Case Report

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Case report on Southeast Asian ovalocytosis: A patient with type 1 renal tubular acidosis and an asymptomatic patient incidentally found

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Abstract

Two male patients were found to have Southeast Asian ovalocytosis - one incidentally and the other one during the investigations of the aetiology for hypokalemic paralysis. Southeast Asian ovalocytosis is found almost exclusively in Southeast Asia (1, 2). Familial renal tubular acidosis can co-exist with south East Asian ovalocytosis in the same patient (2). Anion-exchanger 1 gene AE1 mutation is the underlying pathology and both can originate from the same mutation (2). This can be asymptomatic as in case 1 and can be symptomatic as in case 2. Symptomatic patients need oral potassium and bicarbonate replacement and follow up. After initial clinical assessment and investigations of case 2, he was given intravenous potassium replacement. The correction of metabolic acidosis was made by giving oral sodium bicarbonate 600mg twice daily. Eventually he made full recovery and did not develop further similar episodes.

Key words

Southeast Asian ovalocytosis, Type 1 renal tubular acidosis

Introduction

Southeast Asian ovalocytosis is found almost exclusively in south East Asia (1, 2). Familial renal tubular acidosis can co-exist with Southeast Asian ovalocytosis in the same patient (2). Anion-exchanger 1 gene AE1 mutation is the underlying pathology and both can originate from the same mutation (2). This gene codes for band3, the bicarbonate chloride exchanger which is located in the red cell membrane and alpha intercalated cells in the basolateral membrane of collecting ducts of the kidneys (2). This mutation results in decreased anion transport and manifests with hypokalemic paralysis (4). The combination of Southeast Asian ovalocytosis and distal RTA will occur in individuals who has heterozygous mutations to both of band 3 gene (1).

The clinical syndrome of distal renal tubular acidosis consists of hypokalemia, non-anion gap hyperchloremic metabolic acidosis, inability to lower the urine pH below 5.5 despite ~~of~~ systemic acidosis and also medullary nephrocalcinosis (6). Distal renal tubular acidosis (dRTA) can be primary or secondary. Secondary dRTA can be associated with autoimmune diseases such as primary Sjogren's syndrome and systemic lupus erythematosis and calcium metabolism abnormalities (8, 9). Among RTA syndromes, distal RTA is the most common and manifests due to inability in acidifying urine by the distal part of the nephrons especially collecting tubules and ducts in the presence of normal glomerular filtration rate (9).

Case Presentation

Case1: 18-year-old previously well patient presented with generalized itching and urticaria with background history of multiple allergies to foods and drugs. He complained on and off faintishness and no other significant anemic symptoms. His systemic review was unremarkable. His systemic and general examination was

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unremarkable and no abnormal clinical signs found. His full blood count revealed mild anaemia with haemoglobin 11g/dL,Wbc 8000/uL and platelets 230000/uL with normal differential counts normal red cell indices. We proceeded with blood picture due to mild anaemia and in blood picture; many ovalocytes, numerous stomatocytes and oval cells with transverse banding and irregular haemoglobinisation were seen with normal white cells and platelets and commented as appearances compatible with Southeast Asian ovalocytosis and suggested serum electrolytes, renal function test, liver function test and family screening. His renal and liver functions were within the normal limit and reticount and LDH were normal. His ultra sound KUB was normal. His serum sodium was 138meq/L and serum potassium was 4.1meq/L. His arterial blood gas analysis was normal and during family screening the mother was found to have similar red cell changes. He was diagnosed to have Southeast Asian ovalocytosis and clinically asymptomatic- without haemolysis or acidosis.

Case2: A 40-year-old previously well patient was admitted with sudden onset generalized weakness including all four limbs and fatigability for two days duration. The weakness was prominent in lower limbs than the upper limbs and the proximal part of the lower limbs were affected more than the distal part. He did not develop swallowing difficulty or slurring of speech during his hospital stay. His past medical history and family history were unremarkable. He does not have any features of autoimmune disease and diurnal variation of weakness.

Neurological examination revealed lower limb power was graded as one out of five and upper limb power was two out of five and he had proximal muscle weakness more prominent than distal muscle weakness. His neck muscle power was two out of five. His reflexes were present but diminished comparatively more so in the lower limbs than the upper limbs and plantars were down going bilaterally. He did not have sensory impairment. Coordination could not be assessed due to significant weakness of the limbs. All components of his speech was normal and cognition also normal. The swallowing assessment was normal. His general and systemic examinations were otherwise unremarkable.

His serum potassium on admission was 1.8 mmol/l and he had hypokalemic ECG changes with prominent u waves. His full blood count revealed white blood count of 10,000/uL with normal differential cell count. His haemoglobin was 13g/dL MCV was 82fL.MCH was 32.1pg and MCHC was 35 g/dL. Platelets were 300,000/uL. His capillary blood sugar was 129mg/dl on admission and he has normal HbA1C value.

His arterial blood gas analysis revealed normal anion gap metabolic acidosis. PH was 7.31 and PCO_2 was 35.4 mmhg, PO_2 95mmhg, HCO^{3-} was 19meq/L and base excess was -3.4. His serum osmolality was 284mosm/kg and urine osmolality was 265mosm/kg. His serum sodium was 137mmol/L and chloride was 107mmol/L. His calculated anion gap was 12.8. His urinary PH was 8.28, 7.22 and 7.89 on repeated occasions. Despite normal serum sodium levels his urinary sodium levels in random samples were more than 20 meq/L on all three occasions above and his urinary potassium was 23meq/l despite hypokalemia. His serum creatinine was 104 μmol/L.

His liver biochemistry and liver function tests were normal. ESR was 16mm in 1st hour and C reactive protein was not elevated. His urine full report was normal and did not suggest microscopic haematuria.

He had negative ANA and rheumatoid factors. His ultra sound scan abdomen and KUB were normal and did not reveal any possible nephro calcinosis or renal calculi. His x-ray KUB was normal. He had slightly increased urinary calcium creatinine ratio. Urinary calcium was 8.8mg/dl and urine creatinine was 42.38mg/dl with urine calcium creatinine ratio of 0.2g calcium/g creatinine. He had normal serum protein electrophoresis. His blood picture revealed red cell morphology with many ovalocytes, irregular haemoglobinisation and transverse ridges. Polychromatic cells were not increased and revealed normal white blood cells and platelets. Final comment on the blood picture suggested south East Asian ovalocytosis as the possible cause of the clinical scenario. (figure: 1)

After initial clinical assessment and investigations he was diagnosed as hypokalaemic paralysis and immediately serum potassium was intravenously replaced with 20mmol potassium slow infusion over four hours. He had improvement following replacement and on day 3 of admission he had normal power and no residual weakness. The correction of metabolic acidosis by oral sodium bicarbonate was made by giving 600mg twice daily. Eventually he made full recovery and did not develop further similar episodes. He was arranged with monthly medical clinic follow up with regular serum electrolyte monitoring.

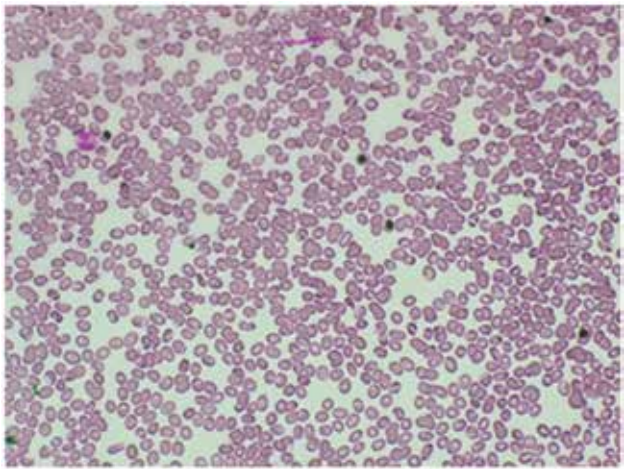

Figure1: Patient's blood film (case2): Polychromatic cells are not increased and revealed normal white blood cells and platelets. Blood picture finally commented as red cell morphology is in keeping with south East Asian ovalocytosis

Discussion

Hypokalaemia is defined as serum potassium levels less than 3.5mmol/L and if potassium is less than 2.5mmol/L it is referred to as severe hypokalaemia (7). The most common serum electrolyte abnormality in distal RTA is hypokalaemia and the symptoms depend on the severity of this electrolyte imbalance (8). Renal based acid base balance is a complex process achieved by bicarbonate reabsorption and hydrogen ion secretion (9).

Presence of recurrent nephrolithiasis, chronic metabolic acidosis, persistently elevated urine pH more than 5.5 and hypercalciuria are suggestive of the presence of distal RTA even though the confirmatory test will be urinary acidification test with either ammonium chloride or furosemide fludrocortisone combination (9). We didn't perform the confirmatory test as it is not available in our setup and currently an outdated practice. But our patient has urinary pH repeatedly more than seven with normal urine sodium excretion despite the presence of normal anion gap systemic metabolic acidosis and evidence of hypercalciuria and hypokalaemia with one episode of hypokalaemic quadriparesis suggested the presence of distal renal tubular acidosis. He did not reveal any features suggestive of endocrine disorders such as primary hyperparathyroidism, or hyperthyroidism. He is clinically unlikely to have any possible autoimmune conditions and his anti-nuclear antibody and rheumatoid factor came as negative. Hence his dRTA is unlikely to be positive due to secondary auto immune aetiology.

Generally metabolic acidosis will lead to hyperkalaemia because hydrogen ions will be exchanged with intracellular potassium and here due to the failure of proton secretion potassium wasting in urine will be high and can end up in hypokalaemia with sometimes paralysis of all four limbs and even respiratory arrest in rare circumstances (9). Symptomatic hypokalemia is not uncommon in distal RTA and our patient also presented with hypokalaemic quadriparesis.

The main goal of treatment is reversal of acidosis which will in turn correct the calciuria, reduced tendency of nephrocalcinosis and electrolyte imbalance (9). Potassium citrate is the drug of choice which can provide both potassium replacement and bicarbonate at the same time (9). We treated him with sodium bicarbonate and potassium chloride oral replacement as potassium citrate is not available in our sector and patient couldn't afford private sector purchase.

Nephrolithiasis occurs only in distal renal tubular acidosis in which hydrogen iron gradient generation and maintenance will be abnormal along distal renal tubules (3). The most common consequence of distal RTA is nephrolithiasis (9). Even though our patient had evidence of hypercalciuria, he didn't develop clinically and radiologically proven nephrolithiasis or nephrocalcinosis. Alkalai therapy is increasing the citrate excretion and hence reducing the tendency of nephrocalcinosis in both

complete and incomplete renal tubular acidosis (3). Primary hyperparathyroididm can cause hypercalciuria, nephrolithiasis and distal renal tubular acidosis with medullary nephrocalcinosis (5).

Southeast Asian ovalocytosis and distal renal tubular acidosis are carrying a common genetic aetio pathology which is anion exchanger 1 gene mutation at band 3 which is coding for bicarbonate chloride exchanger which transporter is common for red cell membrane and alpha intercalated cells in the basolateral membrane of renal collecting ducts(2). In the case of our patient's presentation this might be the most probable underlying aetiology and often this is associated with a familial RTA. We have done family screening for the presence of Southeast Asian ovalocytosis and his elder brother was found to have the same red cell abnormalities.

Southeast Asian ovalocytosis patients will have minimal haemolytic anaemia and they will be asymptomatic in their adult life and found to have resistance to malaria including Plasmodium vivax and Plasmodium falciparum as well (10). Sometimes recurrent hemolytic anaemia and pigmented gall stone disease were reported in adult life. In our patient's blood film there is no evidence of haemolysis and no increased polychromatic cells identified. He did not have symptoms of anaemia in the past as well. The management of this patient was mainly targeted towards type1 renal tubular acidosis rather than ovalocytosis as it is asymptomatic.

The prognosis of type1 renal tubular acidosis mainly depends on the underlying aetiology and in the case of Southeast Asian ovalocytosis it is generally good with proper management and follow up.

Consent

Written informed consent was obtained from the patients for publication of this article.

References

1. JP Vithanage **and** M Ekanayake, A case of distal renal tubular acidosis, Southeast Asian ovalocytosis and possible fluorosis. Ceylon Medical Journal Vol.54 (1) 2009 p.19-20

2. Wrong O, Bruce LJ, Unwin RJ, Toye AM, Tanner MJA. Band 3 mutations, distal renal tubular acidosis, and Southeast Asian ovalocytosis. Kidney International 2002; 62:10-9

3. Buckalew VM. Nephrolithiasis in renal tubular acidosis. The Journal of Urology 1989; 141: 731-7.

4. Kaitwatcharachai, C., Vasuvattakul, S., Yentchitsomanus, P. et al. Distal renal tubular acidosis and high urine carbon dioxide tension in a patient with southeast Asian ovalocytosis. Am J Kidney Dis. 1999; 33: 1147–1152

5. Tom Edward Ngo Lo *and* Iris Thiele Isip Tan, Distal renal tubular acidosis in primary hyperparathyroidism. BMJ Case Rep. 2015; 2015: bcr2014208120.

6. L Naveen, Santoshi Malkarnekar, Adult-Onset Distal Renal Tubular Acidosis with Hypokalemic Quadriparesis in a Patient with Autoimmune Hypothyroidism. Journal of integrate nephrology and andrology.2014,Volume *: 1,*Issue *: 2,*Page *: 82-84*

7. Singer GG, Brenner BM. Fluid and electrolyte disturbances. In: Braunwald E, Fauci AS, Kasper DL, et al, eds. Harrison's principles of internal medicine. 19th ed.

8. Mehmet Celik et al; Patient with Type 1 Distal Renal Tubular Acidosis Secondary to Sjogren's syndrome Presented with Hypokalemic Paralysis. Journal of Medical Cases. Volume 6, Number 6, June 2015, pages 268-270

9. Tim Both, Robert Zietse, Ewout J. Hoorn, P. Martin van Hagen, Virgil A. S. H. Dalm, Jan A. M. van Laar, andPaul L. A. van Daele, Everything you need to know about distal renal tubular acidosis in autoimmune disease. Rheumatology Int. 2014; 34(8): 1037–1045.