We conclude that severe hypercalcemia, extensive generalized bony lytic lesions and suppressed PTH levels may point to an underlying malignancy even in the absence of occult features which should be ruled out by appropriate investigations.

Contributors: KR: reviewed the literature and drafted the manuscript; RS,MJ,VJ: critically reviewed the manuscript. All authors were involved in management of the case and approved the final manuscript.
Funding: None; *Competing interest*: None stated.

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Cytosorb for Management of Acute Kidney Injury due to Rhabdomyolysis in a Child

A 6-year-old girl presented with rhabdomyolysis following a febrile illness. Polymerase chain reaction (PCR) for Influenza B and enterovirus was positive. Her serum creatine kinase (CK) and myoglobin levels were very high. She developed myoglobinuria with oliguria leading to acute kidney injury. Continuous renal replacement therapy along with Cytosorb filter resulted in good outcome.

Keywords: *Cytokine adsorber, Myoglobinuria Treatment*.

Rhabdomyolysis is a potentially life-threatening condition that can result into complications such as hypovolemia, hyperkalemia, metabolic acidosis, acute kidney injury (AKI) and disseminated intravascular coagulation (DIC) [1]. Viral myositis is the most frequent cause of rhabdomyolysis in children [2]. Management of rhabdomyolysis includes aggressive fluid resuscitation and hydration in order to maintain adequate urine output and prevent AKI, and early correction of potentially lethal electrolyte disturbances [3]. For children with ongoing AKI in spite of conservative management, renal replacement therapy is warranted.

A 6-year-old, previously healthy girl presented to us with a febrile illness and profound pain in lower extremities. There was no history of trauma, excessive exercise or insect bite. Investigations showed elevated creatine kinase (CK) level (5169 U/L) and negative dengue serology (NS-1 antigen, IgM and IgG). Child was started on intravenous hydration and oral paracetamol. Her serum creatinine was 0.41 mg/dL. The next day, patient had asystolic cardiac arrest that reverted with cardiopulmonary resuscitation for two minutes. She was put on mechanical ventilation. Child also had coagulopathy that was treated with fresh frozen plasma and platelet transfusions. She was noted to have severe metabolic acidosis, elevated hepatic transaminases (SGOT 10,786 U/L, SGPT 3131 U/L) as well as reduced ejection fraction (35%) on Two-dimension echocardiography (2D-Echo) examination. Her serum creatinine was 0.58 mg/dL. Subsequent laboratory investigations revealed hyperkalemia (serum K^+ 5.9 mEq/L), hypoalbuminemia and further rise in CK level (23586 U/L). Urine microscopic examination revealed ocassional red blood cells and positive urine myoglobin. Sodium bicarbonate infusion was added for alkalization of her urine. Considering very high CK levels, positive fluid balance (3 liters) and dark colored urine, acute renal tubular injury was considered. The child was started on intermittent hemodialysis (HD) with high flux dialyzer (Fx 60). Due to hemodynamic instability, patient was shifted to continuous renal replacement therapy (CRRT) next day in Continuous Veno-Venous Hemofiltration (CVVH) mode. Cytosorb filter was added to remove myoglobin (molecular weight 17kDal) and CK (molecular weight 81kDal). After three days of Cytosorb and five days of continuous CRRT, patient was shifted to intermittent hemodialysis with F×60, as she was

hemodynamically stable. Repeat CK and myoglobin levels revealed decreasing trends, with lowest being (CK 219 U/L, myoglobin 171 ng/mL) by day 27 and day 19, respectively. Pharyngeal swab showed Polymerase chain reaction (PCR) for influenza B and enterovirus positive. During the renal replacement therapy, there were no complications such as bleeding, infection, hypophosphatemia or hypokalemia.

Intermittent hemodialysis was stopped on day 33 as patient's urine output improved; her creatinine also normalized (0.53 mg/dL) by day 44. The trend of CK, myoglobin and serum creatinine is summarized in ***Fig.* 1**. Patient was transferred to ward and subsequently discharged home after a week. On follow-up, six months after discharge, child had gained weight (1.5 kg). Her serum creatinine was 0.26 mg/dl and the estimated glomerular filtration rate (eGFR) was 271 mL/minute.

Incidence of AKI secondary to rhabdomyolysis has been reported variably from 17-35% in adults and 5-50% in children [2,4]. Although renal replacement therapy is rarely needed in rhabdomyolysis, it should be considered when there is severe and resistant hyperkalemia, persistent metabolic acidosis, uremia and ongoing AKI despite conservative treatment. In the present case, we managed AKI associated with rhabdomyolysis with the combination of CRRT and Cytosorb. We added Cytosorb in line with the CRRT circuit in pre-dialyzer position for first 72 hours during CRRT with the intention of removing myoglobin from blood.

Cytosorb is a cytokine adsorbing polymer filter, initially intended as adjunctive treatment for patients with elevated cytokine levels in the setting of severe sepsis and septic shock. It contains hemoadsorption beads made up of polystryrene-divinylbenzene porous particles with a biocompatible polyvinyl-pyrrolidone coating [5]. In addition to cytokines, it has been shown to reduce serum myoglobin in adults with rhabdomyolysis [6]. In the patient discussed, early weaning of inotropic support and rapid improvement in multiorgan dysfunction including coagulopathy suggests the role of extra-corporeal filter therapy.

CRRT in conjunction with CytoSorb represents a novel approach to the treatment of AKI associated with rhabdomyolysis in children. Although early initiation of extracorporeal therapy seems to improve the outcome, currently there is no absolute clarity on identifying patients with rhabdomyolysis needing renal replacement therapy, the levels of CK or serum myoglobin at which RRT should be initiated and the optimum duration of use of Cytosorb in these patients. Data on a larger number of children with rhabdomyolysis need to be evaluated before instituting the above therapy as a standard management protocol.

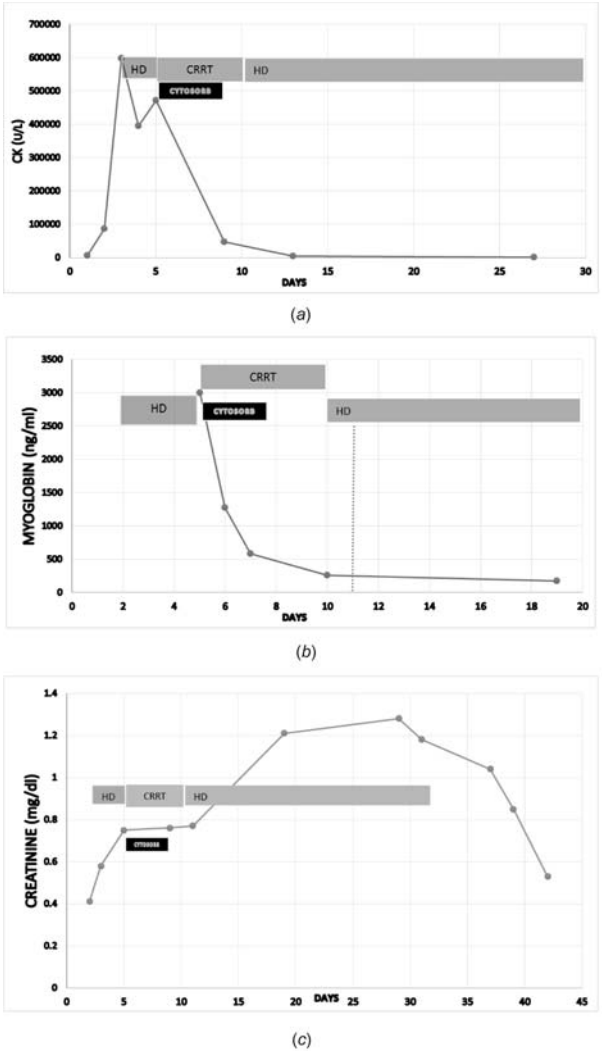

FIG.1 *Trend of serum creatinine kinase (a), myoglobin (b), and creatinine (c) in index patient.*

Contributors: All authors contributed to case management and supervision; SP: drafted the manuscript, which was revised and approved by all authors.

Funding: None; *Competing interest*: None stated.

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Treatment of Multi-drug Resistant Tuberculosis Causing Tubulopathy – Gitelman-like Syndrome

Treatment of multi-drug resistant (MDR) tuberculosis (TB) includes aminoglycosides and ethionamide. A 16-year-old girl presented with sudden onset of paralysis, dyselectrolytemia mimicking Gitelman syndrome, and ethionamide-induced hypothyroidism. Monitoring electrolytes during MDR-TB treatment is recommended to prevent life-threatening complications.

Keywords: *Hypothyroidism, Paralysis.*

Aminoglycosides are commonly used in multi-drug resistant (MDR) tuberculosis. Gitelman syndrome is associated with metabolic alkalosis, dyselectrolytemia with normal blood pressure, and has a high phenotypic variability. Kanamycin used in MDR tuberculosis can cause tubular dysfunction.

A 16-year-old girl presented with progressive weakness of all four limbs for 7 days, numbness and tingling sensations in the hand for 4 days and inability to hold neck for 1 day. There was no history of fever, trauma, backache, headache, loss of bladder/bowel control, parasthesias or similar episodes in the past. She was under treatment for MDR-TB since 2 months with kanamycin, cycloserine, ethionamide, levofloxacin, ethambutol and pyrazinamide. She had a family history of unexplained deaths in two of her six siblings. One sibling had died at the age of 24 during an acute diarrheal illness and the other sibling while on treatment for MDR-TB with similar regimen.

At presentation, she had bradycardia and was normotensive. Systemic examination revealed right sided effusion, generalized hypotonia, areflexia and a soft palpable goitre. Investigations revealed hypokalemia, hypocalcemia, hypomagnesemia, metabolic alkalosis with normal sodium, creatinine, complete blood counts and urine routine (***Table* I**). ECG showed prolonged QTc and PR interval and U waves. She was started on intravenous calcium gluconate, injection magnesium sulphate and intravenous potassium chloride. Paralysis and carpopedal spasms improved after 48-hours of intravenous replacement. Subsequent investigations showed vitamin D levels of 7.5 (normal 50-175), nmol/l and elevated PTH of 120 pg/mL (normal 10-60), and vitamin D3 was added on day 2. Fractional excretion of magnesium was 13.9%, with urinary chloride of 83 meq/L and 24-hour urinary calcium creatinine ratio of 0.21. Attributing these clinical manifestations to kanamycin, the drug was stopped on day 3. Gradually she improved over the next 5 days, intravenous replacements were converted to oral supplements and kanamycin was reintroduced on day 8. She also required thyroxine replacement for her hypothyroidism, which was attributed to ethionamide.

She was discharged in a hemodynamically stable condition on day 10. On follow up at 1 and 2 months, her electrolytes were normal, requiring 8 meq/kg/day of potassium supplement, 1500 mg/day of calcium and 1g of magnesium sulphate per week. As her TSH was still 16 mIU/L, thyroxine dose was increased to 75 mcg/day.

TABLE I LABORATORY PARAMETERS

Investigations	*Day 1*	*Day 3*	*Day 10*	*2 mo*
Serum potassium	2.0	2.5	3.5	4.0
Serum magnesium	1.0	1.1	1.4	1.7
Ionized calcium (4.0-5.0mg/dL)	3.5	3.7	4.0	4.5
pH, HCO3	7.6/ 35	7.56/ 34	7.4/ 30	7.45, 25
Free thyroxine	–	12	–	15
TSH	–	84	–	16
Anti-TPO Ab	–	Negative	–	–

TSH: thyroid stimulating hormone; Anti TPO Ab: anti thyroid peroxidise antibodies; – : not done; Free thyroxine Normal 12-22 pmol/L.