

Crimean Congo Hemorrhagic Fever: Assessment of Four Mild Cases in Kahramanmaraş*

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ABSTRACT: Crimean Congo Hemorrhagic Fever (CCHF), usually acquired through a tick bite, is a viral disease with high mortality and morbidity. Typical symptoms are fever, headache, profound malaise, nausea and hemorrhagic manifestations. In this study, we aim to discuss the clinical features of four patients with CCHF infections diagnosed by ELISA and PCR since 2008 in Kahramanmaraş. Three cases were men and one was woman and mean age was 54 (min-max:34 -74). They came from Andırın region of Kahramanmaraş city. All of them were farmers and had anamnesis of tick bite. The common symptoms in all cases were fever, headache and nausea. Three cases had bleeding symptoms (each one from the nose, teeth and vagina). The fourth case had no bleeding. Common blood test revealed leukopenia, thrombocytopenia, and high liver enzymes (ALT, AST). Three patients had elevated lactic dehydrogenase and two cases had elevated creatinine kinase. Similar medical therapy such as ribavirin, antibiotics, stomach protective and fluid replacement therapy was given to all patients for 7-10 days. No complication was encountered in any patient. They recovered completely. If patients coming from risk zone have got high fever and headache, tick bite must be asked in history taking.

Keywords: Crimean Congo Hemorrhagic Fever, ticks, infection

Kırım-Kongo Kanamalı Ateşi: Kahramanmaraş'ta Dört Hafif Klinik Olgunun Değerlendirilmesi

ÖZET: Kırım-Kongo Kanamalı Ateşi (KKKA) kene ısırmasıyla geçen morbidite ve mortalitesi yüksek bir viral hastalıktır. Tipik semptomları ateş, baş ağrısı, ileri derece halsizlik, bulantı ve kanama kliniği gösterir. Bu çalışmada, Kahramanmaraş'ta 2008 tarihinden itibaren ELİSA ve PCR yöntemi ile KKKA tanısı konulan 4 olgunun klinik özellikleri irdelendi. Olguların üçü erkek, biri kadın idi ve yaş ortalamaları 54 (34-74) idi. Olguların tümü Andırın ilçesinden gelmişti ve çiftçiydi. Olguların tümünde kene ısırığı öyküsü vardı. Tüm olgularda ateş, baş ağrısı ve halsizlik yakınması vardı. Bir olguda burun kanaması, bir olguda da diş eti bir olguda da vajinal kanama öyküsü vardı. Dördüncü olguda ise kanama yoktu. Laboratuvar bulguları incelendiğinde; tüm olgularda lökopeni, trombositopeni, karaciğer enzimlerinde (ALT, AST) yükselme saptandı. 3 olguda Laktik Dehidrogenaz yüksekliği, 2 olguda ise kreatin kinaz yüksekliği belirlendi. Tüm olgularda hastalara 7-10 gün boyunca, ribavirin, antibiyotik, mide koruyucu ve sıvı replasman tedavisi verildi. Hiçbir olguda komplikasyon görülmedi. Olguların tümü şifa ile taburcu edildi. Özellikle riskli bölgelerden gelen ve yüksek ateş ve kanama bulguları olan hastalar, kene ısırığı öyküsü yönünden sorgulanmalıdır.

Anahtar kelimeler: Kırım-Kongo Kanamalı Ateşi, keneler, enfeksiyon

INTRODUCTION

Crimean-Congo hemorrhagic fever (CCHF) which is carried by Hylomma species ticks is a fatal viral infection. The virus belongs to the genus Nairovirus in the Bunyaviridae family (Abram, 1995; Capua, 1998; Saijo, et al., 2002; Papa, et al., 2002; Aidaros, 2003).

Firstly it was seen in Crimean region in 1946 and secondly it was seen Congo in 1956. After that two diseases were realized that they are same disease.

Finally, this disease was mentioned as CCHF after 1969 (Capua, 1998; Aidaros, 2003). Now it was seen more than 30 countries and described in parts of Africa, Asia, Eastern Europe and the Middle East. Originally, CCHF virus had caused epidemics in Middle Black Sea Region in Turkey since 2002, but it has been seen in almost every region of Turkey in recent years.

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Clinical signs

Disease's incubation period is depend on infect way. Incubation time of infection (following bited tick) is generally 1-3 days sometimes more than 9 days. If disease becomes after contact with blood or tissue The early time of incubation period starts on 5-6 days or the late time starts on 13 days. (Aidaros, 2003; OIE, 2009; Swanepoel, et al.1989) There are three different form (mild, moderate and severe). Initial semptom is not spesific. The first semptom is usually headache. Then fever increasing with tremor and cold, sore throat, malasie, fatigue, myalgia, junction pain. (Aidaros, 2003; OIE, 2009) These complaints may be along with vertigo, neck rigidity, photophobia, jaundice, vomiting-nausea, abdominal pain, diarrhea. Patient may have in condition like restless and emotion disorder (Peters, 2005; CDC,1988).

Patiens prone to bleeding . On 3trd-6th days of the disease, on the examination may reveal petechial rash both internal mucosal surface such as mouth, nose, stomach and external surface such as skin. Petechia can progress ecchymosis and it may occur big ecchymosis. It is seen commonly hemorrhagic findings such as epistaxis, haematemesis, melena, haematuria. It is revealed some internal bleeding suh as vaginal bleeding. Infection of the endothelium has a major pathogenic role. It is seen long protrombin time (PT), long activated partial tromboplastin time (aPTT) and long bleeding time, increased fibrin consumption products and low fibrinogen level. In disease's laboraratory findings show leukopenia and thrombocytopenia, but bleeding time can be normal level. Patient having severe clinical condition detected reduction eritrocyte number (Abram,1995; Capua,1998; Saijo,et al., 2002; Papa, et al., 2002).

Hepatic tissue can be affected absolutely. In most cases are detected increased liver enzyme value and hepatomegaly is detected 50% of cases. Serum transaminase value (ALT, AST ve GGT), CPK and LDH are high. (Abram, 1995; CDC,1988).

In serious cases may increase bilirubin, urea and creatinin value. (Abram, 1995). Severe cases can be progress hepatorenal syndrome and lung failure after 5th day (Abram, 1995; Capua,1998; Saijo, et al.,2002; Papa, et al.,2002). In terminal term can be progressed cardiovascular collaps, shock, hepatorenal failure and disseminated intravascular coagulation (DIC). Patients may die from brain failure, renal failure, cardiac failure and liver failure (Joubert, et al.,1985; Burney, et al., 1980). Mean mortality rate is 20-50%. Death is generally occur second weeks of disease. Mild and moderate clinical course can good progress about 9 or 10 days (Abram, 1995; Capua,1998; Saijo, et al., 2002; Papa, et al., 2002). Full recover duration occurs excess 2 weeks. Cured cases don't see sequele. (Aidaros, 2003; OIE, 2009; Swanepoel, et al.1989; Peters, 2005). The laboratory results of the cases at the beginning of clinical symptoms were summarized in Table 1.

Table 1. Laboratory results of the patients at the beginning of clinical symptoms.

Variables	Case 1	Case 2	Case 3	Case 4
<i>AST</i>	167	135	76	101
<i>ALT</i>	234	71	19	73
<i>CK</i>	-*	394	144	255
<i>INR</i>	1.01	1.0	0.98	1.15
<i>PT</i>	13.2	12.5	13.3	16.3
<i>aPTT</i>	25.2	39.5	33	48
<i>Platelet</i>	32.000	16.000	60.000	15.000
<i>WBC</i>	2.2	2.0	1.2	2.16
<i>Fibrinogen</i>	180	280	200	233

*Not detected

Case 1:

AD was fifty years old man and was a farmer. He was hospitalized to Andirin Hospital due to some complaints such as fever, headness, vertigo and nose bleeding. He stayed hospital for care about 5 days. On following, He was given 5 unit blood transfusion owing to nose bleeding. Due to continuing high fever and development bicytopenia patient was sent to our hospital. When the patient came to hospital, his condition was not bad, coopere and had conscious and oriente. On examination, his fever degree was 38.2°C, his blood pressure 80/60 mm/hg and his pulsation was 100/min. There were ecchimosi sites where blood was taken. On patient's anamnesia, there was biting tick. On his laboratory tests were ALT:(alanin transaminaz) 234U/L, AST (aspartat amino transaminaz):167U/L, Na:146 mEq/L, K:4.6 mg/dl, creatinine: 0.6, BUN:18mg/dl, Glukoz:90, Fibrinojen 180mg/dl INR 1.01., protrombin time (PT): 13.2 (%98) sec., active partial tromboplastin time (aPTT 25.2 sec., Hb:12.9gr/dl PLT:32.000/mm³, HCT:% 40.3, WBC: 2200/mm³ (PMNL 42:%, Lenf 47:%, Mon11:%) Patient was taken into isolation room. A consultaion was taken neurology department to investigate his vertigo complaint. Ciprofloksasin and clindamycin antibiotics was started because of his neutropenic parameter. On 5th days of following, the patient neutropenia and thrombocytopenia improved (WBC number:4.95, platelet number:145.000) and his fever became normal. He was discharged antiviral agent Ribavirin was not started, because he had applied very late to hospital. His blood test was determined positive for KKKA IgM and IgG and PCR test.

Case 2:

A G was sixty nine years old man and was a farmer. He was applied to Andirin Hospital due to some complaints such as fever, vomiting vertigo and malaise. The patient detected bicytopenia and fever was sent to our hospital. When the patient came to hospital his condition was not bad, coopere and had conscious and oriente On examination, his fever degree was 38.2°C, his blood tansion 80/60 mm/hg and his pulsation was

100/min. On patient's anamnesia, there was biting tick. On his laboratory tests were ALT: 71U/L, AST:135U/L, creatinine:1.2, BUN:14mg/dl, Lactic dehydrogenase (LDH):483U/L, creatinine kinase (CK):394U/L Fibrinojen 280mg/dl INR 1.01., PT 12.5 (%98) sec, aPTT 32 sec., Hb:16.7gr/dl PLT:77.000/mm³, HCT:% 51.5, WBC: 2000/mm³ (PMNL: 64%, Lymphocyte: 30%, Monocyte: 6%).

Patient was taken into isolation room. The patient was given supportive nutrition, electrolyte fluid therapy, protective stomach therapy and ribavirin treatment. Ciprofloksasin and clindamycin antibiotics was started because of his neutropenic parameter. Hepatomegaly was detected on ultrasonography. On 5th days of following, patient's mouth bleeding was started when thrombocytopenia (platelet score:16.000) and long of blood test was development. Then thrombocyte suspension was given and prednisolene was added to treatment. Thrombocyte numbers elevated high value (72.000) after 2 days. On 8th days of following, (progress on) when his fever became normal and his clinical course was good then he was discharged. His blood test was determined positive for KKKA IgM and IgG and PCR test.

Case 3:

FK was thirty four years old woman and was a farmer. She applied to Andırın Hospital after 3 days bited by tick. She had got some complaints such as fever, vomiting and nausea. On her laboratory test results, Patient was sent to our hospital with KKHA pre diagnosis. When the patient came to hospital, his condition was not bad, coopere and had conscious and oriente On examination, His fever degree was 38.3°C, his blood tansion 80/60 mm/hg and his pulsation was 92/min. On patient's anamnesia, there was biting tick. On laboratory tests were ALT:19U/L, AST:76U/L, Creatinin:0.9, BUN:14mg/dl, LDH:573U/L, CK:144U/L, Fibrinojen 233mg/dl, INR 0.98, PT 13.3 (%98) sec., aPTT 33 sec., Hb:13.7gr/dl PLT:98.000/mm³, HCT:% 51.5, WBC:1200/mm³ (PMNL:50.5%, Lenf:42.5%, Mon:6.6%) .

Patient was taken into isolation room. The patient was given supportive nutrition fluid, electrolyte fluid therapy, protective stomach therapy and ribavirin treatment. Ciprofloksasin and clindamycin antibiotics was started because of his neutropenic parameter. On following trombositopenia continued, thrombocyte number decreased to 60.000 and vaginal bleeding started and it continued 4 days. After ineffective metoclopramide therapy, Ondansetron was added because of more emesis. Fever became normal at the end of third day. Beginning of eight days, WBC (3380/mm³) and platelet (165.000/mm³) increased. On tenth days, the patient was discharged. After improvement of clinical and laboratory value. Her blood test was determined positive for KKKA IgM and IgG and PCR test.

Case 4:

KK was seventy four years old man and was a farmer. He applied Andırın Hospital after 3 days bited by tick. On that time, he had got some complaints such as fever, vomiting and nausea. According to her laboratory test results, Patient was sent to our hospital with KKHA prediagnosis. When the patient came to hospital his condition was not bad, coopere and had conscious and oriente. On examination, His fever degree was 38.2°C, his blood tansion 80/60 mm/hg and his pulsation was 100/min. On patient's anamnesia, there was biting tick. On his laboratory tests were ALT:73U/L, AST:101U/L, Creatinine:0.8, BUN:15mg/dl, LDH:356U/L, CK:255U/L Fibrinojen 200mg/dl INR 1.15 sec., PT 16.3 (%98) sec., aPTT 48 sec., Hb:13.7gr/dl PLT:53.000/mm³, HCT:% 48.8, WBC: 2160/mm³ (PMNL: 65%, Lenf:34%, Mon:1%) .

Patient was taken into isolation room. The patient was given supportive nutrition, electrolyte fluid therapy, protective stomach therapy and ribavirin treatment. Ciprofloksasin and clindamycin antibiotics was started because of his neutropenic parameter. On following neutropenia continued and platelet number decreased to 15.000 value. Platelet suspension was given because of PT elongation and thrombocytopenia. By third days, his fever degree became normal value. After nineth days, WBC (3530/mm³) and thrombocyte (152.000/mm³) number of patient increased (did high gradient). 12th days of following, patient had clinical convelans and normal laboratory value. It was agreed that he would discharge. His blood test was determined positive for KKKA IgM and IgG and PCR test.

DISCUSSION and CONCLUSION

Although, our cases are limited their course were mild form in a study assessing mortality of KKHA cases in Turkey was emphasized (highlighted) some risk factors (Ergonul, et al., 2006; Swanepoel, et al., 1989). Among the mortalities, haematemesis, melena and somnolence were more common, the median platelet count was significantly lower (10.600 /mL-20 000 /mL) the mean prothrombin time (27 h-16 h) and mean activated partial thromboplastin time (73h-44h) were longer, and the mean ALT level (1125-331), the mean AST level (3118-913) and the mean fibrinogen level (119-340) were higher (Ergonul, et al., 2006). The AST /ALT ratio was higher among severe cases than among mild-moderate cases for the first 3 days following admission (p< 0.022, 0.003 and 0.047, respectively). In multivariate analysis, an increased ALT (≥150Ü/L) and AST (≥200) were associated with a fatal outcome (p=0.007). Only one people had got high ALT (234 IU/mL) value. LDH and CPK levels among severe cases were higher than among mild-moderate cases, although this was not statistically significant (p > 0.05), (Ergonul, et al., 2004) .

In our cases were not severe clinical courses such as haematemesis, melena and somnolence Laboratory values was impressed at medium level.

Thrombocytopenia (15-60.000), mild PT elongation (12.5-13), medium aPTT elongation (25-48) The AST/ALT ratio were not high.

Exact assessment is not possible due to case numbers are only four, but Kahramanmaras's cases had mild course.

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