

Follow-up of patients with tick bite in terms of Crimean Congo hemorrhagic fever: Is tick bite enough for diagnosis?

Kene ısırığı olan hastaların izlemi: Kırım Kongo gelişimi için ısırık yeterli mi?

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Abstract

Crimean-Congo hemorrhagic fever (CCHF) is a multi-systemic tick born viral disease caused by a Nairovirus of the Family Bunyaviridae. Findings of disease are with fever, myalgia, chills, headache, vomiting and hemorrhagic manifestations. Infection is transmitted to humans by tick bite or by close contact with freshly slaughtered meat or blood from viremic animals. Since the tests of virus load consume much time, we preferred to study whether the findings obtained from anamnesis and physical exams of patients would be beneficial in predicting the clinical courses of patients. Files of 13 cases, who admitted to our clinic in the years 2006-2007 with the complaint of tick bite, were examined in this study. Anamnesis, physical and laboratory findings were recorded. Eleven of the cases were male. The age average was found to be 8.4 years (3-15). The period of first reference to our clinic was 3.4 days (1-8) on average. Bite size were 0.7 mm (0.4-1.4). The biggest bite was related to an adult tick. While serologic tests from the cases were found to be negative in twelve cases (92.3%), CCHF Immunoglobulin M taken on the third day was positive in one case (7.7%). This case was the one with biggest bite. In conclusion, the severity of the findings of CCHF is in correspondence with the size of virus load transferred. According to this study findings, size of tick and tick bite may be informative about the virus load and indirectly about the clinical outcome. Recording these findings for the future cases would be advised.

Keywords: Tick bite size, Crimean-Congo Hemorrhagic Fever, children

Özet

Kırım Kongo kanamalı ateşi (KKKA) multisistemik kene kaynaklı Bunyaviridae ailesinden Nairovirus kaynaklı bir viral hastalıktır. Hastalığın bulguları arasında ateş, miyalji, titremeler, baş ağrısı, kusma ve hemorajik bulgular yer alır. Enfeksiyon insanlara keneler vasıtasıyla veya yeni enfekte olmuş et veya viremik hayvanların kanlarına yakın temas ile bulaşır. Hastalığın tanısında kullanılan testlerin sonuçlanması uzun sürebildiğinden bu çalışmada anamnez ve erken klinik ve laboratuvar bulgularının hastalığın seyri hakkında faydalı bilgiler verebileceğini düşünülerek bu bulgular analiz edildi. Kayıtlarına ulaşılabilen 2006-2007 yıllarında kene ısırığı nedeniyle başvurmuş olan 13 çocuk hastanın anamnez, fizik inceleme ve laboratuvar bulguları kaydedildi. Hastaların 11 tanesi erkekti. Ortalama başvuru yaşı 8,4 yıl (3-15 yıl) idi. Isırktan sonra hastaneye ortalama başvuru süresi 3,4 gün (1-8) idi. Ortalama ısırık boyutu 0,7mm (0,4-1,4mm) idi. En büyük ısırığın bir erişkin keneye ait olduğu saptandı. Bu hastada aynı zamanda KKKA açısından seropozitiflik saptandı. Diğer 12 hastanın KKKA immunoglobulin M sonuçları negatif olarak saptandı. Sonuç olarak, KKKA bulgularının ciddiyeti hastaya ulaşan virüs yükü ile paraleldir. Bu çalışmanın sonuçlarına göre kenenin ve ısırığın boyutu hastaya aktarılan virüs yükünün ve klinik seyrin erken dönemde tahmin edilmesine yardımcı olabilecek bilgilerdir. Bu hasta grubunda başvuru süresi ve ısırığın boyutunun kaydedilmesi bu hastaları ilk gören klinisyenlere tavsiye edilebilir.

Anahtar kelimeler: Kene ısırığı boyutu, Kırım Kongo Kanamalı Ateşi, çocuklar

Introduction

Crimean-Congo hemorrhagic fever (CCHF) is a tick-borne often fatal multi-systemic viral zoonosis caused by a Nairovirus of the Family Bunyaviridae (1-5). CCHF is an endemic infection which occurs in Eastern Europe, Asia, Africa and the Middle East. Sporadic cases are being reported in many parts of the world (1-4). CCHF is transmitted to humans by; tick bite, crushing infected ticks, close contact with freshly slaughtered meat or a patient with CCHF during acute phase and blood from viremic animals such as

sheep, cattle and goats or nosocomially (1-5). Ticks are second only to mosquitoes as vectors of human infectious diseases in the world (6). Tick is a parasite fed with blood, with no eyes, unable to fly or jump (3). Nymphs are immature ticks. Among thirty tick species, Hyalomma has importance in terms of public health since they are able to vector the Nairoviruses (6).

Crimean-Congo hemorrhagic fever begins with such symptoms as acute high fever, myalgia, chills, headache, nausea, vomiting, diarrhoea, hemorrhagic manifestations such as hemophagocytosis and then

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could lead to capillary leak syndrome and even hypotensive crisis due to severe haemorrhage in gastrointestinal system, nose, mouth and uterus (7). CCHF is listed under hemorrhagic fever group with a fatality level of 30% (8-80%) (2).

Definite diagnosis can be made specifically by the isolation of virus from blood and tissues, and by manifesting viral antigens and antibodies. Virus can be isolated through such cell cultures as tissue and blood specimens VeroE6, BHK-21, SW 13 in the first 5 days of the disease. Among the serologic methods, Elisa A is frequently utilized. With this method, immunoglobulin M antibodies from the 5th-7th days of the disease, and immunoglobulin G antibodies from the 10th day can be established in the serum. Ig M antibodies could remain positive in serum for 4 months, and this period is 5 years for Ig G antibodies. Polymerized chain reaction (PCR) which is a test finding the viral antigen on the first 5-6 days plays a significant role in diagnosis (5,8). The severity of findings of the disease is correlated with the amount of virus load transferred to the patient (9,10). Elisa studies used for diagnosis and sophisticated PCR methods are used to quantify the virus load but these tests consume much time and clinical findings of the disease are not specific at the initial stage of CCHF.

Although many children apply to the emergency department with tick bite every child does not develop CCHF. Diagnostic tests of CCHF are studied at sophisticated central laboratories and results appear after a period. In this time period the lack of diagnostic follow up laboratory tests makes the management of the these children with the suspicion of CCHF a stumbling point. In patients with clinically deteriorated faster, we had observed that the size of tick bite was bigger and removal time was later. In order to check this observation scientifically we planned to compare the patients' application findings such as the size of tick bite and laboratory deterioration follow up results. In most clinical instances objective data related with tick type, tick bite size and removal time are not efficiently recorded.

The objective of this study was to investigate the clinical follow-up results of children with tick bite and search the relation of clinical and laboratory parameters with the tick bite size and maturation stage of tick and serologic diagnostic tests (10).

Materials and Methods

Clinical findings and files of 13 cases who admitted to department of pediatrics with the complaint of tick bite during time period of 2006-2007 with the complaint of tick bite were analyzed. Anamnesis related with type of tick, period before removal of tick, physical (bite size) and laboratory findings at application and follow-up results were recorded. The means of recorded values related with anamnesis,

physical and laboratory findings of cases with laboratory deterioration at initial and follow-up period were compared with the findings of cases without laboratory deterioration. Eleven of the cases were male, and 2 of them were female. The age average was found to be 8.4 years (3-15 years). Eight cases were admitted from Ankara and its districts (61.5%), two of them were from Çankırı (15.3%), one from Yozgat (7.6%), one from Ordu (7.6%), and one from Kırıkkale (7.6%). Local ethics committee was approved the study.

Results

The period of first admission from tick bite to our clinic was 3.4 days (1-8 days) on average. Mean tick bite size was 0.7 mm (0.4-1.4). The biggest size was related to an adult tick. Ticks were removed by physicians in the hospital in seven cases (53.6%), and families of patients in other six (46.2%).

In history of one case, there was vertigo, nausea, myalgia, and feeling of numbness on the bitten spot (7.6%). Physical exam revealed subaxillary fever of 38.2°C in three cases (23%). In another case, a three-day thrombocytopenia (85.000/mm³) and leucopenia (3200/mm³) were observed in laboratory findings (7.6%).

In seven of 13 cases different laboratory parameters were deteriorated and there was only one serology positive case in this group. In one case (7.6%), a six-day high level of liver transaminases, an average two-day high level PT and PTT in 6 cases were other observations. While serologic tests from the cases were found to be negative in twelve cases (92.3%), CCHF IgM taken on the third day was positive in one case (7.7%). Even though this case did not have any clinical complaints, transaminases were high (ALT 83 U/L, AST 98 U/L). In the follow-up of the case with negative hepatitis markers, laboratory findings went back to normal on the fifth day. During their hospital stay, contact isolation was applied to all the cases. The average hospital stay of the cases was 7.3 days. All the cases were reported to the Ministry of Health. Mean time of tick removal is 3.46 hours (1-8 hr), 10 of 13 ticks were seen by clinicians and typed. 7 of 10 ticks were nymphs, 3 of 10 were adult ticks, mean size of tick bite was 0.83 mm (0.4-1.8 mm). The largest bite size was 1.8 mm (patient 10, Table 1) and it was detected on serologically positive patient. Mean bite size in patients with laboratory deterioration were higher than the patients without laboratory deterioration (1.14±0.36 (0.8-1.4) and 0.48±0.36 (0.4-0.6) mm consecutively), (p<0.05), (Table 2). Also the mean removal time was higher in cases with laboratory deterioration (4.71±2.28 (2-8) and 2±1.26 (1-4) hours consecutively), (p<0.05), (Table 2).

Table 1. Clinical and laboratory characteristics of patients

No	Case	Tick removal time (hours)	Tick Type	Bite Size (mm)	Clinical Symptoms	Clinical Signs	Lab Deterioration	Serology
1	Y.E.A	8	Nymph	0.9	-	-	PT,PTT	-
2	K.Ö	7	Unknown	0.8	-	-	PT,PTT	-
3	M.E.A	3	Nymph	0.4	-	-	-	-
4	S.E	4	Nymph	0.4	-	-	-	-
5	M.Ç	6	Unknown	1.1	-	Fever	PT,PTT	-
6	O.Ö	4	Nymph	0.8	-	-	PT,PTT	-
7	N.G.Y	1	Nymph	0.5	-	-	-	-
8	S.A	1	Nymph	0.5	-	-	-	-
9	B.A	3	Adult	1.2	-	-	WBC,PT,PTT	-
10	H.İ.İ	2	Adult	1.8	-	-	AST,ALT	+
11	A.T	2	Adult	0.6	-	Fever	-	-
12	B.K	3	Unknown	1.4	+	Fever	PT,PTT	-
13	H.E.S	1	Nymph	0.5	-	-	-	-

Table 2. Comparison of Patients According to Laboratory Deterioration

	Laboratory Deterioration		p
	(+) (n=7)	(-) (n=6)	
Bite size(mm) mean±SD (min-max)	1.14±0.36 (0.8-1.4)	0.48±0.36 (0.4-0.6)	<0.05
Removal time (hour) mean±SD (min-max)	4.71±2.28 (2-8)	2±1.26 (1-4)	<0.05

Discussion

The results of this retrospective study reveal that every tick bite does not progress to the CCHF disease. Clinical presentation findings gathered during the emergency service such as type and removal type of tick and size of tick bite might be valuable for assessing and predicting about clinical prognosis.

It was significant to see that the bite size on our serologically positive CCHF patient was the largest (patient 10, Table 1). The results of this study as shown in Table 2 reveals that the ticks with big bite size and lately removed seems to be causing higher frequency of laboratory deterioration ($p < 0.05$). The incubation period of CCHF, which generally follows an asymptomatic course, is 1-3 days (maximum 9) and 5-13 days in nosocomial infection. In this asymptomatic period the findings such as size of bite and removal time may be used as simple but rough clues for deterioration risk of patient clinic they may reflect clinical and laboratory outcome and assessing the prognostic course of the case. From the fifth day on ward, hepato-renal and pulmonary failure and disseminated intravenous coagulation picture might develop due to liver and endothelial exhaustion and thrombocytopenia. Death mostly occurs on the 5th-14th days (5).

Based on the findings obtained from a previously conducted study, if the virus count is 1×10^9 copy/ml and above the disease will have a fatal course (9,10). This is probably true for adult ticks which are bigger in size (12 mm) compared to nymphs (5 mm) and able to suck more blood. Again, if the tick stays longer on human skin, the amount of transferred viral load and infection risk would also increase. Even clinicians do not see the ticks they may decide about the type of tick by examining the size of tick bite. This information may be useful in case of crowded populations in order to predict clinical

outcome and help for deciding about the cases for follow up and hospitalize.

The case number of our study is relatively small but since the reported paediatric cases in literature are small in number the findings could be meaningful for the clinicians who are scarcely seeing this group of patients.

Because species and size of the tick bites, and the time period after the bite could help in predicting the severity of clinical courses of the patients, keeping a record of these data would create an opportunity for making diagnosis early and predicting the clinical progress of patients especially the ones with worse prognosis supporting appropriate treatment.

References

- Mostafavi E, Pourhossein B, Chinikar S. Clinical symptoms and laboratory findings supporting early diagnosis of Crimean-Congo hemorrhagic fever in Iran J Med Virol 2014;86(7):1188-92.
- Ergonul O. Crimean-Congo haemorrhagic fever. Lancet Infect Dis 2006;6(4):203-14.
- Gozalan A, Esen B, Fitzner J, Tapar FS, Ozkan AP, Georges-Courbot MC, et al. Crimean-Congo haemorrhagic fever cases in Turkey. Scand J Infect Dis 2007;39(4):332-36.
- Karti SS, Odabasi Z, Kortten V, Yilmaz M, Sonmez M, Caylan R, et al. Crimean-Congo hemorrhagic fever in Turkey. Emerg Infect Dis 2004;10(8):1379-84.
- Whitehouse CA. Crimean-Congo hemorrhagic fever. Antiviral Res 2004;64(3):145-60.
- Ahmed J, Alp H, Aksin M, Seitzer U. Current status of ticks in Asia. Parasitol Res 2007;101(Suppl 2):S159-62.
- Papa A, Bino S, Liagami A, Brahimaj S, Papadimitriou E, Pavlidou V, et al. Crimean-Congo hemorrhagic fever in Albania, 2001. Eur J Clin Microbiol Infect Dis 2002;21(8):603-6.
- Vorou R, Pierrotsakos IN, Maltezou HC. Crimean-Congo hemorrhagic fever. Curr Opin Infect Dis 2007;20(5):495-500.
- Cevik MA, Erbay A, Bodur H, Eren SS, Akinci E, Sener K, et al. Viral load as a predictor of outcome in Crimean-Congo hemorrhagic fever. Clin Infect Dis 2007;45(7):e96-100.

10. Duh D, Saksida A, Petrovec M, Ahmeti S, Dedushaj I, Panning M, et al. Viral load as predictor of Crimean-Congo hemorrhagic fever outcome. Emerg Infect Dis 2007;13(11):1769-72.

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