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Case Series

Acute Kidney Injury Due to Cholera: A Case Series

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Abstract:

Worldwide, an estimated 1.3 to 4 million people are affected by cholera every year. Cholera is an acute infectious disease caused by ingestion of food and water contaminated by Vibrio cholerae. The clinical course of cholera varies from mild diarrhea to severe complications such as hypokalemia, hyponatremia or hypernatremia, metabolic acidosis, and acute kidney injury. The disease can be fatal if timely treatment is not initiated. We discuss here, two cases who presented to our tertiary care hospital with history of pain abdomen and multiple episodes of watery diarrhea. Both cases later developed acute renal failure secondary to severe gastroenteritis. The aetiology of the gastroenteritis was later confirmed to be cholera. Both cases presented with history of profuse watery diarrhoea with vomiting, on admission signs of volume depletion in the form of sunken eyes, reduced skin turgor and capillary filling time > 3 seconds were observed in both the cases. There was history of consumption of sea food from the local street vendor, but no history of movement outside the place of residence within last one week prior to onset of symptoms. Laboratory investigations revealed raised haemoglobin, PCV, raised blood urea and serum creatinine, hyperkalaemia; and anion gap. Despite aggressive rehydration, both the cases developed acute kidney injury. Renal ischemia secondary to dehydration leading to acute tubular necrosis may have caused the acute kidney injury with elevated urea/creatinine levels in our patients. Both our patients were successfully managed by intravenous infusion of fluids, electrolytes, sodium bicarbonate and appropriate antibiotics, followed by hemodialysis. Both the cases were discharged without any further complications as they showed signs of recovery of renal function.

Keywords: Cholera, Kidney, Gastroenteritis, Hypovolaemia.

Introduction

Worldwide, an estimated 1.3 to 4 million people are affected by cholera every year. Cholera is an acute infectious disease caused by ingestion of food and water contaminated by Vibrio cholerae. [1,2] The clinical course of cholera varies from mild diarrhea to severe complications such as hypokalemia, hyponatremia or hypernatremia, metabolic acidosis, and acute kidney injury. [3] Untreated electrolyte imbalance, metabolic acidosis, and acute kidney injury can prove to be fatal. [4] Prompt and aggressive prevention of these complications, entails administration of intravenous fluids. [5] Several researchers from across the world have contributed to literature highlighting acute kidney injury in cholera patients. [6,7] Acute gastroenteritis may lead to acute kidney injury via a prerenal mechanism of hypoperfusion. Acute kidney injury has multiple aetiopathogenic mechanisms; and is a multifactorial illness. [8] Vibrio cholera is a gram-negative bacterium, the toxin producing strains of which cause the acute secretory diarrhoeal illness named cholera. Resource-limited settings with inadequate access to clean water as in many countries in Africa and Asia favour endemicity of cholera. Profound fluid and electrolyte losses in the stool and vomitus, volume depletion and the rapid development of hypovolemic shock are the hallmark of severe cholera. Complications include acute renal failure, metabolic acidosis, circulatory failure, arrhythmias. The disease can be fatal if timely treatment is not initiated. [3] The genus Vibrio is a member of the family Vibrionaceae. Vibrio species are ubiquitously distributed in marine and estuarine environments all over the world. Of the 37 recognized species, only twelve species are potential human pathogens causing diarrhea, septicemia and extra intestinal infections, e.g. wound infections [3,9]. Vibrio species are facultative anaerobes, motile by a single polar flagellum, are oxidase positive; and do not produce gas from glucose. [3,10] Ingestion of water and

food contaminated with vibrio cholerae causes the diarrhoeal disease cholera. [3,11] Out of the over 200 recognized serogroups of V. cholerae, the most common serogroups are O1 and O139, which cause epidemic cholera. [3,12] We discuss here, two cases who presented to our tertiary care hospital with history of pain abdomen and multiple episodes of watery diarrhea. Both cases later developed acute renal failure secondary to severe gastroenteritis. The aetiology of the gastroenteritis was later confirmed to be cholera.

Case reports

Case 1: A 44 year old male resident of north central India presented to the emergency department of a large tertiary care hospital with approximately 20 episodes of severe watery diarrhea small bowel type of one day duration. It was associated with 08 episodes of non-bilious non-projectile vomiting. There was history of consumption of sea food from local food stall. There was no history of movement outside place of residence in last one week prior to onset of symptoms. On examination there were signs of volume depletion in the form of reduced skin turgor, feeble pulse and capillary filling time of >3 seconds. BP was 80/40 mmHg with postural drop of 20 mmHg. On abdomen examination there was no tenderness over the abdomen. Investigations revealed Hb: 15.2 gm/dl, PCV: 45, TLC: 15000/mm^3 with 90% Neutrophils. Routine biochemical investigations revealed urea 80 mg/dl, serum creatinine 4.2 mg/dl. Blood and urine culture were sterile, while stool RE revealed numerous pus cells. Arterial blood gas analysis revealed pH: 7.19, PCO_2: 25, HCO3: 11.8, PAO_2: 106, Na: 153 meq/l, K: 5 meq/l, lactate 4.2 mmol/L, Cl: 95.meq/l. This was suggestive of high anion gap metabolic acidosis and hyperkalemia. Patient was managed with aggressive hydration with half normal saline, Inj ceftriaxone 2 gm once a day and Inj Metronidazole 500 mg three times in a day. His course was complicated by ongoing diarrhea with a frequency of 10-12 episodes per day and abdominal cramps. Subsequent investigations revealed worsening of azotemia and acidosis.

The stool was subjected to Biofibre gastrointestinal panel (Film array multiplex PCR) assay which revealed vibrio cholera .Further microbiological investigations of stool revealed pale non-lactose fermenting colonies which on thiosulfate citrate bile salt sucrose agar was confirmed by their yellow appearance to be vibrio cholera.. The serology was determined by slide agglutination test which revealed cholera serogroup O1. Antibiogram revealed sensitivity to Inj ceftriaxone and doxycycline and resistant to aminoglycoside group of antibiotics. USG revealed normal sized kidneys with increased echotexture and normal cortico medullary differentiation. Patient developed features of intravascular volume depletion due to ongoing volume loss; and had evidence of advanced azetomia and metabolic acidosis. He underwent three sessions of haemodialysis with ultrafiltration 500 ml in each. He gradually improved with recovery of his urine output and was discharged on day 14 of the illness with regular follow-up.

Case 2: A 40 yrs old young male in good health presented with recurrent episodes of 15 - 20 loose stools per day small bowel type associated with 08 - 10 episodes of vomiting. His stool was watery with no associated blood in stools. He gave history of consumption of foods in the form of prawns from the street vendor. There was no history of movement outside place of residence in last one week prior to onset of symptoms.

Clinically he was pale with sunken eyes, JVP was reduced, capillary filling time was > 3 sec and BP was 80/40 mmHg, Temp-101˚F. He was managed with antibiotics, IV normal saline. His investigation revealed Hb-15 mg/dl, PCV - 46 TLC-11300, blood urea-82, serum creatinine-3.9 mg/dl, Na/K :147/5.1 meq/L, CPK-6121 IU/L Stool RE showed vibrio cholera by multiplex PCR. Stool for hanging revealed rod like bacilli with darting motility. His stool culture typing revealed non O1, non O13 vibrio cholera species. USG revealed that both kidneys were of normal size with increased echotexture and normal cortico medullaty differentiation.

The patient was managed with intravenous hydration with 0.9% normal saline, sodium chloride 0.9 % and inj ceftriaxone and doxycycline. Inspite of fluid resuscitation, the patient had a downhill course and developed oliguria with metabolic acidosis. Arterial blood gas analysis revealed pH:7.2, HCO3 12, pCO_2:24, lactate 4.4 mmol/L and an anion gap of 16,urine revealed specific gravity of 1.010, no active sediments and granular casts were seen on microscopy. He was treated with IV sodium bicarbonate supplementation. He also had high CPK level and hyperkalemia with ongoing fever. Patient remained oliguric and was managed with 03 sessions of haemodialysis via right triple lumen IJV 13 cm covidien catheter and subsequently improved. He was discharged on day 19 with improving renal function. Laboratory reports of case 1 and case 2 are tabulated in table 1 and 2 respectively.

Table 1: Laboratory reports of case 1 of acute kidney injury due to cholera

	Hb (gm %)	PCV (%)	Blood Urea mg%	Serum Creatinine (mg %)	Na^+ (meq/l)	K^+ (meq/l)	Lactate (mmol/l)	CPK (IU/ml)
Day 1	14.0	46	88	5.9	153	3.3	4.6	310
Day 2	14.1	44	112	6.4	147	5.2	6.2	288
Day 4	12.1	39	102	72	141	5.7	6.6	260
Day 7	10.9	37	84	7.4	137	4.9	1.2	179
Day 10	10.1	35	53	5.1	135	43	0.8	114
Day 14	92	35	48	3.4	131	4.1	-	-
Day 21	9.1	34	40	1.1	134	4.0	-	-

Table 2: Laboratory reports of case 2 of acute kidney injury due to cholera

	Hb (gm %)	PCV (%)	Blood Urea mg%	Serum Creatinine (mg %)	Na^+ (meq/l)	K^+ (meq/l)	Lactate (mmol/l)	CPK (IU/ml)	Ca++ (mg %)
Day 2	15.0	48	81	4.7	147	5.1	4.6	371	7.2
Day 4	13.0	46	41	8.1	141	5.9	1.2	266	7.1
Day 7	11.0	37	52	7.2	135	5.1	1.0	188	7.3
Day 14	10.0	35	41	6.7	133	4.1	0.8	166	79
Day 19	9.1	35	41	3.4	136	4.0	0.5	104	7.8
Day 21	9.0	3.5	35	1.7	141	3.8	-	101	-

Discussion

Untreated cholera can become life-threatening with severe complications such as refractory shock, acute kidney injury, coma, and death. Both our patients had developed complicated cholera with severe electrolyte imbalance leading to acute kidney injury. Neutrophilic leukocytosis can be attributed to the systemic inflammatory response to the Vibrio cholerae infection. Besides, both the patients had high hemoglobin and hematocrit levels, on account of the hemoconcentration secondary to hypovolaema due to profuse diarrhoea. Several biochemical and acid-base abnormalities such as hypokalaemia, hyponatraemia, low chloride levels, and metabolic acidosis with a high anion gap are often associated with cholera. [1] Both our patients also developed metabolic acidosis, low bicarbonate, hypokalaemia, hyponatremia, and hypocalcemia. Previous researchers have reported that cholera as well as other severe gastrointestinal infections can cause renal complications. [2]Acute oligoanuric kidney injury can develop due to varying aetiology, i.e. due to Vibrio cholerae infection itself or secondary to diarrhoeal volume depletion. [2] Intravenous fluids and antibiotics to manage cholera patients with severe dehydration is the standard management protocol recommended by World Health Organization (WHO). [1] Besides, patients presenting with severe acute kidney injury refractory to conservative treatment may require renal replacement therapies. [13] In sync with the above standard management protocol, aggressive intravenous hydration, antibiotics, and haemodialysis were carried out, to which both our patients showed complete recovery. Antibiotics along with administration of intravenous fluids and oral rehydration salts form the standard management protocol of cholera [14]. V. cholera isolates from primary culture are identified by colony appearance, Gram stain, biochemical tests, serology (agglutination with specific antisera), 16S rRNA PCR, specific PCR and sequencing. [15,16,17] Epidemic strains of V. cholerae O1 are differentiated into El Tor and classical biotypes, which are further subdivided into Inaba, Ogawa and Hikojima serotypes. Strains which do not belong to serogroup O1 are generally referred to as V. cholerae non O1.7 V. cholerae carries several virulence-related genes which provoke pathogenic processes in the infected hosts. Cholera toxin (CT), is the key virulence factor of serogroups O1 and O139 include which is responsible for profuse watery diarrhea. [7,14] In both our cases, severe diarrhea lead to acute kidney injury with elevated urea/creatinine levels and both the patients recovered without relapse due to treatment with intensive infusions of fluids, electrolytes, sodium bicarbonate and appropriate antibiotics.

Conclusion

Patients with nausea, vomiting, and diarrhea are frequently encountered in the emergency department of all hospitals. Majority of these will be self-limiting viral infections, requiring little or no intervention. Clinicians often become complacent when faced with patients presenting with chief complaints of “nausea, vomiting, and diarrhea” and prematurely close their historical and diagnostic evaluations, presuming it to be another viral diarrhoea. Observing the patient’s vital signs and appearance is of paramount importance.

Regardless of the presenting complaints, patients with a toxic look require early and aggressive management. Eliciting the key historical facts; and exploring other aetiologies if it does not fit the typical clinical picture of viral acute gastroenteritis is imperative.

Hospitals are responsible to public health authorities to ensure that appropriate health service agencies are informed whenever a notofiable disease is diagnosed. Mechanisms do exist for public notification and prevention and control of further spread of disease, however, these rely on prompt and accurate reporting. The coordination of all cholera research groups and robust establishment of international networking is warranted for the battle against cholera. In the present era several effective measures in controlling the infection and spread of the disease are available. Natural disasters such as floods and earthquakes lead to unhygienic environment and overcrowding. Thus, V. cholerae prevails unnoticed in the environment during inter-epidemic periods out running our efforts at prevention and control of the disease. Updated knowledge regarding the history and pathogenicity of Vibrio cholera in relation to its epidemiology and evolution is required. In conclusion, we report two cases of complicated cholera who developed severe electrolyte imbalance and acute kidney injury. Renal ischemia secondary to dehydration leading to acute tubular necrosis may have caused the acute kidney injury with elevated urea/creatinine levels in our patients. Both our patients were successfully managed by aggressive intravenous infusion of fluids, electrolytes, sodium bicarbonate and appropriate antibiotics, followed by hemodialysis. Both our patients recovered without relapse. Due to hemodialysis therapy and appropriate medical management, there was no mortality in our cases.

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