Author contributions

JAS conceived the idea. ZI, PM and JAS wrote the article and approved the final version.

Competing interests

The authors have no competing interests to declare.

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Current Referee Status: ✓ ✓ ✓

Version 1

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This is a well constructed and executed Case Report which is informative both with regards to the uncommon complication and the primary inherited kidney disease it pertains to. It is likely to be of interest and utility for clinicians who may encounter a patient with Gitelman Syndrome. The background, case history and discussion are cohesive, add to the knowledge base and are important for advancing the understanding and clinical management of this rare disease.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Competing Interests: No competing interests were disclosed.

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Nicholas G Larkins
Princess Margaret Hospital, Perth, WA, Australia

A well written article describing an interesting presentation of an uncommon condition. The case would be useful to other clinicians, as there is some important discussion of magnesium preparations.

I note the authors reference another case report published this year by themselves of a 37 year female with chonedrocalcinosis and GS. These could have been combined, with a more substantial discussion for a more useful contribution to the literature.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Competing Interests: No competing interests were disclosed.

Referee Report 16 May 2016

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Coralie Bingham
Renal Unit, Royal Devon and Exeter Hospital, Exeter, UK

A well written case report about an unusual complication of a rare disease. The genetic background to this disorder is covered. I think this report will be useful to other clinicians who may rarely see a case of Gitelman syndrome. There is a clear discussion of the medical management strategy used in this patient which lead to an improvement of symptoms and the avoidance of surgery. I think this report adds to knowledge about this rare disease and merits indexation.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Competing Interests: No competing interests were disclosed.