Investigation of Cases with Tick Attachment at the Emergency Department

Acil Servise Gelen Kene Tutunması Olgularının İncelenmesi

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Geliş Tarihi/*Received:* 17.07.2012
Kabul Tarihi/*Accepted:* 12.07.2013

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ABSTRACT Objective: Tick-borne diseases and especially Crimean-Congo Hemorrhagic Fever (CCHF) are serious epidemiological problems in many parts of the world. In this study, we aimed to emphasize the importance of an emergency approach to treat these diseases and to stress the importance of identifying characteristics of patients who are admitted to the hospital for tick attachment. **Material and Methods:** This study included 336 patients who admitted to Uludag University Medical Faculty Hospital Emergency Department (ED) and presented with tick attachment between April 2009 and May 2010. Patient demographics, clinical and laboratory findings and follow-up data were recorded. Laboratory parameters of hospitalized patients and non- hospitalized patients were statistically compared. **Results:** The mean age of the patients was 43.85±13.88 years. Males comprised %50.9 of the patients. The most common months for hospital admission for tick attachment were July (33.0%) and August (32.4%). Of total, %49.1 of the patients acquired the tick in urban areas while %35.4 of them acquired it in the rural areas such as picnic areas, forest, field or animal shelters. The tick attachments were found in the lower extremities in 27.4% of the patients. In 65.5% of patients, the tick was removed by a physician in the ED using a forceps (54.2%) which was the most commonly used tool for tick removal. Laboratory parameters [aspartate transaminase (AST), alanine transaminase (ALT), lactate dehydrogenase (LDH), creatine phosphokinase (CK), white blood cell, neutrophil and platelet counts, prothrombin time (PT), activated partial thromboplastin time (aPTT) and the international normalized ratio (INR)] of the hospitalized patients who were suspected CCHF were statistically significantly different when compared to the ones who were not hospitalized. **Conclusion:** In tick attachment cases who admitted to the ED, decreased levels of thrombocyte, leukocyte and neutrophil counts and increased levels of AST, ALT, LDH, CK, aPTT, PT and INR are significant for CCHF. An emergency department physician should be alert for these results.

Key Words: Ticks; emergency medicine; hemorrhagic fever virus, Crimean-Congo

ÖZET Amaç: Kene vektörlüğü ile bulaşan hastalıklar özellikle Kırım-Kongo Kanamalı Ateşi (KKKA) dünyanın birçok yerinde ciddi bölgesel epidemiyolojik problemdir. Bu çalışmada Uludağ Üniversitesi Tıp Fakültesi (UÜTF) hastanesi Acil Servis (AS)'ine kene tutunması nedeniyle başvuran olguların demografik özelliklerinin belirlenmesi, izlem ve tetkik sonuçlarının değerlendirilmesi ve kene tutunmasına acil yaklaşımın öneminin vurgulaması amaçlanmıştır. **Gereç ve Yöntemler:** Çalışmaya Nisan 2009- Mayıs 2010 tarihleri arasında UÜTF AS'ine kene tutunması şikayeti ile başvuran 336 hasta alındı. Hastaların demografik özellikleri, klinik, laboratuar bulguları ve izlem verileri kaydedildi. Hastaneye yatırılan ve taburcu edilen hastaların laboratuar parametreleri istatistiksel olarak karşılaştırıldı. **Bulgular:** Çalışmaya alınan hastaların yaş ortalaması 43,85±13,88'idi. Hastaların %50,9'u erkekti. En sık başvuru Temmuz (%33,3) ve Ağustos (%32,7) aylarında oldu. Hastaların %49,1'inde kene tutunması yerleşim yerinde, %35,4'ünde piknik alanları, hayvan barınağı, orman, tarla gibi kırsal alanlarda meydana gelmişti. Olgularının %27,4'ünde kene alt ekstremiteye tutunmuştu. Kenelerin %65,5'i AS'de doktor tarafından çıkarılmıştı ve çıkartma yöntemi olarak en sık %54,2 oranında forseps kullanılmıştı. KKKA şüphesi ile hastaneye yatırılan olguların laboratuar parametreleri [aspartat transaminaz (AST), alanin transaminaz (ALT), laktat dehidrogenaz (LDH), kreatin fosfokinaz (CK), lökosit, nötrofil, trombosit, aktive parsiyel promboplastin zamanı (aPTZ), protrombin zamanı (PT), international normalize ratio (INR)], hospitalize edilmeyen olgularınkinden istatistiksel olarak anlamlı derecede farklı idi. **Sonuç:** Acil servise başvuran kene tutunması olgularının laboratuar incelemesinde trombosit, lökosit ve nötrofil sayılarının düşük olması; AST, ALT, LDH, CK, aPTT, PT ve INR değerlerinin yükselmesi, KKKA hastalığı açısından önemlidir. Bir acil hekimi bu açıdan uyanık olmalıdır.

Anahtar Kelimeler: Keneler; acil tıp; hemorajik ateş virüsü, Kırım-Kongo

doi: 10.5336/medsci.2012-31397

Turkiye Klinikleri J Med Sci 2013;33(5):1209-15

Because the incidence of tick-borne diseases, especially Crimean-Congo Hemorrhagic Fever (CCHF) has been increasing in our country and worldwide, understanding tick and tick-borne diseases is becoming increasingly important. It is well recognized that ticks are the most important vectors of disease in Europe, and when compared to the other vectors, they play role in the transfer of a great number of pathogens.[1,2]

The main diseases transmitted by ticks are ricketsiosis, typhus, tick-borne encephalitis, babesiosis, Lyme disease, borreliosis, ehrlichiosis, tularemia and viral hemorrhagic fever. In areas endemic with ticks, increasing the public awareness for these diseases is very important for public health.[3] Since CCHF is a not a well known disease causing death in recent years in our country, it is recommended that people with cases of tick adhesion should seek medical attention. It is extremely important to understand the properties of tick-borne diseases and tick vectors to prevent disease transmission.

In this study, we aimed to emphasize the importance of an emergency approach to treat this disease and to stress the importance of identifying characteristics of patients who are admitted to the hospital for tick attachment and the importance of identifying patient demographics.

MATERIAL AND METHODS

This study was performed at the Emergency Department (ED) at the Uludag University Medical Faculty, and was approved by the Medical Research Ethics Committee (2009-8/33). In this prospective and observational study, we examined the characteristics of tick-borne diseases between April 2009 and May 2010. Three hundred and thirty-six patients who were over 18 years of age, complained of a tick-borne disease, and signed the informed consent form voluntarily participated in this study. Non-hospitalized patients were excluded from follow-up.

Patients complaining of the tick-borne disease were evaluated in the ED by the resident responsible for this study, and then treated with necessary interventions. Ticks were removed by a resident in the ED and the region of attachment was cleaned with antiseptic solutions. Patients were evaluated for tetanus prophylaxis, and if necessary, prophylaxis was administered.

Complete blood count (CBC), urea, creatinine, aspartate transaminase (AST), alanine transaminase (ALT), lactate dehydrogenase (LDH), creatine phosphokinase (CPK), prothrombin time (PT), activated partial thromboplastin time (aPTT) and the international normalized ratio (INR) were evaluated from venous blood samples obtained from the patients. Doxycycline (100 mg) twice daily for 3 days was prescribed to the patients with normal laboratory results, and the non-hospitalized patients with a recommendation to contact the Department of Infectious Diseases. The patients with pathologic results were consulted with the Infectious Diseases Department.

The information of the patients who participated in the study included: age, gender, date of birth, occupation, date of arrival, tick contact date, place the event occurred, tick's attachment place on the body, method of removal, tick's shape, presenting complaint and physical examination findings.

We compared the laboratory parameters (CBC, urea, creatinine, AST, ALT, LDH, CPK, PT, aPTT and INR) of hospitalized and non-hospitalized patients.

STATISTICAL ANALYSIS

SPSS 13.0 packet program was used for the statistical analysis. According to the specifications of variation in this study, descriptive statistics and frequency distributions were calculated. All data were expressed as the mean±standard deviation (SD), minimum-maximum value and median value. Categorical variables were compared with the Mann Whitney U test. A statistical significance of $p<0.05$ was considered to be statistically significant.

RESULTS

The 336 patients enrolled in this study had a mean age of 43.85±13.88 years. Females comprised 49.1%

of the study population. Regarding the age distribution, the most common age range in patients presenting with a tick attachment was 30-39 years (28%) (Figure 1). According to the arrival month, July (33.0%) was the most common month for presentation and the others were August (32.4%) and September (21.7%) (Figure 2).

We determined where the tick attached in each patient, and the results showed that 49.1% were acquired from urban areas 16.6% were acquired in a field, 8.6% were from a forest, 7.4% were acquired in a park and 3.3% were from a animal shelters. The remaining 15.5% were acquired in other places. The site of tick attachment was the lower extremities in 27.4%, upper extremities in 16.4% and abdomen 14.6% of the patients (Figure 3). Of the patients with ticks on their body, 65.5% visited the ED and 19% of them brought the tick with them after removing the tick by themselves. Sixteen percent of the patients gave a tick bite history. For removing ticks, forceps were used in 54.2% of patients, a punch biopsy was performed in 6.8%, a rope method was used in 2.7% of patients and the remaining 36.3% of patients used other methods to remove the tick (e.g., patients and their relatives used tweezers or a needle).

In our study, 30 patients had other complaints in addition to tick attachments. These complaints were classified as fatigue (3.2% of cases), fever (2.6%), abdominal pain (1.4%), nausea and vomiting (1.1%), joint pain (1.1%), flu-like symptoms (1.1%), bleeding (0.9%), headache (0.9%), rash (0.9%), diarrhea (0.6%), myalgia (0.3%) and other symptoms (3.5%). Seven of 30 patients were hospitalized and 23 patients were non-hospitalized

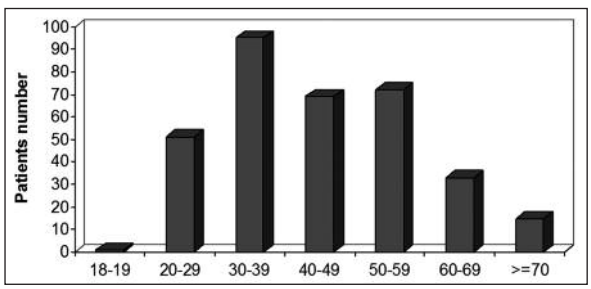

FIGURE 1: The distribution of patients according to age groups.

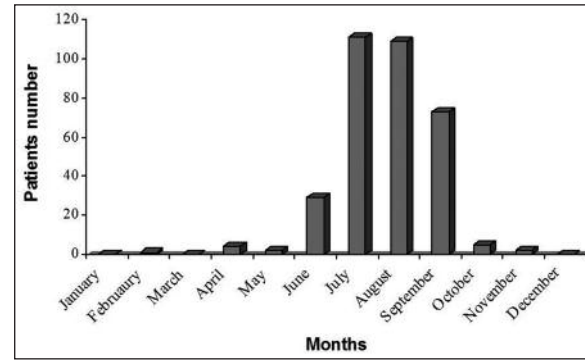

FIGURE 2: The distribution of patients according to the months.

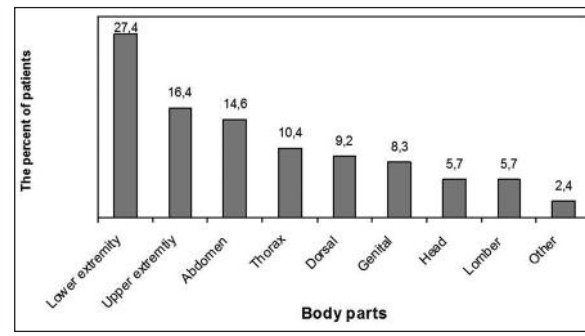

FIGURE 3: Results for the distribution of tick-based adhesion to body parts

with further recommendations. Nine patients had positive physical examination findings, including subfebrile fever in five patients, hypotension in four patients, rash in three patients and epistaxis in two patients.

Comparison of laboratory test results between hospitalized and non-hospitalized patients revealed that AST, ALT, LDH, CK, WBC, neutrophil, platelet, PT, aPTT and INR values were statistically significantly different between these two groups ($p < 0.05$) (Table 1). During this study in our hospital, six patients had a presumed diagnosis of CCHF-rickettsial infection and one patient was referred to the State Hospital for treatment. The remaining 329 patients were prescribed doxycycline and discharged with the recommendations to consult the Infectious Diseases Department. Laboratory parameters in 7 patients with a presumed diagnosis of CCHF included leukopenia (82.6%) in 6 patients, thrombocytopenia (71.4%) in 5 patients and 1 patient had a low hemoglobin level (14.2%).

TABLE 1: Comparison of biochemical parameters.

Biochemical Parameters	Hospitalized patients (n=7) Median (minimum-maximum)	Non-hospitalized patients (n=329) Median (minimum-maximum)	p
AST (IU/L)	71 (24-3580)	20 (10-68)	<0.001*
ALT (IU/L)	35 (14-1383)	18 (10-123)	0.019*
LDH (IU/L)	406 (198-3624)	198 (17-435)	0.001*
CK (IU/L)	617 (34-1526)	102 (9-1305)	0.019*
WBC (K/mm^3)	3070 (730-5540)	7240 (1240-15200)	<0.001*
Neu (K/mm^3)	1580 (254-3840)	4020 (1440-12700)	<0.001*
RBC (K/mm^3)	4.84 (1.72-5.24)	4.71 (3.14-6.55)	0.368
Hgb (g/dl)	12.7 (2.82-15.40)	13.8 (7.82-18.7)	0.143
Hct (%)	37.9 (9.46-47)	40.5 (26.8-55.1)	0.114
Plt (K/mm^3)	107000 (8780-255000)	257000 (31000-2930000)	<0.001*
PT (sec)	11.7 (10-19.7)	11 (8.55-18.9)	0.038*
aPTT (sec)	25 (23.2-40.6)	23.4 (10.4-48.7)	0.018*
INR	1.12 (0.97-2.12)	0.99 (0.3-11.2)	0.004*

AST: Aspartate aminotransferase; ALT: Alanine transaminase; LDH: Lactate dehydrogenase; CK: Creatine phosphokinase; PT: Prothrombin time; aPTT: Activated partial thromboplastin time; INR: International normalization ratio; WBC: Beyac blood cells; Neu: Neutrophil; RBC: Red blood cells; Hgb: Hemoglobin; Hct: Hematocrit; PLT: Platelet; IU: International unit; K: Concentration, *p<0.05.

DISCUSSION

Ticks can transmit a variety of viruses, bacteria or parasites that can cause serious infections or diseases in humans and animals.[4] One of these diseases is CCHF. CCHF threatens public health and can lead to epidemics and carries a risk of high fatality (10-50%).[5] In Africa, Asia, Western Europe and the Middle East, CCHF is known as a fatal viral infection. In our country, after a medical staff member died in 2002, research was initiated to help recognize this disease for the first time.[6] Written and visual media has reported on tick adhesions and deaths. Thus, in a society with serious concerns regarding this issue, the population has developed an awareness of ticks and tick-borne diseases. In addition, the cases admitting to Emergency Services increased.[7-11]

In the literature, there have been various studies based on demographic characteristics of patients with tick-borne diseases.[12-14] The mean age of the patients ranged between 6.7 and 46.5 years in these studies.[12-17] Because the patients in the pediatric age group were observed by the Children's Emergency Service, they were not included in this study. The average age of patients was 43.85±13.88 years (min: 18 years, max: 79 years) and most applicants were 30 -39 years old (28%), which is consistent with the reported findings. When the sex distribution of patients with tick-borne disease is considered, different ratios were observed in men and women.[12-14] Although some studies suggest that males and females were equally affected, other studies revealed that there was a higher incidence in men.[13,17-21] For example, a study from Sri Lanka determined that there was a high incidence in women.[14] Our study indicatesd that 49.1% of cases were women and 50.9% of cases were men.

Some occupations, such as forestry, farm work and animal husbandry may be classified as risk factors for tick attachment and tick-borne diseases. Additionally, activities such as gardening, picnicking, hiking, fishing and hunting can increase the risk for tick attachment and tick-borne diseases.[22] However, in recent years, tick attachment is not just a problem for people living in rural areas; it is also a problem for people living in big cities. The risk of tick attachment depends upon several parameters including the prevalence of a tick species, their abundance, and their preferences towards humans as hosts. Al et al. reported that 82.05% of patients were living in rural areas, handled animals

or visited rural areas in the last two weeks.[13] Other studies also reported that patients with tick attachment, admitted to the hospital, were living in villages or rural areas.[16,18] In our study, 49.1% of the patients with tick attachment were living in urban areas and the remainder of cases (50.1%) acquired ticks from picnic areas, farms, forests and animal shelters; these rates are close to those reported in the literature.

In our country, several studies have evaluated patients who live in a different geographic regions and admitted to the hospital for tick attachments. The results showed that the tick settled on various places on the body. There are several studies investigating tick attachments according to body parts.[13,23] Gunduz et al. determined that tick bites were present on the leg, foot, abdomen and groin region in 67 patients.[23] Al et al. found that the most common regions were the head, neck, legs and thighs.[13] Additionally, in the other studies, Taskesen et al. showed that the most common region was the leg (37%) and the body (21%).[10] Sümer found that the leg (34.52%) and the body (11.9%), were the most common regions for tick attachment and Kandis et al. showed the leg (23.2%) as the most common region for tick attachment.[16,18] It is important to know the most common locations for tick attachments to prevent them. It is said that because 20% of ticks were attached to the body in a location where they cannot be visualized by the patient, in order to detect tick attachments in endemic areas, it is necessary to examine the entire body surface.[23] In our study, we found tick attachments on the lower extremities (27.4%), upper extremities (16.4%) and abdomen (14.6%). We believe that the reason for the common observations of ticks on these parts of the body is because it is easy for the tick to attach to the host while he/she is close to the ground. It is especially easy for the tick to attach to uncovered parts of the host's body.

In the examination of cases to determine the intensity of tick attachments in Turkey, the most frequent attachments were reported in August.[24] However, studies in Turkey showed the increase in activities of vector ticks due to the temperature. Furthermore, the disease shows seasonal features and has generally been reported during June-September in the Black Sea region and during April-August.[25] Kartı et al. described that most patients visited the hospital in May and August.[6] Al et al. reported that the ratio was highest (69.23%) in June and July.[13] On the other hand, Arıkan et al., Kandiş et al., and Sümer reported that the tick attachment ratio was the highest in May and August.[16,18,19] In our study, patients presenting with tick attachments were most common in July (33.0%) and August (32.4%), as reported in the literature.

Removal of ticks must be performed as soon as possible and by a physician.[11] Al et al. reported that 64.1% of ticks were removed in a hospital by a doctor and 35.9% of the ticks were removed by the patient or their relatives.[13] According to Kandis et al., 552 patients (86.1%) were admitted to the hospital with tick attachments and ticks were removed by a physician in the ED.[16] Yardan et al. also determined that 25.1% of patients with tick attachments had their ticks removed by a doctor in a heath facility unit.[15] The other 38.8% of patients had their ticks removed by a doctor working in an ED. In our study, we discovered that in the majority of cases with tick attachments, the ticks were removed in a health facility unit or were removed by the patient himself or by a relative. Two hundred and twenty-two patients (65.5%) participating in this study were admitted to the hospital with a tick on their body and the tick was removed at the ED by the physician working in the ED.

Today, the most recommended method for tick removal is mechanical removal. Ticks cannot be removed with bare hands.[11] Patients with suspected non-removable ticks should have their tick removed with an excisional biopsy to preserve the purity of the tick, and the remaining tissue should be removed. After removing the tick, the area should be cleaned with a disinfectant. The best method for removing the tick is use of blunt forceps. Celebi et al. used forceps to remove ticks in 70% of cases and used the tickmatic in 30% of cases.[26] In our study, 54.2% of cases in the ED used forceps to remove the ticks. In the other cases (36.3%), tweezers or needles were used by the patient or a relative, to remove the tick.

CCHF disease transmitted by vector ticks is usually characterized by fever and bleeding and leads to severe clinical pathology in humans, and sometimes to death. The disease includes fever, widespread pain in the body, nausea, vomiting, abdominal pain, diarrhea, bleeding and bruising. Additionally, intra-abdominal bleeding, abdominal pain and acute abdomen syndrome may occur.[27,28] In the study by Al et al., except for one case, none of the 39 cases were associated with tick attachments.[13] Patients admitted to the hospital with complaints such as fatigue, abdominal pain and subfebrile fever were not connected with a tick-bite and therefore they were not hospitalized. Six patients with pathologic physical examinations and laboratory findings, who also had more than one complaint, were treated in our hospital. One patient had been hospitalized in the state hospital infectious diseases clinic. Nine patients in this study had pathologic evidence on physical examination. The results indicated subfebrile fever in five patients, hypotension in four patients, rash in three patients and epistaxis in two patients. However, in two patients with a hyperemic rash caused by the tick's attachment, there were no laboratory findings suggestive on CCHF- Rickettsia disease; these patients were not hospitalized.

Increased levels of AST, ALT, LDH and CK and low platelets and white blood cell counts are important in patients with tick attachment and for tick-transmitted diseases in terms of biochemical tests.[28] In CCHF cases, leukopenia, thrombocytopenia, AST, ALT, LDH, PT and APTT increases are noted in various publications.[28,29,30] In our study, when we compared biochemical parameters of the hospitalized and non-hospitalized patients, AST, ALT, LDH, CK, WBC, neutrophils, platelets, PT, aPTT and INR values were significantly higher in the hospitalized patients. Seven of the patients with a presumed diagnosis of CCHF were hospitalized and test results confirmed a diagnosis of CCHF in 3 patients. All patients were discharged and only 3 of these patients had a definitive diagnosis of CCHF as a result of further investigations.

LIMITATIONS

The limitations of this study are as follows: study is performed in a single center, including patients only ≥18 years of age and not classifying the ticks.

CONCLUSION

In tick attachment cases who admitted to the ED, decreased levels of trombocyte, leukocyte and neutrophil counts and increased levels of AST, ALT, LDH, CK, aPTT, PT and INR are significant for CCHF. An emergency department physician should be alert for these results.

Ticks should be removed as soon as possible, the area should be cleaned and alcohol should be poured on the tick. One should try to keep the tick alive during removal. Asymptomatic patients with CCHF should be informed about tick attachments and outpatient visits should be performed as early as possible.

REFERENCES

1. Parola P. Tick-borne rickettsial diseases: emerging risks in Europe. Comp Immunol Microbiol Infect Dis 2004;27(5):297-304.
2. Estrada-Peña A, Jongejan F. Ticks feeding on humans: a review of records on human-biting Ixodoidea with special reference to pathogen transmission. Exp Appl Acarol 1999;23(9): 685-715.
3. Randolph SE. Evidence that climate change has caused 'emergence' of tick-borne diseases in Europe? Int J Med Microbiol 2004; 293(Suppl 37):5-15.
4. Göksu K, Tüzer E. [The importance of diseases caused by ticks and ticks]. İstanbul Univ Vet Fak Derg 1981;7(1):69-113.
5. Vatansever Z, Gargili A, Aysul NS, Sengoz G, Estrada-Peña A. Ticks biting humans in the urban area of Istanbul. Parasitol Res 2008;102(3):551-3.
6. Karti SS, Odabasi Z, Korten V, Yilmaz M, Sonmez M, Caylan R, et al. Crimean-Congo hemorrhagic fever in Turkey. Emerg Infect Dis 2004;10(8):1379-84.
7. Ergönül O. Crimean-Congo haemorrhagic fever. Lancet Infect Dis 2006;6(4):203-14.
8. Yilmaz GR, Buzgan T, Irmak H, Safran A, Uzun R, Cevik MA, et al. The epidemiology of Crimean-Congo hemorrhagic fever in Turkey, 2002-2007. Int J Infect Dis 2009;13(3):380-6.
9. Yilmaz GR, Buzgan T, Torunoglu MA, Safran A, Irmak H, Com S, et al. A preliminary report on Crimean-Congo haemorrhagic fever in Turkey, March-June 2008. Euro Surveill 2008; 13(33):1-2. pii: 18953.
10. Taşkesen M, Okur N, Taş MA. [The evalution of 19 patients who were admitted for the tick bite]. Dicle Med J 2008;35(2):110-3.

11. Kara A. [Tick removal]. Turkish Pediatric Journal 2008;51(3):117-22.
12. Tezer H, Şaylı TR, Bilir ÖA, Demirkapı S. [Is a tick bite of concern in children? Our Data for 2008]. J Pediatr Inf 2009;3(2):54-7.
13. Al B, Yıldırım C, Söğüt Ö, Yeşilkaya A. [The evalution of 39 tick bitings who admitted to Batman State Hospital emergency department in seven months]. Journal of Academic Emergency Medicine 2008;7(3):40-3.
14. Dilrukshi PR, Yasawardene AD, Amerasinghe PH, Amerasinghe FP. Human otoacariasis: a retrospective study from an area of Sri Lanka. Trans R Soc Trop Med Hyg 2004;98(8):489-95.
15. Yardan T, Baydın A, Başol N, Duran L, Sünbül M. [Epidemiologic evalution of patients admitted to emergency department due to tick bites]. J Exp Clin Med 2009; 26(4):153-6.
16. Kandiş H, Katırcı Y, Uzun H, Güneş H, Kara İH, Geyik MF. [Demographic and epidemiologic features of tick bite cases who have applied to emergency service in an endemic region]. Düzce Medical Journal 2010;12(1):18-23.
17. Parlak AH.[Preventive medicine in tick-borne diseases].Turkiye Klinikleri J Dermatol-Special Topics 2010;3(2):34-9.
18. Sümer A. [The evalution of the patients who were admitted to the emergency department of Kaş State Hospital because of tick biting]. Kafkas Univ Vet Fak Derg 2010;16(1):49-53.
19. Arıkan İ, Tıraş Ü, Saraçoğlu D, Taşar MA, Dallar Y. [Evaluation of the cases appealed as Crimean-Congo haemorrhagic fever]. Ege Journal of Medicine 2009;48(1):29-31.
20. Edlow JA, McGillicuddy DC. Tick paralysis. Infect Dis Clin North Am 2008;22(3):397-413, vii.
21. Onguru P, Akgul EO, Akinci E, Yaman H, Kurt YG, Erbay A, et al. High serum levels of neopterin in patients with Crimean-Congo hemorrhagic fever and its relation with mortality. J Infect 2008;56(5):366-70.
22. Goodman JL. Clinical approach to the patient with a possible tick borne illness. Tick Borne Diseases of Humans. 1st ed. Washington: ASM Press; 2005. p.87-101.
23. Gunduz A, Turkmen S, Turedi S, Nuhoglu I, Topbas M. Tick attachment sites. Wilderness Environ Med 2008;19(1):4-6.
24. Gargılı A, Kar S, Yılmazer N, Cerit C, Sonmez G, Sahin F, et al. Evaluation of ticks biting humans in thrace province, Turkey. Kafkas Univ Vet Fak Derg 2010;16(Suppl -A):S141-S146.
25. Akyazı R, Ecevit O. [Ticks and Crimean Congo haemorrhagic fever]. J Fac Agric OMU 2006;21(3):340-9.
26. Çelebi S, Aydın L, Hacımustafaoğlu M, Çelik U, Çakır D, Emir BR, et al. [Evaluation of children cases admitted for tick bite in Uludag University Medicine of Faculty]. J Pediatr Inf 2010;4(4):133-7.
27. Swanepoel R, Gill DE, Shepherd AJ, Leman PA, Mynhardt JH, Harvey S. The clinical pathology of Crimean-Congo hemorrhagic fever. Rev Infect Dis 1989;11(4):794-800.
28. Ergün H, Çiftçi E. [Crimean-Congo hemorrhagic fever]. Turkiye Klinikleri J Pediatr Sci 2007;3(2):23-6.
29. Ozkurt Z, Kiki I, Erol S, Erdem F, Yilmaz N, Parlak M, et al. Crimean-Congo hemorrhagic fever in Eastern Turkey: clinical features, risk factors and efficacy of ribavirin therapy. J Infect 2006;52(3):207-15.
30. Whitehouse CA. Crimean-Congo hemorrhagic fever. Antiviral Res 2004;64(3):145-60.