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Hemoperitoneum is A Rare Clinical Manifestation of Crimean-Congo Hemorrhagic Fever in Children

Hemoperitoneum, Çocuklarda Kırım-Kongo Kanamalı Ateşinin Nadir Görülen Bir Klinik Belirtisidir

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ABSTRACT

Hemoperitoneum is a manifestation of abdominal bleeding of non-traumatic origin, leading to the outpouring of free blood into the abdominal cavity or retroperitoneal space. This condition is defined as a rare complication occurring in children with Crimean-Congo hemorrhagic fever (CCHF). To highlight the hemoperitoneum in children with CCHF and raise awareness of a rare complication among clinicians. A retrospective analysis was conducted on detected cases of CCHF in children, focusing especially on the features of the pre-hemorrhagic and hemorrhagic periods of the disease. Clinical cases with rare symptoms in children, such as hemoperitoneum, are described. The clinical picture of CCHF in children may manifest as a rare complication such as hemoperitoneum. The outcome of the disease depends on the severity of the hemorrhagic syndrome, the timeliness of etiologic and hemostatic therapy, and treatment and prevention of possible complications.

Keywords: Crimean-Congo hemorrhagic fever, hemoperitoneum, children, hemorrhagic syndrome

ÖZ

Hemoperitoneum, travmatik olmayan kökenli abdominal kanamanın bir belirtisidir ve karın boşluğuna veya retroperitoneal boşluğa serbest kan dökülmesine yol açar. Kırım-Kongo kanamalı ateşi (KKKA) olan çocuklarda görülen nadir bir komplikasyon olarak tanımlanmaktadır. KKKA olan çocuklarda hemoperitonu vurgulamak ve klinisyenler arasında nadir görülen bir komplikasyon hakkında farkındalık yaratmak. Çocuklarda tespit edilen KKKA vakalarının, özellikle hastalığın hemorajik öncesi ve hemorajik dönemlerinin özelliklerinin, çocuklarda hemoperiton gibi nadir semptomları olan klinik vakaların retrospektif bir analizi tanımlanmıştır. Çocuklarda KKKA klinik tablosu hemoperiton gibi nadir görülen bir komplikasyon olarak kendini gösterebilir. Hastalığın sonucu hemorajik sendromun ciddiyetine, etiyotropik ve hemostatik tedavinin zamanlamasına, olası komplikasyonların tedavisine ve önlenmesine bağlıdır.

Anahtar Sözcükler: Kırım-Kongo kanamalı ateşi, hemoperiton, çocuk, hemorajik sendrom

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INTRODUCTION

Crimean-Congo hemorrhagic fever (CCHF) is a tick-borne infection that is caused by the CCHFV virus from the Bunyaviridae family (1). CCHF is an endemic disease in some countries, and is one of the diseases prioritized for their pandemic potential (2-4). Possible ways of transmitting the virus to humans are through the bite of infected ticks or direct contact with infected blood or other body fluids (5). Currently, it is known that with CCHF there is a high mortality rate, which varies according to various data from 20 to 30% in hospitalized patients (6). However, according to various authors, despite the high mortality from CCHF, children still carry the disease in a milder form than adults (2,6). In addition, during the COVID-19 pandemic, many researchers found an increase in the number of cases of CCHF in children who manifested a more severe disease course and were mistakenly diagnosed as manifestations of coronavirus infection (2). In this study, we describe clinical cases of CCHF in children with a clinical manifestation of hemoperitoneum.

CASE REPORT

Case 1

An 11-year-old female child was admitted to the Hospital of Infectious diseases on 13.05.2019. Upon admission, she complained of an increase in body temperature to 38.1°C, runny nose, weakness, and headache. When collecting anamnesis, it was established. On 10.05.19, the girl was bitten by a tick in the yard of her house. Her parents went to the hospital, where medical workers successfully removed the tick. On 13.05.19, the child had fever up to 39.5°C, headache, runny nose, weakness, and the parents returned to the infectious hospital, where a general blood test was taken and showed that platelets were within the normal range $-272 \times 10^9/L$. The girl was hospitalized with a diagnosis of acute respiratory viral infection (ARVI) in severe form. The patient had a tick bite. Treatment of ARVI was started. At the beginning of the disease, febrile manifestations, manifestations of intoxication syndrome, and catarrhal symptoms characteristic of viral respiratory infection were noted; the normal number of platelets remained in blood tests. The dynamics of the girl's condition worsened on the 4th day: there was poor health; abdominal pain; vomiting once; leg aches; facial hyperemia; pronounced scleritis; conjunctivitis; 1-2 elements of petechial rashes on the abdomen; and hematomas at injection sites. Anemia, thrombocytopenia, up to $96 \times 10^9/L$, increased alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase were noted in blood tests. Signs of hypocoagulation were indicated by the coagulogram. The doctors diagnosed CCHF with moderate severity as a probable case. Etiotropic therapy with ribavirin was prescribed according to the scheme (initially 30 mg/kg, then 15 mg/kg every 6 hours for 4 days). On the 5th day, despite the treatment, hemorrhagic rashes appeared on the skin in the area of the knee joints, the upper half of the chest, and hemorrhages in the injection sites, pronounced abdominal pain, and joint pain. There has been excessive bleeding from the genital tract, unrelated to the menstrual cycle. Until now, the girl had no manifestations of regular menstruation. The "coffee grounds" type of discharge was noted from the nasogastric probe. In the analysis of feces for latent blood, a strongly positive result was obtained. As can be seen, the patient developed a severe hemorrhagic syndrome:

pallor of the skin and mucous membranes, "cold sweat", dizziness, weakness, darkening of the eyes, tachycardia, arterial hypotension, a hemorrhagic rash, uterine and gastrointestinal bleeding, and the clinical picture includes symptoms of hemoperitoneum, such as: abdominal pain; bluntness in sloping places; auscultation reveals muffling of intestinal noises. On the 6th day of the disease, against the background of continuing bleeding, the child had complaints of severe headaches, loss of consciousness, symptoms of coma, and acute cerebral circulation disorders of hemorrhagic type: difficulty swallowing; speech; weakness of the limbs with left-sided hemitype; impaired coordination. Anemia, leukopenia, thrombocytopenia with counts up to $40 \times 10^9/L$, and an increase in Erythrocyte sedimentation rate levels were observed in blood tests. On the 7th day, an ultrasound examination of the abdominal cavity revealed reactive cholecystitis, pericholecystitis, splenomegaly, free fluid in the pelvis in an amount of 72 cm³, and in the abdominal cavity in an amount of 30 cm³. Conducting the tests yielded positive results: the virus RNA was detected by polymerase chain reaction (PCR), and immunoglobulin M (IgM) antibodies were detected by ELISA. During ongoing treatment, positive changes were observed in blood tests as an increase in the number of platelets to $133 \times 10^9/L$, hemoglobin to 74 g/L, and erythrocytes to 2.9×10^{12} . On the 10th day of the illness, a positive ELISA test result for the CCHF virus was received again. The final clinical diagnosis was established for the child of CCHF, confirmed case, severe form with abdominal bleeding (gastric, intestinal, uterine). Complications: Hemoperitoneum. An acute disturbance of cerebral circulation due to hemorrhagic type occurs. The treatment included ribavirin with etiotropic purpose, freshly frozen plasma, immunized plasma with antibodies to the CCHF virus, hemostatic therapy, replacement therapy with blood components, and symptomatic therapy. Against the background of therapy, the general condition stabilized; the child came out of a coma and began to react to external stimuli; hemorrhagic and intoxication syndromes were stopped; sleep and appetite were restored. On the 22nd day of the illness, the child was discharged home with a significant improvement in condition under the supervision of a district doctor.

Case 2

A 12-year-old male child from a village arrived at the district residence in the Turkestan region on 9th July 2022, with complaints of fever up to 38-39°C, weakness, muscle pain, and headache. From the anamnesis on 7th January 2022: the boy independently removed the attached tick from the surface of the left thigh, while he himself crushed it and threw it away, but did not tell the matter about what had happened. On 7th April 2022 his body temperature rose to 38°C. The boy's mother gave antipyretics on her own, soldered fluids, the condition with a "cold disease". There was no improvement chills, weakness, muscle pain, headache joined the child's dynamics on 7th September 2022. The child's mother was infected on the same day. The boy was hospitalized in the infectious diseases department with a diagnosis of CCHF, a probable case. On subjective examination, the condition was regarded as severe due to intoxication syndrome, preserved consciousness, meningeal, and unwanted neurological symptoms. Hyperemia of the throat was noted; tonsils were loose, somewhat edematous, without plaque; the tongue was wet and covered with a white coating. The skin is clean, dry, warm to the touch, somewhat hyperemic, slightly puffy, the sclera is injected,

petechiae, ecchymosis, hemorrhages at the injection site without manifestations. Symptoms of «burning» were negative. The oxygenate saturation is 95%. Heart sounds are muffled, quickened. Pulse 96 in 1 min., arterial pressure 112/73 mmHg. The abdomen is soft accessible on palpation, somewhat sensitive in the epigastric region the symptoms of “acute abdomen” are negative. The liver was enlarged, and palpable below the edge of the costal arch by 1.5 cm the edge was light, b painless. Diuresis has been saved. Fecal occult blood test positive result. The institution conducted a laboratory blood test upon detection of severe thrombocytopenia $46 \times 10^9/L$, anemia Hb -85 g/L, leukopenia $L - 3.39 \times 10^9/L$, hypoproteinemia of total protein - 7.8 g/L, increase in ALT enzymes - 296.3 IU/L, AST - 51.1 IU/L. In the coagulogram manifestations of hypocoagulation: a decrease in the prothrombin index 59.3% increase in international normalized ratio 1.68 of prothrombin time - 21.9 seconds prolongation of blood clotting time beginning 07:25 minute/second - 08:50 minute/second. With the condition of the child, stable nutrition was maintained, weakness, lethargy, drowsiness persisted, hemorrhagic syndrome on the skin and mucous membranes manifested itself, there were no violations, weak sensitivity to palpation of the abdomen, repeated examination of the children’s surgical syndrome of the acute state of “acute abdomen”. At the height of the disease, blood tests revealed a violation of hemostasis, a sharp increase in the enzymes ALT: 234.2 IU/L and AST: 697.1 IU/L, and a moderate increase in bilirubin up to $37 \mu\text{mol/L}$. Tests for markers of viral hepatitis are negative. The child was also examined by a hematologist and diagnosed with CCHF, a probable case. Syndrome of intravascular coagulation. Secondary thrombocytopenia. Ultrasound of the gastrointestinal tract detected the presence of free fluid in the abdominal cavity and a significant amount in the small pelvis. The patient has been diagnosed with ascites, hepatomegaly, diffuse changes in the liver parenchyma. When conducting a specific examination of CCHF, the analyses gave positive results: the PCR method revealed the RNA of the CCHF virus and ELISA detected IgM antibodies. The child was diagnosed with Crimean-Congo hemorrhagic fever, a confirmed case, a severe form characterized by abdominal bleeding (gastric, intestinal). Complication: hemoperitoneum. The child received CCHF therapy in accordance with the medical protocol for the diagnosis and treatment: with the delivery of receipts of ribavirin with an etiotropic purpose (initially 30 mg/kg, then 15 mg/kg for about 6 hours for 4 days), fresh frozen plasma, immunized plasma with antibodies to the CCHF virus, hemostatic therapy, replacement therapy with blood components, symptomatic therapy. On the background of treatment, blood tests returned to normal: total protein - 65 g/L, ALT - 7.5 IU/L, AST - 6 IU/L, total bilirubin - $8.4 \mu\text{mol/L}$, restoration of coagulogram parameters. On the 16th day of hospitalization, the child was discharged with improvement under the supervision of a local doctor, with recommendations for recovery.

DISCUSSION

The results of clinical manifestations are manifested by rare manifestations of CCHF in children in the form of hemoperitoneum and hemorrhagic stroke. Clinical presentation of hemorrhagic syndrome CCHF in areas experiencing leakage, with noted individual deviations. If in the first case we have an extended and vivid picture in a girl: hemorrhagic rashes on the skin, hemorrhages at injection sites, gastrointestinal and uterine hemorrhages, severe abdominal

pain, symptoms of hemoperitoneum, further development of coma against the background of acute cerebrovascular accident due to hemorrhagic pressure, then in the second patient, the clinic of hemorrhagic syndrome was without signs of hemorrhage on the skin and mucous membranes, in the presence of confirmed hemoperitoneum, more restrained abdominal symptoms. Epidemiological anamnesis was decisive in the diagnosis of the disease; the identification of initial foci in the blood test showing a sharp decrease in the level of platelets; a positive fecal occult blood test; PCR; and ELISA-confirmation of a specific examination for CCHF.

At the moment, there are several studies focused on CCHF in children, but they do not describe rare cases of hemoperitoneum. In one study conducted by scientists from Türkiye, a rare complication of CCHF was found as hemophagocytic lymphohistiocytosis with an unusually severe course (2). In another study, rare ocular symptoms were evaluated in children diagnosed with CCHF, and an increased tortuosity of retinal vessels was revealed (7). There is also a report of a rare case of myocarditis in a child with CCHF, which completely regressed after the convalescent period of the disease (8). In the modern literature, there is evidence of a rare complication in the form of reversible bradycardia occurring during the clinical course in children with CCHF (9,10).

Due to the scarce data available in the literature on the CCHF in children, it is noteworthy that, in most cases, the course of the disease in pediatric patients is much easier than in adults (11). At the same time, the disease is most often observed in older male children, and the main factor in the onset of the disease is direct contact with livestock (5). However, clinicians need to be wary of children with CCHF on the rare severe complications.

CONCLUSION

The probability of the disease of children with children increases during the active season of ticks, which are carriers of infection, if they have lived in natural focal areas, been bitten by a tick, or had contact with a confirmed case. The clinical picture of CCHF in children may have similarities with the manifestations of this infection in adults. Among the rare symptoms, hemoperitoneum is possible. The outcome of the disease depends on the severity of the hemorrhagic syndrome, the timeliness of etiotropic and hemostatic therapy, treatment and prevention of possible complications. In severe cases, timely initiation of etiotropic and hemostatic therapy gives a chance for a successful outcome.

Ethics

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: B.F.A., A.G.N., P.T.V., A.D.S., U.G.A., B.Y.B., Concept: B.F.A., A.G.N., Design: B.F.A., A.G.N., Data Collection or Processing: B.F.A., A.G.N., Analysis or Interpretation: B.F.A., A.G.N., U.G.A., Literature Search: P.T.V., Writing B.F.A., A.G.N., P.T.V., U.G.A., B.Y.B.

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