Acute confusion and ataxia in the emergency department with an unexpected underlying diagnosis

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A 54 year old man presented to the Emergency Department with a one day history of confusion and unsteadiness. He had been unwell in the week preceding this presentation with nausea, poor appetite and vomiting.

He had been diagnosed with hypertension as a teenager. He took anti-hypertensives intermittently and had not taken them for more than 6 months preceding this presentation. He had otherwise been well with no admissions and little contact with medical services. He had no history of smoking, alcohol or illicit drug use. He had no other drug prescriptions besides Propranolol 40mg twice daily and Hydrochlorthiazide 25mg daily. He had no history of taking herbal medication. There was no family history of hypertension. Amongst his 3 siblings and parents, there was no history of sudden death or unexplained ill health at a young age.

On examination he had conjunctival pallor, was drowsy with a Glasgow Coma Score of 14/15 (E-4, M-6, V-4). He was noted to have "half and half nails". His vital signs were: blood pressure 162/88mmHg, pulse rate 124 beats/min, respiratory rate 21 breaths/min and temperature 36.4 °C. The cardiovascular and respiratory examinations were normal. Abdominal examination revealed a palpable bladder up to the level of the umbilicus. He had no neck stiffness, the cranial and peripheral nerves examination was normal. A random blood glucose carried out in the emergency department was 146mg/dl and his oxygen saturations were normal. A bladder catheter was inserted.

Questions

1. What is the likely cause of this man's confusional state?

2. What differential diagnoses should be considered for the underlying cause?

3. What urgent investigations should be carried out?

Answers

1. The most likely cause of this presentation is a metabolic encephalopathy. He does not have features of acute or chronic liver disease making hepatic encephalopathy unlikely. His blood glucose is normal and there are no pointers towards pulmonary disease. An infective etiology is unlikely as he is afebrile, has no neck stiffness and no focal neurological signs. However, infection cannot be completely ruled out at this stage. There is no history to suggest intoxication or poisoning. The symptoms of nausea and vomiting, plus the finding of clinical anaemia and "half and half" nails make uraemic encephalopathy most likely.

2. The differential diagnosis of kidney failure in this patient needs to include renal and post-renal causes. The finding of probable anaemia makes chronic or "acute on chronic" kidney failure most likely. He has chronic poorly controlled hypertension and hypertensive kidney disease is a possibility. The history of onset of hypertension at a young age is unusual and raises the possibility of a secondary cause of hypertension. This may suggest that he has long standing kidney disease. Chronic renal conditions with onset in teenage years and slow progression include renal hypoplasia/dysplasia, glomerulonephritis and reflux nephropathy.The most likely cause of acute kidney injury in this man is obstructive uropathy. He has a palpable bladder and is in the age group where urinary outflow obstruction due to prostate pathology is common. Other causes of chronic kidney disease that can present at this age include diabetic nephropathy, chronic use of nephrotoxic drugs and multisystem diseases (myeloma, vasculitis).

3.Urgent investigations must include measurement of urea, creatinine and electrolytes, urine dipstick and microscopy, full blood count (FBC), liver function tests, HIV testing and a renal ultrasound. Blood cultures and a lumbar puncture for cerebrospinal fluid analysis should also be done to rule out infective causes of confusion. If these tests are unremarkable brain imaging should be considered.

The creatinine was 18.3mg/dL (Normal range 0.7 – 1.2mg/dL), potassium 8.3mmol/L (3.5 -5 mmol/L), sodium 136mmol/L (135 – 145 mmol/L) and chloride 103mmol/L (98 – 107mmol/L). The haemoglobin concentration was 7.3g/dL, mean cell volume (MCV) 74 fL, white blood cells (WBC) 7.6×106/μL and platelets 277×106/μL. A urine dipstick from a catheter sample showed protein + and blood +++.

The serum albumin was 3.0mg/dL and the rest of the liver function tests were normal. The HIV test was negative. Cerebrospinal fluid analysis revealed no WBC, 190 red cells/hpf (the lumbar puncture was traumatic), normal glucose and protein, India Ink stain negative and no growth on culture. Magnetic resonance imaging of the brain was normal.

An urgent abdominal ultrasound scan carried out before catheterization showed a grossly distended bladder but with normal bladder wall thickness, suggesting acute urine retention and a normal prostate. Both kidneys were enlarged with multiple bilateral kidney cysts. There was no hydronephrosis . There were no cysts in the liver.

Final diagnosis: Acute on chronic kidney injury due to urinary retention on a background of chronic kidney disease secondary to adult polycystic kidney disease.

Further Progress

Hyperkalaemia of this magnitude is a medical emergency. He was immediately treated with intravenous calcium gluconate and intravenous insulin and dextrose. The hyperkalemia did not respond to initial management and he was subsequently referred for urgent haemodialysis for refractory hyperkalaemia and suspected uraemic encephalopathy.

After 3 haemodialysis treatments via a temporary dialysis

catheter in the right femoral vein, the encephalopathy resolved and the creatinine and potassium levels fell (see table 1). He maintained a good urinary output throughout the course of admission (40 – 60cc/hr) after bladder catheterisation.

The patient was discharged and followed as an outpatient. Over the next 2 months, his renal function deteriorated and he became progressively uraemic. He was eventually started on regular twice weekly haemodialysis sessions via a semi permanent internal jugular haemodialysis catheter. Five months after the initiation of dialysis, the patient had an episode of fever and massive hemoptysis for which the underlying cause was not clear. Despite aggressive resuscitation, intubation and admission to the intensive care unit, he died in August 2012.

Discussion

Acute Confusion and Uraemic Encephalopathy

In both acute and chronic kidney disease, encephalopathy may result from uraemia and drug toxicities. The severity and progression of uraemic encephalopathy depends on the rate of decline of kidney function and not necessarily on the absolute creatinine or blood urea nitrogen levels. Symptoms are usually reversible with dialysis.

The mechanism of uraemic encephalopathy is multifactorial and is thought to result from hormonal imbalances, the accumulation of uraemic toxins and oxidative stress[2].

Acute presentations of autosomal dominant polycystic kidney disease to the emergency department are rare but have been described with features such as vomiting, abdominal pain and kidney failure[3].

Autosomal Dominant Polycystic Kidney Disease

Background

Autosomal dominant polycystic kidney disease (ADPKD) is an inherited disorder that affects all races equally with an estimated worldwide prevalence of 1 in 800 live births[3]. The responsible genes lie on chromosome 16 (PKD1 gene) accounting for 85% of ADPKD cases and chromosome 4 (PKD2 gene) accounting for 15% of ADPKD cases[4].

Offspring of affected parents have 50% risk of inheritance each but in up to a fourth of newly diagnosed cases, patients report no familial history of the disease suggesting that many cases go undetected[5] or that spontaneous mutations may occur.

Presentation

Kidney manifestations include enlarged kidneys with fluid filled cysts, haematuria, proteinuria, nephrolithiasis and flank pain. Kidney failure characteristically appears in between the fourth and sixth decades of life[4]

Cysts can occur anywhere along the nephron and are thought to result from an imbalance between cellular proliferation and apoptosis[2]. Cysts can rupture spontaneously or secondary to trauma into the kidney tubules causing hematuria. They may also become secondarily infected[7]. ADPKD is also associated with high circulating vasopressin levels and vasopressin resistance.

Hypertension occurs in 60% of ADPKD patients before any significant glomerular filtration rate (GFR) decline and results from activation of a local intra-kidney renin angiotensin aldosterone system as a result of ischaemia from expanding kidney cysts[4,6].

Cysts can also occur in the liver (60% of APKD patients), seminal vesicles, pancreas and arachnoid membrane[3,4]. Hepatic cysts are more common in women but are not known to cause liver failure.

Other extra-renal manifestations include intracranial aneurysms, mitral valve prolapse and diverticulosis. The risk of aneurysm rupture increases with a prior or family history of ruptured aneurysm[4,5].

Diagnosis

Kidney sonography is most commonly used to diagnose ADPKD. Diagnostic criteria include at least two unilateral or bilateral cysts in individuals younger than 30 years; two cysts in each kidney in individuals 30–59 years; and four cysts in each kidney in individuals 60 years or older3. CT Scan and MRI may also be used. The use of genetic testing is limited by hundreds of intragenic PKD1 and PKD2 mutations.

Differential Diagnosis

Other polycystic kidney disorders include inherited conditions such as familial nephronophthosis and medullary cystic kidneys both of which are characterized by bilateral small kidneys, salt wasting and polyuria. Autosomal recessive polycystic kidney disease is much rarer than ADPKD and often causes fetal and neonatal deaths due to tremendous bilateral kidney enlargement, impaired lung function and pulmonary hypoplasia[3]. Acquired cysts may develop as a result of aging and dialysis.

Management

Antihypertensives are recommended for adults with hypertension with target BP 130/80mmHg particularly with angiotensin converting enzyme inhibitors or angiotensin receptor blockers which have been shown to preserve kidney function in APKD[7]. More recently, a study on vasopressor receptor antagonist drugs demonstrated reduction in the decline of kidney function and slowed progression of total kidney volume when tolvaptan was compared to placebo in APKD patients[9].

Infected kidney or hepatic cysts may require prolonged antibiotic therapy or drainage. Haematuria is often managed conservatively with hydration and bed rest. Flank pain is managed with analgesics avoiding nephrotoxic agents[5].

ADPKD patients progressing to end-stage kidney disease require renal replacement therapy which includes dialysis and kidney transplantation. Transplantation, when possible, is the treatment of choice[4].

The above case illustrates an unusual presentation of confusion with an unexpected underlying diagnosis. Kidney disease should be considered as a metabolic cause of acute confusion and renal function tests should be obtained in all such cases.

References

1. Chalela JA et al. Acute Toxic Metabolic Encephalopathy in Adults. UpToDate, September 2010

2. Scaini G, Kozuchovski G, Streck EL. Mechanisms underlying uremic encephalopathy. Rev Bras TerIntensiva. 2010; 22(2):206-211

3. Silman, Eric F MD; Chakravarthy, Bharath MD, MPH; Vaca, Federico E MD, MPH; &Langdorf, Mark I MD, MHPE. (2009). Polycystic Kidney Disease with Kidney Failure Presenting as Incarcerated Inguinal Hernia in the ED. Western Journal of Emergency Medicine, 10(1).

4. Wilson PD. Polycystic Kidney Disease. N Engl J Med 2004;350:151-64

5. Torres VE, Harris PC, Pirson Y. Autosomal dominant polycystic kidney disease. Lancet 2007; 369: 1287–301
6. Grantham JJ. Autosomal Dominant Polycystic Kidney Disease. N Engl J Med 2008;359:1477-85
7. Elhassan E, Masoumi A, Schrier RW.Progress on Autosomal Dominant Polycystic Kidney Disease. Arab Journal of Nephrology and Transplantation. 2009 May;2(2):27-44
8. Torres VE et al. Tolvaptan in Patients with Autosomal Dominant Polycystic Kidney Disease. N Engl J Med 2012;367:2407-18.

Table 1: Serial Electrolytes Pre- and Post-hemodialysis

Date	20/3/12 (admission)	28/3/12 (after 2nd dialysis session)	31/3/12 (after 3rd dialysis session)	3/4/12 (on discharge)
Creatinine (mg/dL)*	18.39	9.43		13.6
Potassium (mmol/L)	8.3	4	3.6	5.0
Sodium (mmol/L)	137	137	142	137
Chloride (mmol/L)	103	104	104	97
Urea (mg/dL)		118		99
Phosphate (mmol/L)				0.87
Bicarbonate (mmol/L)				21
Calcium (corrected) (mmol/L)				1.48

**normal values for Creatinine (0.7 – 1.2mg/dL), Potassium (3.5 -5 mmol/L), Sodium(135 – 145 mmol/L) and Chloride (98 – 107mmol/L), Urea (8 – 25mg/dL), Phosphate: (0.81 – 1.45 mmol/L), (Bicarbonate (22-31mmol/L), Calcium (2.1 -2.5)*