

Syndrome of Inappropriate Antidiuretic Hormone Associated with Crimean-Congo Hemorrhagic Fever

Kırım-Kongo Hemorajik Ateşi Olan Vakada Uygunsuz Anti-diüretik Hormon Sendromu

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ABSTRACT

Crimean-Congo hemorrhagic fever (CCHF) is a potentially fatal systemic disease in children caused by a tick-borne virus. Many different clinical and laboratory findings are seen in *CCHF*. We report here an atypical presentation of *CCHF* with hyponatremia. *CCHF* with electrolyte imbalance is not reported before.

A 4-year-old girl presented with fever, fatigue and unconsciousness with hyponatremia.

Based on the clinical and epidemiological findings, virus infection was suspected. Hyponatremia is has never been reported in *Crimean-Congo hemorrhagic fever (CCHF)*, as was observed in this case.

The diagnosis was confirmed by detection of IgM antibody to *CCHF* virus and positive Real-Time PCR. We report the first case of imported *CCHF* presenting as hyponatremia. This electrolyte imbalance has never been reported before in *CCHF* in children, and the clinician should consider this entity in complications to explain unconsciousness. (*Türkiye Parazitoloj Derg 2014; 38: 275-7*)

Keywords: *Crimean-Congo hemorrhagic fever*, electrolyte imbalance, syndrome of inappropriate antidiuretic hormone (SIADH)

Received: 05.03.2014

Accepted: 17.07.2014

ÖZET

Kırım Kongo Hemorajik Ateşi (KKHA) çocukluk çağında fatal seyirli kene tutunması sonucu ortaya çıkan klinik tablodur. Çok çeşitli klinik ve laboratuvar bulguları ile karşımıza çıkabilir. Bu yazıda atipik bir prezentasyon olan hiponatremi ve bilinç bulanıklığı ile başvuran olgu sunulmuştur. KKHA'nde hiponatremi daha önce bildirilmemiştir.

Olguda 4 yaşında kız hasta ateş, halsizlik ve hiponatremiye bağlı bilinç bulanıklığı ile başvurdu. Hastanın kırsal kesimden başvuruyor olması ve Tokat yöresinde KKHA vakalarının çok sayıda olmasından dolayı KKHA virüsü enfeksiyonundan şüphelenildi. KKHA virüsüne karşı IgM antikorlarının ve Real-Time PCR ile virüsün saptanması ile tanı doğrulandı.

Bu vakayı daha önce KKHA vakalarında elektrolit dengesizliğinin bildirilmemiş olması ve hiponatreminin neden olabileceği bilinç bulanıklığı ve konvülsiyon gibi klinik tablolarla karşılaşılabileceğini vurgulanmak amacıyla sunduk. (*Türkiye Parazitoloj Derg 2014; 38: 275-7*)

Anahtar Sözcükler: Kırım-Kongo hemorajik ateş, elektrolit dengesizliği,uygunsuz anti-diüretik hormon sendromu

Geliş Tarihi: 05.03.2014

Kabul Tarihi: 17.07.2014

This study is presented in the 3th PUADER Congress, 30 April-4 May 2014, Antalya, Turkey.

Bu çalışma "3. PUADER Kongresi"nde sunulmuştur, 30 Nisan-4 Mayıs 2014, Antalya, Türkiye.

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DOI: 10.5152/tpd.2014.3603

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INTRODUCTION

Crimean-Congo hemorrhagic fever (CCHF) is a tick-borne fatal systemic disease caused by Nairovirus, which belongs to the Bunyaviridae family and causes severe diseases in humans, with the reported mortality rate of 5-30% (1). Crimean-Congo hemorrhagic fever virus (CCHFV) is transmitted to humans through bites of infected ticks or direct contact with viremic animals, humans, or contaminated secretions (2). CCHF has a short incubation period and is characterized by a sudden onset of fever, fatigue, headache, dizziness, nausea, vomiting, diarrhea, abdominal pain and elevated liver enzymes, leucopenia, thrombocytopenia, coagulopathy and other hemorrhagic manifestations develop, ranging from petechiae to large areas of ecchymosis (2, 3).

There are many etiologic factors underlying unconsciousness. In all these factors, electrolyte imbalance, especially hyponatremia, is a very important entity. Hyponatremia symptoms are nausea, anorexia, emesis, malaise, lethargy, confusion, agitation, headache, seizures, muscle cramps, weakness, coma, and decreased reflexes. Most symptoms of hyponatremia are due to the decrease in extracellular osmolality (4).

CASE REPORT

A 4-year-old previously healthy girl was admitted to the pediatric emergency department of Gaziosmanpaşa University Medical Practice and Research Center (a tertiary health care facility in the region). Her complaints started 4 days before admission, with fever, fatigue and lethargy. She had no history of tick bite.

On admission, her body temperature was 38.9°C, blood pressure was 90/60 mmHg, heart rate was 125 beats/min. White blood cell (WBC) count was $3.3 \times 10^3/\mu\text{L}$, hemoglobin (Hb) 11.3 g/dL, and platelet count $46 \times 10^3/\mu\text{L}$, aspartate aminotransferase (AST) 266 IU/L, alanine aminotransferase (ALT) 110 IU/L, creatine kinase (CK) 277 IU/L and lactate dehydrogenase (LDH) 567 IU/L, creatinine 0.39 mg/dL, glucose 86 mg/dL, Na 124 mmol/L, K 4.86 mmol/L, blood urea nitrogen (BUN) 6.9 mg/dL, albumin 3.6 g/dL, prothrombin time (PT) 10.3 s, activated partial thromboplastin time (aPTT) 40.3 s, urine Na 217 mmol/L. Following the morning of admission, it was seen that she had maculopapular rashes, and she was still lethargic on examination. WBC was $2.9 \times 10^3/\text{L}$, Hb 11g/dL and platelet count $22.7 \times 10^3/\text{L}$, Na 124 mmol/L, K 3.8 mmol/L, AST 239 IU/L, ALT 95 IU/L. The patient was then administered 1 unit of platelets. On another morning, platelet count was $44 \times 10^3/\text{L}$, but she had epistaxis and abdominal pain. Because of this coagulopathy, apheresis thrombocyte was given, and she had nasal acking. Abdominal ultrasound imaging revealed that liver craniocaudal length was 105 mm and had slightly increased, and she had splenomegaly. Thereafter, platelet count was $66.7 \times 10^3/\text{L}$, and bleeding was stopped. On the same day, sodium deficit was calculated. Na replacement treatment was administered. Serum osmolality was 237.2 mOsm/kg H₂O, and urine osmolality was 413 mOsm/kg H₂O, and urine Na level was 217 mmol/L. Blood pressure was within the normal range, she had no edema and hypervolemia. After day, Na level was 130 mmol/L, and lethargy was started to recruit. She was oriented and cooperative. The following day, Na level was 137 mmol/L. We decided that lethargy was associated with hyponatremia. After 5 days from admission, Na level reached 139 mmol/L, platelet count $115 \times 10^3/\text{L}$ and WBC $6.910^3/\text{L}$, Hb 10.1g/dL, AST 53 IU/L, ALT 45 IU/L, LDH 431 IU/L, Na 138 mmol/L,

K 4,5 mmol/L, Cl 101 mmol/L. She had no bleeding, and skin eruptions disappeared. Diagnosis was confirmed with blood sample tested in Refik Saydam National Public Health Agency Virology Reference and Research Laboratory by TaqMan based on one-step real-time PCR. Her IgM was positive and IgG was negative for CCHF.

DISCUSSION

Hyponatremia is life-threatening clinical condition. Although many clinical features are described in CCHF, hyponatremia has never been reported before. The CCHF cases in Turkey has increased dramatically in recent years (1). Because of endothelial damage in CCHF, it can be seen with many different clinical manifestations, laboratory findings, and complications (5). CCHFV infection course has 4 distinct phases: incubation, prehemorrhagic, hemorrhagic, and convalescence period. The incubation period for CCHF differs from 2 to 9 days (6).

The majority (82%) of patients have a history of tick bite. Fever (100%), hemorrhagic symptoms (76%), nausea-vomiting (60%), tonsillopharyngitis (50%), malaise (50%), myalgia (46%), and maculopapular rash (24%) are the most common presenting clinical features (4). Hyponatremia or any electrolyte imbalance has not been reported before. In this case, our patient was admitted to hospital with fever and lethargy. Lethargy is not a common complaint in CCHF, and also, electrolyte imbalance has not been reported before with CCHF (4).

Specific mechanisms underlie the pathogenesis of CCHF infection, and these mechanisms have not been clearly explained. Major targets of the CCHF virus are mononuclear phagocytes, hepatocytes, and endothelial cells (7). This shows that the virus may attack nearly all the systems in our body. Because of this, as a clinician, we can meet many different laboratory findings and clinical manifestations. Laboratory findings in CCHF show elevated liver enzymes, CK, LDH, increase in PT, aPTT, C-reactive protein (CRP) and D-dimer levels, decrease in fibrinogen levels, leukocytosis, leukopenia, and thrombocytopenia, and hepatomegaly and splenomegaly can be seen as clinical evidence.

Hyponatremia is the most common and serious disorder of electrolyte imbalance in hospitalized patients. Acute hyponatremia can cause substantial morbidity and mortality if not treated. The etiology of hyponatremia is various, and infections are common, which underlie this disorder. Our patient was euvoletic and had no edema. One of the criterion for diagnosing SIADH is decreased effective osmolality of the extracellular fluid ($\text{Posm} < 275 \text{ mOsm/kg H}_2\text{O}$). Inappropriate urinary concentration ($\text{Uosm} > 100 \text{ mOsm/kg H}_2\text{O}$ with normal renal function) at some level of plasma hypo-osmolality. Clinical euvolectmia, as defined by the absence of signs of hypovolemia (orthostasis, tachycardia, decreased skin turgor, dry mucous membranes) or hypervolemia (subcutaneous edema, ascites). Elevated urinary sodium excretion ($> 30 \text{ mmol/L}$) while on normal salt and water intake (8). According to these criteria, our patient had SIADH.

CONCLUSION

In conclusion, this is the first case report of CCHF accompanied by SIADH in children. No CCHF-related hyponatremia has been reported in the literature. Because of this, clinicians must be careful of electrolyte imbalance in children who are diagnosed

with CCHF. Electrolyte levels must be checked on admission and daily during hospitalization. This case report showed that SIADH can develop in children diagnosed with CCHF. Hyponatremia may be the cause of lethargy, and this can be regulated with sodium replacement treatment.

Informed Consent: Hastanın kimlik bilgileri ortaya koyan herhangi bir veri kullanılmamıştır. Hastadan onam alınması gereken herhangi bir girişim yapılmamıştır. Yerel etik kurula danışılmıştır ve bu vaka sunumu için onam alınmasına gerek görülmemiştir.

Peer-review: Externally peer-reviewed.

Author contributions: Concept - S.Ö., N.Ö.K., E.S.; Design - S.Ö., N.Ö.K., E.K., R.Y.; Supervision - S.Ö., N.Ö.K., E.S., E.K., R.Y.; Funding - S.Ö., N.Ö.K., E.S., E.K., R.Y.; Data Collection and/or Processing - S.Ö., N.Ö.K., E.K.; Analysis and/or Interpretation - S.Ö., N.Ö.K., E.S., E.K., R.Y.; Literature Review - S.Ö., N.Ö.K., R.Y.; Writer - S.Ö., N.Ö.K., R.Y.; Critical Review - E.S., E.K., R.Y.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

Hasta Onamı: Hastanın kimlik bilgileri ortaya koyan herhangi bir veri kullanılmamıştır. Hastadan onam alınması gereken herhangi bir girişim yapılmamıştır. Yerel etik kurula danışılmıştır ve bu vaka sunumu için onam alınmasına gerek görülmemiştir.

Hakem Değerlendirmesi: Dış Bağımsız

Yazar Katkıları: Fikir - S.Ö., N.Ö.K., E.S.; Tasarım - S.Ö., N.Ö.K., E.K., R.Y., E.K.; Denetleme - S.Ö., N.Ö.K., E.S., E.K., R.Y.; Kaynaklar

- S.Ö., N.Ö.K., E.S., E.K., R.Y.; Veri Toplanması ve/veya işleme - S.Ö., N.Ö.K., E.K.; Analiz ve/veya Yorum - S.Ö., N.Ö.K., E.S., E.K., R.Y.; Literatür taraması - S.Ö., N.Ö.K., R.Y.; Yazıyı Yazan - S.Ö., N.Ö.K., R.Y.; Eleştirel İnceleme - E.S., E.K., R.Y.

Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

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