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Case Report

Hoffman's syndrome: delayed onset and progression in elderly - a case report

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ABSTRACT

Hoffmann's syndrome (HS) is typically characterized by myopathy and linked to hypothyroidism. It is distinguished by hypothyroidism, muscle weakness, and pseudohypertrophy of particular muscles. In the present case report, a 70-year-old man was brought to the hospital with major complaints of hematuria and swelling in both legs, and a small wound on his right leg. He had a known history of type 2 diabetes mellitus with irregular medication. The hematological investigation reveals abnormalities, including an irregular Q-wave, an inverted T-wave, and low voltage in the limb leads, as identified by electrocardiography (ECG). Troponin I was negative, cardiac indicators were aberrant, and the creatine kinase myocardial band (CK-MB) level was 132 U/l. To manage the symptoms and stabilize the patient's condition, he was treated initially with antibiotics, metformin, metoprolol, furosemide, aspirin, and clopidogrel. Contrarily, the leg swelling did not improve. Later, the hematological investigation revealed that abnormal thyroxine levels (T3-0.26 ng/ml, T4-0.5 ng/ml, and TSH-60.0 mIU/l) and prominent right leg swelling were associated with chronic kidney disease (CKD) and Hypothyroidism. The swelling and cellulitis gradually reduced after intravenous meropenem and oral thyroxine treatment. He was continuously monitored, and signs and symptoms steadily improved. In this instance, it is crucial to stress that, particularly in the absence of obvious signs of hypothyroidism, a differential diagnosis of musculoskeletal problems should be taken into consideration when a patient presents with leg swelling, and early detection of Hoffman's disorder leads to a more effective treatment outcome.

Keywords: Hoffmann's syndrome, Hypothyroidism, Muscle weakness, Myopathy

INTRODUCTION

In Hypothyroidism, the lower levels of thyroid hormones lead to severe complications and lead to severe morbidity and mortality, if not treated. This condition is substantially diagnosed through laboratory examinations and measuring TSH, T3, and T4 levels. The lower levels of thyroxine and elevated thyroid-stimulating hormone (TSH) are defined as clinical or overt primary hypothyroidism.[1] Kocher-Debre-Semelaigne syndrome (KDSS), Hoffmann's syndrome (HS), atrophic form, and myasthenic syndrome (MS), these myopathies are linked to hypothyroidism.[2] Around 75 of people with hypothyroidism and 67 of people with hyperthyroidism experience neuromuscular symptoms, which are frequent in thyroid problems.[3] Grown-ups with HS have hypothyroidism, presenting with pseudohypertrophy of specific muscles and muscle weakness. In addition to low serum thyroid hormone (THL) and elevated thyroid-stimulating hormone (TSH), there's also an increase in muscle enzyme, which indicates rhabdomyolysis in HS.[4]

CASE REPORT

In the present case study, a 70-year-old male patient was admitted to the hospital with complaints of swelling in both legs, a wound on his right leg, difficulty walking, irritability, and hematuria. These symptoms have gradually developed over the past two days. There was no history of trauma or surgery, but the patient had a known history of type 2 diabetes mellitus for which he was not on regular medication. His general and systemic examinations were largely unremarkable, except for a local examination of the legs, which revealed bilateral swelling. Further investigations were conducted to identify the underlying conditions.

Hematological investigations

Initial hematological and liver function tests indicated abnormal findings (Table 1). Also, Electrocardiography (ECG) revealed an abnormal Q-wave, an inverted T-wave, and a low voltage in the limb leads. Cardiac markers were abnormal, troponin I was negative, and creatine kinase myocardial band (CK-MB) was positive.

Therapeutic management

The patient was initially prescribed a combination of medications, aimed at subsiding the symptoms of bilateral leg swelling, a wound on the right leg, difficulty walking, elevated capillary glucose levels, and increased creatine kinase myocardial band. The prescribed treatment regimen included intravenous (IV) fluids, antibiotics, antiplatelet agents, antihistamines, analgesics, antihypertensives, and antidiabetics over three days in the general surgery ward (Table 2). However, contrary to the aim of the treatment, there was no reduction in the leg swelling.

Further, hematological investigations (mean corpuscular volume (MCV) of 112.2 fl, haemoglobin 12.5 g/dl, platelets 68,000/µl, troponin I, urea 72 mg/dl, and creatinine 2 mg/dl) and abnormal thyroxine levels (T3-0.26 ng/ml, T4-0.5 ng/ml, and TSH-60.0 mIU/l) revealed that hypothyroidism. On observation, the right leg was more prominent than the left. Based on these findings, the patient was diagnosed with bilateral lower limb cellulitis, sepsis, acute kidney injury (AKI), diabetic nephropathy, coronary artery disease, and volume-overloaded status, with a history of inferior wall myocardial infarction.

The prescribed antibiotics (ceftriaxone and metronidazole) were switched to higher antibiotics (meropenem), along with alkalinizing agents and endothelin receptor antagonists, in addition to medications previously administered (Table 3). The swelling due to cellulitis gradually reduced, and further investigation was conducted to monitor the signs and symptoms. The patient was subsequently transferred to the general ward and continued the treatment to treat sepsis, AKI, diabetic nephropathy, coronary artery disease, old inferior wall myocardial infarction, and volume overload.

Table 1: Laboratory investigations.

Parameters	Observed value		Reference range
	Initial (Day 1)	Later (Day 4)	
Hematological investigation			
White blood cell (WBC)	14.8×10^3/µl	-	$4.0\text{-}11.0\times 10^3$/µl
Red blood cell (RBC)	3.50×10^6/µl	-	$4.5\text{-}5.9\times 10^6$/µl
Haemoglobin (Hb)	13.5 g/dl	12.5 g/dl	13.5-17.5g/dl
Platelet	87×10^3/µl	68×10^3/µl	$150\text{-}400\times 10^3$/µl
lymphocytes	8%	-	20-40%
Neutrophils	87.4%	-	40-70%
Monocytes	4.6%	-	2-8%
Eosinophils	4.6%	-	1-4%
Mean corpuscular haemoglobin (MCH)	38.6 pg	-	27-32 pg
Mean corpuscular haemoglobin concentration (MCHC)	34.2 g/dl	-	32-36 g/dl
Mean corpuscular volume (MCV)	-	112.2 fl	80-100 fl
Biochemical Investigation		-	
Total bilirubin	1.6 mg/dl	-	0.3-1.2 mg/dl
Direct bilirubin	0.4 mg/dl	-	0.1-0.3 mg/dl
Aspartate aminotransferase (AST)	124 IU/l	-	5-40 IU/l
Alanine aminotransferase (ALT)	92 IU/l	-	7-56 IU/l
Total protein	6.3 g/dl	-	6.4-8.3 g/dl
Albumin	3.1 g/dl	-	3.5-50 g/dl
Alkaline phosphatase	98 U/l	-	44-147 U/l
Capillary blood glucose	160 mg/dl	-	<140 mg/dl
Urea	39 mg/dl	72 mg/dl	15-40 mg/dl
Creatinine	1.6 mg/dl	2 mg/dl	0.7-1.3 mg/dl

Continued.

Parameters	Observed value		Reference range
	Initial (Day 1)	Later (Day 4)	
Cardiac biomarkers			
Troponin I	Negative	Negative	
Creatine kinase myocardial band (CK-MB)	132 U/l	-	0-25 U/l
Thyroid function tests			
Total T3	-	0.26 ng/ml	0.8-2.0 ng/ml
Total T4	-	0.50 µg/dl	5.0-12.0 µg/dl
Thyroid stimulating hormone (TSH)	-	60 mIU/l	0.4-4.0 mIU/l

Table 2: Initial therapeutic management.

Drug	Dose and frequency
Injection ceftriaxone	1g IV and then b.d till day 3
Injection metronidazole	500 mg IV t.d.s for 7 days
Injection ranitidine	50 mg IV b.d for 7 days
Tablet paracetamol	500 mg b.d for 7 days
Tablet aspirin	150 mg o.d for 7 days
Tablet clopidogrel	75 mg o.d for 7 days
Tablet atorvastatin	20 mg h.s for 7 days
Tablet metoprolol	50 mg b.d for 7 days
Tablet metformin	500 mg b.d for 7 days
Tablet furosemide	40 mg b.d for 7 days (morning and afternoon half dose)

Table 3: Therapeutic management of Hoffmann's syndrome (from day four).

Drug	Dose and frequency
Tablet thyroxine	100 mcg, o. d
Tablet metformin	500 mg, b. d
Tablet aspirin	150 mg, o.d
Tablet clopidogrel	75 mg, o. d
Tablet atorvastatin	20 mg, o. d
Tablet furosemide	40 mg, to be taken in the morning and half dose in afternoon
Tablet ranitidine	150 mg, b.d, morning and evening before meals
Injection meropenem	500 mg in 100 ml NS IV t.d.s, initiated on day 4 for 3 days
Tablet sodium bicarbonate	500 mg t.d.s initiated on day 4 for 3 days
Tablet calcium carbonate	300 mg o.d initiated on day 4 for 3 days

DISCUSSION

In patients with diabetes mellitus, cellulitis affects the deeper subcutaneous layers of the skin. The infected area, which is typically seen on the thigh, is characterized by warmth, redness, swelling, soreness, and discomfort.[5] The diagnosis of abscess or cellulitis is typically based on medical history and physical examination, although the latter has variable reliability in assessing the presence and severity of abscesses, particularly for smaller or deeper collections. Misdiagnosing an abscess as cellulitis may lead to inadequate treatment and a return visit due to antibiotic failure, while misidentifying cellulitis as an abscess may result in unnecessary incision and drainage, causing discomfort, anxiety, and a potential need for procedural sedation.[6] Hoffmann syndrome was initially described by Hoffmann in 1897 in an adult who experienced muscle stiffness and difficulty relaxing the muscles after thyroidectomy.[7] The hallmark symptoms of muscular (pseudo-) hypertrophy are uncommon manifestations of hypothyroidism.[8] Hypertrophy may result from an increase in connective tissue and enlargement and proliferation of muscle fibres. In Hoffmann's syndrome, hypothyroidism is typically primary, often due to Hashimoto's thyroiditis, whereas secondary hypothyroidism rarely presents with this syndrome.

Muscle biopsy is generally not necessary to confirm the diagnosis.[9] Previous reports on Hoffmann syndrome indicate that while the calf muscles are typically affected, any muscle group, including those in the thighs, arms, and forearms, can also be involved.[10] The mechanism behind this involves increased deposition of glycosaminoglycans and enlargement and proliferation of muscle fibers. Additionally, there is a shift in the muscle fibre type from fast-twitch type II to slow-twitch type I, resulting in delayed muscle contraction.[11] Creatine kinase (CK) is a key biochemical marker of myopathy. However, reports were showing that elevated CK levels were found in

patients with mild hypothyroidism.[10] Other enzymes, such as aldolase, AST, and LDH, play supporting roles in the absence of liver dysfunction. Although the precise cause of high CK levels in hypothyroidism is unknown, it is believed to be caused by direct cellular injury, a reversible impairment in glycogenolysis, and decreased CK clearance.[12] If Hoffmann's syndrome appears without other signs of hypothyroidism, a high level of caution is necessary.[13]

Hoffmann's syndrome affects the muscles, causing weakness, stiffness, and fatigue due to hypothyroidism, with dry and swollen skin but without redness, warmth, or fever. In contrast, cellulitis is a skin infection characterized by red, swollen, warm, and painful areas, often accompanied by fever and chills, and typically does not involve muscle pain.

CONCLUSION

In this case, it is important to emphasize that when a patient presents with leg swelling, a differential diagnosis of musculoskeletal symptoms should be considered, especially in the absence of overt manifestations of hypothyroidism. The consideration of hypothyroidism, along with routine measurement of serum TSH levels, is crucial when evaluating patients with progressive muscle weakness and swelling. Early identification of Hoffmann syndrome facilitates more effective treatment, and regular monitoring of serum TSH levels can aid in the prompt diagnosis of this condition.

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