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Pentavaccine Induced Acute Kidney Injury in a Resource Poor Setting - A Case Report

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ABSTRACT

Background: Vaccination is a cost-effective way of preventing disease and promoting health. Most vaccines have little or no side effects. Although most vaccine adverse events are self-limiting and non-life threatening, some may be severe with long term health implications. Massive proteinuria with Nephrotic syndrome (NS) and severe Acute kidney injury (AKI) secondary to acute interstitial nephritis and membranous nephropathy have been reported rarely following the 2009 H1N1 infuenza vaccine. There has been no reported case of massive proteinuria with severe AKI following Pentavalent vaccination in Nigerian children.
Case summary: We report a previously healthy two months old female who developed sudden onset generalized urticarial rash, acute pulmonary oedema, anuria, proteinuria (++), haematuria(+) and severe AKI (serum creatinine- 140umol/L, urea- 7.3umol/L, potassium-4.5umol/L; following vaccination with pentavalent vaccine. Symptoms resolved following fluid management and diuretics. A month later, she had another episode of AKI with massive proteinuria within 24 hours of a 2nd dose of Pentavalent vaccine. She also responded well to conservative management and has remained stable post discharge. She is still being followed up. It is possible that some cases of NS with AKI and glomerulonephritis may be secondary to hitherto unrecognized underlying pathology such as Vaccine induced membranous nephropathy (VIMN).
Conclusion: Thus, vaccine induced AKI should be suspected in children who develop sudden-onset AKI following immunization particularly in resource-poor centers where biopsy and electron microscopy are not readily available,

Key words: *Penta vaccine, Membranous nephropathy, Vaccination*

INTRODUCTION

Vaccination is one of the most cost-effective ways of preventing disease and promoting health[1]. Evidences for the huge benefits of vaccination include the eradication of small pox, the marked reduction in childhood mortality and morbidity due to vaccine preventable diseases such as measles, pertussis, tetanus, diphtheria, chickenpox, *Haemophilus influenza* meningitis and pneumonia, Rota virus etc. Majority of vaccines are safe with little or no known side effects. Most side effects are self-limiting and non-life threatening. However, some adverse events following vaccinations may be severe and life threatening with long term health implications[2]. Severe vaccine associated adverse events affects mostly the immune system (anaphylaxis), the central nervous system (seizures) the digestive system (vomiting, diarrhea, hepatitis). Massive proteinuria with NS and severe AKI soon after receiving the 2009 H1N1 influenza vaccine has been reported in adults in which Kidney biopsy showed membranous nephropathy (MN) and acute

interstitial nephritis (AIN)[5]. Acute kidney injury following pentavalent (DPT, PERTUSIS, TETANUS, HBV and HIB) vaccine has rarely been reported. Long-term prognosis is guarded because approximately 50% of patients may have evidence of progressive kidney disease.[6] In resource-poor settings such as ours where biopsy and electron microscopy are not readily available, suggestive clinical features shortly within 24-72 hours of vaccination, combined with heavy proteinuria (+++) and deranged kidney function should alert clinicians of a possible vaccine mediated kidney injury

CASE SUMMARY

AC was a previously healthy 5kg two months old baby with a history of sudden onset of generalized urticarial rash for 5 days, generalized body swelling for 3 days, reduced urine output for 1 day, fast/laboured breathing 12 hours prior to presentation. There was no preceding history of fever, diarrhoeal illness, use of nephrotoxic agents nor envenomation. She had received the first dose of Pentavalent vaccine a day prior to onset of symptoms. She had no previous hospitalization nor underlying medical conditions. Genotype was unknown. Pregnancy, delivery and neonatal history were essentially normal. There was no family history of kidney diseases. At presentation, she was ill looking, pale, in respiratory distress with intercostal and sub-costal recessions, tachypnoeic with respiratory rate of 80 cycles per minute and mildly cyanosed (SpO2 - 86%). She had generalized oedema. Pulse was full volume, regular and synchronous, blood pressure was 60/30mmHg, Apex beat was not displaced, she had normal heart sounds. She was conscious but lethargic, with mild hypotonia. Other CNS (Central nervous system) signs were normal. Abdomen was full with mild ascites evidenced by shifting dullness. Her urine output was 0.3mls/kg/hour. Initial investigations revealed: Urinalysis - proteinuria +, haematuria +, Specific gravity 10.25. (other parameters were normal - nitrite negative, leucocyte - negative), CRP was elevated 33mg/dl. Blood film for malaria parasite showed scanty trophozoites of P. falciparum. EUCr (serum electrolytes, urea and creatinine) - serum creatinine-140umol/L, urea- 7.3mmol/L, potassium($K+$)- 4.5 mmol/L, Sodium(Na^+)-132 mmol/L, Chloride(Cl^-)- 99 mmol/L, Bicarbonate (HCO_3^-)20 mmol/L. Full blood count showed moderate anaemia (PCV - 28 %). Total white cell count/ differentials were unremarkable. Chest x-ray showed features of pulmonary oedema. Abdominal/pelvic ultrasound scan showed mild ascites, bilateral renal parenchymal echogenicity. There were no features of obstructive lesions of the urinary tract.

A working diagnosis of 'Acute kidney injury with pulmonary oedema? cause? acute malaria, to rule out sepsis' was made. Blood culture and urine cultures yielded no bacterial growth. She received appropriate fluid management, intravenous antibiotics, antimalarial and oral haematinics. Repeat EUCr and urinalysis 3 days later showed normalization of laboratory parameters. Her urine output had increased to 1.2mls/kg/hour. She was discharged home in stable condition after 1 week on admission. A month later, she was re-admitted on account of generalized urticarial rash, poor suck, body swelling, reduced urine output, and worsening respiratory distress within 24 hours of a 2nd dose of Pentavalent vaccine. There was no history of diarrhoea, vomiting or cough. On examination, she was febrile, (temp - 38^{0}C) lethargic, very pale, cyanosed (SpO2-80%), facial puffiness, non-pitting leg oedema, and in respiratory distress with signs of heart failure. Her weight was 6.2kg. Her blood pressure was 70/40mmHg. She had an episode of seizure at presentation aborted by parenteral diazepam. An initial diagnosis of "Recurrent AKI secondary to vaccine associated adverse event" was made. Her urine output 0.4ml/kg/min. Serial EUCr showed worsening azotaemia: Urea - 6.2mmol/L, Creatinine -105 umol/L, K^+-

5.5mmol/L, Na^+-130 mmol/L, HCO_3^- 20-mmol/L, Cl^- -98 mmol/L); Urinalysis showed proteinuria^{+++}, Urine protein/ creatinine ratio was - 2.5. Serum protein: total (55 g/L) and albumin (35g/L) were at the lower limit of normal. Serum cholesterol level was within normal range. FBC was essentially normal. Urine and blood culture yielded no bacterial growth. CRP was raised (35mg/dl). She was commenced on conservative management. Due to a low hematocrit, she was transfused with sedimented red blood cells twice under lasix cover. Her clinical condition improved steadily with urine output increased to 2ml/kg/hr by the 8th day of admission, resolution of heart failure, fever and improvement in appetite. Pre-discharge urinalysis and EUCr showed (Proteinuria trace for 3 consecutive days, creatinine–54umol/L, urea - 2.8mmol/L, K^+ - 3.7mmol/l, Na^+ - 140mmol/l, Cl^- - 104mmol/L, HCO_3^- -24mmol/L). She was discharged after 2 weeks on admission. She is still on follow up and has remained stable. Parents declined the 3rd dose of Pentavalent Vaccine.

DISCUSSION

Vaccination is one of the most cost-effective ways of preventing disease and promoting health[1]. Evidence for the huge benefits of vaccination include the eradication of small pox, the marked reduction in childhood mortality and morbidity due to vaccine preventable diseases such as measles, pertussis, tetanus, diphtheria, chickenpox, Hemophilus influenza meningitis and pneumonia, Rota virus etc. Majority of vaccines are safe with little or no known side effects.[1,2] Most side effects are self-limiting and non-life threatening. However, some adverse events following vaccinations may be severe and life threatening with long term health implications[2]. Severe vaccine associated adverse events affects mostly the immune system (anaphylaxis), the central nervous system (seizures) the Digestive (vomiting, diarrhea, hepatitis). The presence of urticarial rash, fever, anuria, anorexia and seizures in our patient points to affectation of these target organ systems. Massive proteinuria with NS and severe AKI soon after receiving the 2009 H1N1 influenza vaccine has been reported in adults in which Kidney biopsy showed membranous nephropathy (MN) and acute interstitial nephritis (AIN)[5]. More recently, Luo et al reported AKI occurring after COVID-19 vaccines more common in those with co-morbidities an in the elderly.[7] Acute kidney injury following pentavalent (DPT, PERTUSIS, TETANUS, HBV and HIB) vaccine has rarely been reported. Our patient had nephrotic range proteinuria. Most cases of nephrotic syndrome in children are classified as idiopathic. Kidney biopsy was not done due to lack of expertise and equipment for immunofluorescence assay and electron microscopy. It is possible that some cases of idiopathic glomerulopathy including idiopathic nephrotic syndrome may be secondary to hitherto unrecognized underlying pathology such as vaccine induced membranous nephropathy (VIMN). VIMN is a rare but serious glomerulopathy in paediatrics. Long-term prognosis is guarded because approximately 50% of patients may have evidence of progressive kidney disease.[6] In our patient, reduced urinary output, simple urinalysis showing massive proteinuria (+++) and rising creatinine was sufficient in identifying kidney injury. It remains speculative which of the 5 components of the pentavalent vaccine could be the culprit.

Vaccine related adverse events reporting is a useful way of monitoring vaccine safety and which helps to strengthen vaccine uptake[4.] The timing of onset of symptoms such as urticarial rash, fever, anuria and body swelling and laboratory evidence of deranged kidney function tests and heavy proteinuria following vaccination, are suggestive of immune mediated AKI should raise concern about possible vaccine-induced AKI from VMN. VIMN should be suspected in children who develop sudden-onset AKI following immunization; as it

was with our patient following the 2 doses of Pentavaccine she received.

CONCLUSION

Repeated episodes of generalized urticarial rash, fever, body swelling and anuria with deranged kidney function and nephrotic range proteinuria shortly after vaccination with pentavalent vaccines points to a possible immune mediated vaccine induced kidney injury. It is possible that some cases of glomerulonephritis and nephrotic syndrome with AKI may be secondary to hitherto unrecognized underlying pathology such as vaccine induced membranous nephropathy (VIMN). In resource-poor centers where biopsy and electron microscopy are not readily available, vaccine induced AKI should be suspected in children who develop sudden-onset AKI following immunization. Prompt diagnosis and appropriate management are necessary for a favourable outcome.

Declaration by Authors

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