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Primary hyperaldosteronism presenting as hypokalemic periodic paralysis

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Abstract

Hypokalaemic periodic paralysis is episodic painless muscle weakness associated with areflexia (1). Hypertension and hypokalaema are the classic presentation of primary hyperaldoteronism though some patients can be normokalaemic (2). Hypokalaemic paralysis is occasionaly seen in patients with hyperaldosteronism (1). This middle aged female presented with her 3rd episode of hypokalaemic periodic paralysis and later diagnosed to have primary hyperaldosteronism due to unilateral adrenal hyperplasia, cured after adrenalectomy.

Key words: primary hyperaldosteronism, periodic paralysis, hypokalaemia.

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Case

A forty year old previously healthy female was admitted to the medical casualty with painless weakness of both lower limbs for 4 days duration. Weakness was more in proximal muscles and it was progressive over time.Bilateral upper limbs were involved by fourth day of illness. She did not feel numb over the muscles of weakness. She did not have diplopia, dysarthria or dysphagia and she did not feel breathless. Symptoms did not demonstrate a diurnal variation. Bladder and bowel habits were normal. There were no similar illnesses in the family.

She has had 2 similar, but less severe episodes about 1 and 3 months ago respectively. The weakness improved spontaneously without medical attention.She was well between episodes, without residual weakness.She was clinically euthyroid.

On examination, she was not pale. She was not dyspnoic and saturation on breathing ambient air was 100%. Her motor system examination revealed flaccid quadriparesis. Proximal muscles were weaker than the distal muscles. Tendon reflexes were diminished in both upper and lower limbs. Sensory and joint position sensations were intact with flexor plantar response. Cranial nerves, cerebellar functions and fundoscopy examination were normal.Her blood pressure on admission was 210/130mmHg, with a pulse rate of 90 beats per minute. Rest of the cardio vascular, abdomen and respiratory system examination were unremarkable.

Her basic investigations revealed hypokalaemia with metabolic alkalosis (table 1). ECG showed U waves from V2 to V5. Her complete blood analysis, liver functions and inflammatory markers were normal. Hypokalaemia was corrected with intravenous potassium chloride infusion with cardiac monitoring. Patient made a complete recovery.

Her thyroid enzyme profile was normal. Further investigations were performed to confirm the possibility of hyperaldosteronism.Calculated urine potassium to creatinine ratio was 16.52 mmol/mmol (normal value <2 mmol/mmol)(3) . Serum aldosterone and renin levels in upright position demonstrated suppressed serum renin levels and a high serum aldosterone to renin ratio, suggestive of primary hyperaldosteronism (table 2). Low dose dexamethasone suppression test ruled out the possibility of associated Cushing's syndrome. Renal artery duplex excluded renal artery stenosis. Contrast enhanced CT abdomen was also unable to show any evidence of adrenal abnormality.

Variable	Patient's Value	Reference Range

Table 1: Laboratory data – Basic investigations

$PaCO_2$(mmHg)	26	38-42
PaO_2(mmHg)	100	94-100
HCO_3(mmol/L)	27	22-28
S. Potassium (mmol/L)	1.9	3.5-5.1
S. Sodium (mmol/L)	141	136-142
S. Calcium (Albumin corrected µmol/L)	8.9	8.6-10.3
S. Magnesium (mg/dL)	2.11	1.9- 2.5
Urine Sodium (mmol/L)	183	40-220
Urine Potassium (mmol/L)	21.6	13-62
Urine Potassium to Creatinine ratio (mmol/mmol)	16.52	<2mmol/mmol
S. Creatinine (µmol/L)	58	58-96
Blood urea (mg/dL)	15	

Table 2: second line investigations

Variable	Patient's Value	Reference range
Serum Aldosterone –Upright (pg/mL)	201	34.7 -275
Serum Renin – Upright (pg/mL)	1.2	5.4-34.6
Serum Aldosterone/ Renin ratio	163	<50
Low dose dexamethasone suppression test		
basal 9am cortisol (µg/dL)	274	240- 620
cortisol at 48 hours	20.7	<50

Primary hyperaldosteronism was confirmed by saline infusion test. In this test, 0.9% NaCl is infused intravenously, at a rate of 500ml per hour, for a duration of 4 hours. Serum Aldosterone levels are measured sequentially every hour, in the upright position (Table 3).Failure to suppress serum aldosterone levels over time confirms primary hyperaldosteronism.

Adrenal venous sampling was performed later to isolate the side of adrenal hyper secretion (Table 4).

Lateralization of the test was interpreted in terms of lateralization index[4].

Lateralization index = $\frac{\text{Aldosterone/Cortisol}_{\text{Dominant)}}}{\text{Aldosterone/Cortisol}_{\text{(Non dominant)}}}$

Lateralization index values greater than 3 to 5 are considered to define lateralized aldosterone production (4). Our patient had a lateralization index value of 12.9, left side adrenal gland being the dominant gland.After the diagnosis of hypersecretion of aldosterone from left adrenal gland, patient was referred to surgical team for left sided aderenalectomy. Aderenalectomy was performed and histology revealed a multiple foci of adrenal cortical hyperplasia.

Discussion

Periodic paralysis is characterized by painless episodes of muscle paralysis (1). These attacks are typically sudden onset muscle weakness with preservation of consciousness. Bulbar muscles and respiratory muscles are occasionally involved.

Main differential diagnoses for hypokalaemic periodic paralysis are thyrotoxic periodic paralysis, myasthenia gravis, metabolic myopathies and secondary hypokalaemia due to gastro intestinal, renal and other losses(5). High urinary potassium to creatinine ration, high trans-tubular potassium gradient and severe hypokalaemia indicate secondary causes (3).

Primary hyperaldosteronism is renin – independent hypersecretion of aldosterone from adrenal glands. The classical symptoms at presentation are hypertension and hypokalaemia(1). Though hypokalaemia is conventionally considered as a feature of primary hyperaldosteronism, hypokalaemia is not seen in around 20% of patients (2). Hypokalaemic periodic paralysis is occasionally associated with hyperaldosteronism(1). The percentage of patients with primary hyperaldosteronism, presenting with hypokalaemic periodic paralysis lies within a range of 1 to 49 in case series (8).

Table 3: Laboratory data – saline infusion test – serum Aldosterone levels after infusing 0.9% NaCl

Serum aldosterone (ng/dl)	Reference value	Patient's value
1st hour	Expected fall in normal population <	21.89
2nd hour	5	20.09
	Suggestive of primary hyperaldosretonism >10	
3rd hour		20.84
4th hour		10.79

Table 4: Laboratory data –Adrenal venous sampling

	Left adrenal vein	Right adrenal vein	IVC
Cortisol (nmol/L)	>1700	>1700	364
Aldosterone (ng/dL)	292.4	22.6	17.3
Aldosterone to cortisol ratio	0.17	0.013	21.01

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It is reported more frequently in East Asians (8).

Commonest causes of primary hyperaldosteronism are aldosterone producing adenomas and idiopathic hyperaldosteronism. Unilateral adrenal hyperplasia and adrenal carcinoma are not commonly seen. Inherited causes of primary hyperaldosteronism such as familial hyperaldosteronism account for less than 1% of all causes (6). Aldosterone to renin ratio is used to detect cases of suspected primary hyperaldosteronism. Several confirmatory tests such as oral sodium loading test, saline infusion test and furosemide upright test are used with varying sensitivity and specificity for diagnosis(7). The diagnosis was confirmed in our patient by saline infusion test as described above.

Adrenal venous sampling performed by an experienced interventional radiologist, isolates unilateral cases of hyperaldosteronism(4).CT imaging is helpful in detecting adrenal space occupying lesions, especially in patients with other co morbidities, as it is a noninvasive procedure. Despite of its usefulness in diagnosis, it carries significant false positive and false negative rates. Idiopathic adrenal hyperplasia can be falsely interpreted as normal in CT. Also, non-functioning adrenal macro adenomas are common in the elderly, and can be misinterpreted as functioning tumours(7).

Surgical treatment is the treatment of choice for patient with unilateral adrenal hyperplasia, which cures the disease.

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