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A CASE OF HEPARIN INDUCED HYPOALDOSTERONISM MANIFESTING AS REFRACTORY HYPERKALEMIA.

General of Medicine

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ABSTRACT

Heparin is used extensively in the treatment and prevention of thromboembolic events. Most common side effects with heparin treatment include easy bleeding, bruising, Heparin Induced Thrombocytopenia (HIT) and Heparin Induced Thrombocytopenia and Thrombocytosis (HIIT). Rarely, it leads to life threatening complications; one among them is hyperkalemia. We report a case of 44 year old female presented with deep vein thrombosis who on treatment with heparin developed treatment resistant hyperkalemia.

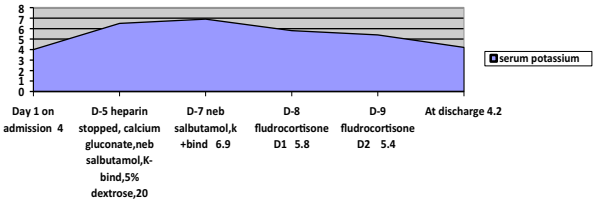
KEYWORDS

CASE REPORT:

A 44 year old female was admitted with history of swelling of the left leg for 2 weeks which was progressive and associated with pain. No history of shortness of breath, chest pain, fever, loss of weight and appetite was present. She was a known case of diabetes mellitus on regular treatment. Her past medical history revealed no recent immobilization, surgeries, any trauma, intake of birth control pills nor over the counter medications. Family history was insignificant. On examination, her vitals were stable. General Examination revealed painful pedal edema in left leg which extended till the upper thigh. Systemic Examination revealed no abnormality.

Routine investigations including complete blood count, renal and liver function test and coagulation profile were normal. Serum electrolytes at the time of presentation were normal as shown in table. Electrocardiogram and x-ray chest were normal. Venous doppler of the left lower limb showed a deep vein thrombosis involving the external iliac vein and common iliac vein. Extensive evaluation to find out the underlying cause for DVT including antiphospholipid antibodies turned out to be negative. Clinical Examination as well as imaging of the abdomen and chest did not reveal any focus suggestive of malignancy.

She was started on heparin (80U/kg) IV bolus followed by infusion at 18U/hr with frequent monitoring of aPTT. On day 2 of hospital admission, she was switched over to heparin 5000 units IV 6th hourly. She was also managed with tramadol and other supportive measures. All the basic investigations were repeated on 4th day which incidentally revealed elevated serum potassium (6.1 meq/l). She was stared on anti-hyperkalemic measures as shown in the graph below.



As the patient had hyperkalemia after starting heparin, the possibility of heparin induced hyperkalemia was suspected and heparin was stopped. Despite of stopping heparin for 3 days, hyperkalemia persisted. Evaluation for hyperkalemia showed normal ABG with a TTKG (Trans tubular potassium gradient) of 2.04. Since TTKG values were below 3, patient was suspected to have mineralocorticoid deficiency and plasma aldosterone was measured which was found to be low(2 ng/dl). 50 µg of fludrocortisone was started and within 48 hours, there was marked improvement in serum potassium. Repeat TTKG was 5.2. At the time of discharge serum potassium was 4.2.

She was switched over to oral anticoagulant dabigatran after heparin was stopped and continued for 6 months. At 6 months follow up, RFT and electrolytes were normal. Evaluation for DVT did not reveal any underlying cause.

	Day 1 (on admission)	Day 4	Day 5	Day 7	Day 8 (fludrocor-tisone started)	Day 9	At the time of discharge
SODIUM (meq/l)	129	128	126	124	129	130	134
POTASSIUM (meq/l)	4.0	6.1	6.5	6.9	5.8	5.4	4.2

DISCUSSION:

Hyperkalemia has been defined as the elevation of serum potassium concentration greater than 5.5 meq/l. Incidence of hyperkalemia has been estimated to be around 1.3% to 10% in hospitalized patients and one tenth of those patients having values greater than 6.0 meq/l (1). Among the various causes of hyperkalemia impaired renal secretion and excretion rank the most common. Medications causing hyperkalemia account for twenty seven to seventy five percent of cases as reported by Evans et al.2

Heparin Induced Hyperkalemia(HIH) is rare entity and has been increasingly reported recently(3). Heparin most commonly causes bleeding and Thrombocytopenia. Recently studies have shown that heparin and related substances cause suppression of aldosterone with resultant natriuresis. HIH has been reportedly occurred with dosage of even 5000 units on twice daily dosing(4). Exact mechanism of heparin induced hypoaldosteronism remains unknown. Heparin has increased specificity on the Zona glomerulosa leading to reduction in aldosterone production, decreased steroidogenesis and reduced affinity of Angiotnsin II receptors in the Zona glomerulosa with resultant reduction in excretion of potassium (3,5,6). Suppression of Aldosterone can be detected in 1-3 days after starting heparin and most of the casesare reported on 3 to 5 days after initiation. Heparin continuation further results in adrenal hemorrhage and insufficiency. Measurement of plasma aldosterone levels as well as determining potassium concentration at the cortical collecting tubule (cannot be estimated directly) by TTKG (Trans Tubular Potassium Gradient). TTKG is a measure of secretory activity of Potassium in the distal tubules. TTKG values lower than 5 in Hyperkalemic patients is typically suggestive of hypoaldosteronism(7).

Diagnosis is confirmed by measurement of serum Aldosterone levels and indirectly demonstrating improvement in TTKG with administration of mineralocorticoid such as Fludrocortisone. Fludrocortisone has been proved to be effective in cases of Heparin induced Hypoaldosteronism (8). In our case Hyperkalemia was resistant to conventional measures which probed to workup regarding HIH and our diagnosis was confirmed through low measured levels of aldosterone levels and low TTKG value which improved with treatment on fludrocortisone.

Though on patients with Heparin, altered levels of aldosterone are common, only those who are unable to compensate (by increasing renin production) develop Hyperkalemia. Early identification and treatment of Heparin induced Hypoaldosteronism would result in significant reduction in morbidity and mortality. Therefore it is vital to monitor electrolytes (sodium and potassium) during initial 3 -5 days of starting treatment with Heparin and weekly thereafter (8).

CONCLUSION:

HIH is a rare complication of heparin therapy and it may persist despite discontinuation of the drug. The physician should be aware of this, as conventional therapy for hyperkalemia in this scenario is ineffective in some of the patients (9). Measurement of electrolytes after initiation of heparin should be done as a routine especially in patients with underlying kidney disease or in presence of co-morbid illness.

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