Journal of Turgut Ozal Medical Center 2016;23(3):302-5
OLGU SUNUMU/CASE REPORT DOI: 10.5455/jtomc.2016.03.035

A case of paralytic rabies mimicking Guillain-Barre syndrome

Guillain-Barre sendromunu taklit eden paralitik kuduz olgusu

Seher Erdogan[1], Ahmet Rauf Goktepe[2], Mehmet Bosnak[1], Alper Dai[3]

[1]Gaziantep University, Faculty of Medicine, Department of Pediatric Intensive Care, Gaziantep, Turkey
[2]Gaziantep University, Faculty of Medicine, Department of Pediatrics, Gaziantep, Turkey
[3]Gaziantep University, Faculty of Medicine, Department of Pediatric Neurology, Gaziantep, Turkey

Abstract

Rabies is an acute, fatal viral infection of the central nervous system, and one of the oldest zoonotic diseases in human history. A Syrian boy aged 14 had been hospitalized for 2 days with a preliminary diagnosis of Guillain-Barre syndrome because of muscle weakness that spread rapidly to the upper extremities. He was transferred to our unit when the muscle weakness worsened. Respiratory failure developed following admission to the ICU, and the patient was intubated and given ventilator support. Ascending paralysis and albuminocytologic dissociation in the cerebrospinal fluid (CSF) examination suggested a preliminary diagnosis of Guillain-Barre syndrome and plasmapheresis treatment was initiated. No clinical improvement was achieved despite plasmapheresis. On the 10th day of hospitalization, we learned that he had been bitten on the ankle by a stray dog in Syria 2 months ago and had not received prophylaxis. Suspecting that this might be a case of rabies, body fluid samples of the patient were sent to the National Reference Laboratory. The patient died on the 12th day of admission. A postmortem brain biopsy was taken, and Negri bodies were detected.

This case report emphasizes that rabies should be considered in the differential diagnosis of patients presenting with paralysis.

Keywords: Rabies; Guillain-Barre Syndrome; Encephalomyelitis.

Öz

Merkezi sinir sisteminin akut seyirli, öldürücü bir viral enfeksiyonu olan kuduz, insanlık tarihinin en eski zoonotik hastalıklarından birisidir. 14 yaşında Suriye'li erkek hastanın, hızla üst ekstremitelere yayılan kas güçsüzlüğü yakınmaları nedeniyle Guillain-Barre sendromu öntanısı ile 2 gün yatırılarak izlendiği, kas güçsüzlüğünün ilerlemesi üzerine ünitemize sevkedildiği öğrenildi. Solunum yetmezliğinin gelişmesi üzerine hasta entübe edilerek ventilatör desteği verildi. Asendan paralizi olması ve BOS incelemesinde albüminositolojik disosiasyon saptanması nedeniyle Guillain-Barre sendromu öntanısı ile plazmaferez tedavisi başlandı, ancak 5 kez plazmaferez tedavisi uygulanmasına karşın klinik iyileşme saptanmadı. Ancak yatışının 10. gününde, hastanın 2 ay önce Suriye'de bir sokak köpeği tarafından ayak bileğinden ısırıldığı ve profilaksi yapılmadığı öğrenildi. Kuduz hastalığından şüphelenilerek alınan vücut sıvı örnekleri, Refik Saydam Hıfzıssıhha Laboratuvarı'na gönderildi. 12. gününde dolaşım yetmezliği gelişti, hasta kaybedildi. Postmortem beyin biyopsisi alındı, beyin dokusunda Negri cisimciği saptandı.

Bu çalışmada, paralizi ile gelen olguların ayırıcı tanısında kuduzun da düşünülmesi gerektiği vurgulanmıştır.

Anahtar Kelimeler: Kuduz; Guillain-Barre Sendromu; Ensefalomiyelit.

Received/Başvuru: 05.03.2016
Accepted/Kabul: 11.05.2016

Correspondence/İletişim
Seher Erdogan
Gaziantep University, Faculty of Medicine, Department of Pediatric Intensive Care, Gaziantep, Turkey
E-mail: seher70@gmail.com

For citing/Atıf için
Erdogan S, Goktepe AR, Bosnak M, Dai A. A case of paralytic rabies mimicking Guillain-Barre syndrome. J Turgut Ozal Med Cent 2016;23(3):302-5

2016;23(3):302-5
DOI:10.5455/jtomc.2016.03.035

INTRODUCTION

Rabies, an acute and fatal viral infection, is one of the oldest known zoonotic diseases in human history (1). The rabies agent is a neurotropic RNA virus contained in an envelope from the family Rhabdoviridea of the genus Lyssavirus (2). Twenty-nine cases were reported in Turkey between 1995 and 2004. Althought there has been no decrease in the number of cases of rabies risk contact, prophylaxis is administered to approximately 100,000 people a year following rabies risk contact (3). Transmission of the virus to humans often occurs though bites by infected animals, although cases have also been reported to following organ and tissue transplantation and transmission through injured skin and mucosa (4, 5). Patients may present with severe (encephalitic) or paralytic rabies. The paralytic form is rarer, and is seen in 20% of all cases (6).

This study emphasizes the need to consider rabies in the differential diagnosis of patients who present with paralysis by reporting the case of a Syrian migrant who was referred from another health institution with a preliminary diagnosis of Guillain-Barre syndrome, and was subsequently diagnosed with the paralytic form of rabies.

CASE REPORT

A Syrian boy aged 14 initially presented at a hospital in Syria because of vomiting, headache, and high fever beginning that had been present for 1 week along with muscular weakness that had begun in the feet 3 days ago and spread rapidly to the upper extremities. The patient crossed the Turkish border and he had been hospitalized for monitoring with a preliminary diagnosis of Guillain-Barre syndrome at a health institution in Gaziantep 2 days previously. Antibiotic and intravenous immunoglobulin (IVIG) therapy had been administered. He was referred to the Gaziantep University Pediatric Intensive Care Unit (PICU). On admission, his body temperature was 36.5°C, heart rate 115/min, blood pressure 125/75 mmHg, and respiration rate 22/min. He was confused, and had a Glasgow coma score of 11. There were no findings of meningeal irritation, and cranial nerve examination was normal. The lower and upper extremities were hyponotic and deep tendon reflexes were absent. Babinski's sign was weak. Respiratory insufficiency developed 3 h after admission to the pediatric intensive care unit (PICU), and the patient was intubated and administered ventilator support. Nifedipine was added to treatment because the hypertension persisted.

At laboratory examinations, serum glucose, electrolytes and biochemistry, and blood cell counts were normal. HSV 1 and 2 IgM, CMV IgM, HAV IgM, HBsAg, anti-HIV, anti-HCV and EBV IgM were negative in serum. Salmonella and brucella agglutination tests and *Mycobacterium tuberculosis* polymerase chain reaction (PCR) were also negative in serum. In the CSF examination, protein was 75 mg/dL, sugar 79 mg/dL and simultaneous serum glucose 123 mg/dL. Six cells per mm^3 (4 lymphocytes and 2 granulocytes) were observed in CSF smear. No growth was observed in CSF, blood or urine culture. Cerebral magnetic resonance imaging (MRI) revealed an arachnoid cyst in the right temporal region, increased contrast in the meningeal areas, and suppression in neighboring sulcal areas (Figure 1).

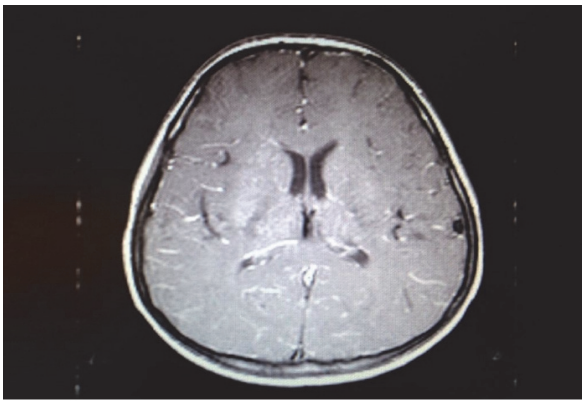

Figure 1. Increased contrast in the meningeal areas and suppression in neighboring sulcal areas in brain CT.

Findings consistent with severe sensorimotor polyneuropathy progressing with severe axonal degeneration and demyelination were observed at electromyography (EMG). Plasmapheresis was initiated with a preliminary diagnosis of Guillain-Barre syndrome on the basis of the presence of ascending paralysis and albuminocytologic dissociation in the CSF examination. However, no clinical improvement was determined after performing plasmapheresis for five times.

The family had arrived as migrants and were unable to provide clear answers to our questions. However, on the 10^{th} day of hospitalization, we learned that the patient had been bitten in the ankle by a stray dog in Syria 2 months ago and that prophylaxis had not been administered. A skin biopsy was taken from the hairline on the back of the neck on the suspicion of rabies, and urine, tear, saliva, and CSF specimens were sent to the National Reference Laboratory. The patient was isolated, and support treatments were maintained. However, the patient died due to respiratory collapse on the 12^{th} day. The family gave permission for postmortem a brain biopsy to be taken. Negri bodies were determined in the brain tissue, the direct fluorescent antibody (DFA) test was negative in skin biopsy, and the virus was isolated in CSF, urine, and saliva. Paralytic rabies was diagnosed on the basis of these findings.

DISCUSSION

Rhabdovirus can be transmitted though bites by infected animals or by their licking of damaged skin or mucous membranes, and can also be transmitted through transplantation of infected human or animal organs and tissues. The mean incubation time is 1-3 months, although this can range between a few days and a few years. The incubation period is shorter in the event of bites to the face or head, deep wounds, in children, and in subjects using corticosteroids (7). The incubation time in our patient was approximately 60 days, we think that this incubation time was prolonged because he was bitten on the ankle. Following the incubation period, the

2016;23(3):302-5
DOI:10.5455/jtomc.2016.03.035

prodromal period begins, in which symptoms non-disease specific symptoms such as lethargy, lack of appetite, mild fever, sore throat, headache, nausea, vomiting and fear occur, which persists for a few days. The prodromal period is followed by the neurologic phase, which concludes within 2-7 days. Encephalitic rabies, the classic form, is characterized by hydrophobia, aerophobia, pharyngeal spasm, and hyperactivity. The encephalitic form develops in 80% of rabies cases. The paralytic form of rabies is more common in individuals with inactivated and irregular inoculations and after bat bites (8). Hydrophobia and hyperactivity are not characteristically present, but hydrophobia and severe rabies findings may develop in some patients in the terminal period.

Paralytic rabies mimics Guillain-Barre syndrome when it progresses with quadriparesis. Early diagnosis is difficult because the major findings appear in the late period in this form. Some characteristics may assist the differentiation of Guillain-Barre syndrome and paralytic rabies; 1) Fever is always present in paralytic rabies. In Guillain-Barre syndrome, however, there is no fever in the period when muscle weakness is seen unless complications such as aspiration pneumonia develop. 2) In paralytic rabies sensory functions are healthy, except for paresthesia in the area of the bite. 3) Quadriparesis, which is more pronounced in the proximal muscles, and urinary incontinence are always present in the early stages of paralytic rabies. Urinary incontinence in Guillain-Barre syndrome is rare, and both the proximal and distal muscles are affected, particularly in the early phases. 4) Myoedema is seen in both the early and late phases of paralytic rabies. It is not observed in Guillain-Barre syndrome. 5) Generalized and focal fasciculations are common in cases of paralytic rabies (9). In 2005, Sheikh et al. (10) published a case of paralytic rabies that progressed with acute axonal neuropathy and very closely resembled Guillain-Barre syndrome. The authors emphasized that the clinical and pathologic characteristics of paralytic rabies and Gullain-Barre syndrome may be very similar and that this may derive from the infectious and immunologic etiologies, which lead to similar morphologic changes in the nerves. In our patient, no fever was observed on admission to the intensive care unit or in the following days. Muscle weakness began from the lower extremities and followed an ascending course. No myoedema or fasciculation were observed. Plasmapheresis was started when no response was obtained to IVIG because CSF examination and EMG findings in our hospital supported a diagnosis of Guillain-Barre syndrome. However, no clinical response was achieved.

The acute neurologic phase is followed by generalized flask paralysis, respiratory and circulatory collapse, and coma. Patients require mechanical ventilator support during this period, and death generally occurs within 2 weeks.

Diagnosis in patients with rabies is to a large extent based on suspicion, history, and clinical findings. Diagnosis is only possible antemortem in approximately 50% of cases. In the advanced stages, pleocytosis, increased protein levels, and normal glucose levels may be seen in CSF. Positivity in the DFA test, which tests for rabies-specific antigens in saliva, corneal epithelial cells, brain tissue, and skin tissue taken from the hairline on the back of the neck, antibody levels in CSF above 100 IU/mL, virus isolation from CSF, urine, saliva and respiratory secretions in the 2nd or 3rd week of symptoms, and RT-PCR test positivity in saliva and brain tissue are diagnostic (11-13). Urine and serum specimens have low diagnostic sensitivity. Observation of Negri bodies in brain tissue and neuronal tissues is pathognomonic for rabies, but may not be determined in all cases of rabies.

Human rabies immunoglobulin (HRIG) and inoculation after the disease have started to provide no benefit. Symptomatic and supportive treatment may be administered. Antiviral agents such as amantadine, ribavirin, and tribavirin have been studied in animal experiments, but no effectiveness has been determined (14). Patients die within 2 weeks after entering the comatose period.

The number of Syrian migrants in Turkey is increasing all the time due to the civil war in Syria. One of the consequences of the unavailability of health services in Syria due to the war is that cases of rabies have become more frequent in Turkey, although it is not an endemic region. Patients with suspected infection must be isolated, contact with infected secretions and tissues must be avoided, protective measures must be taken by health personnel in particular, and those with a history of contact must receive regular prophylactic inoculations.

Rabies must be considered in differential diagnosis of patients with rapidly worsening, acute onset Guillain-Barre syndrome that fails to respond to standard treatment.

REFERENCES

1. Dede T, Kocabaş E. An important public health problem as yet unsolved in the world and our country: Rabies. J Pediatr Inf 2008;3:109-16.
2. Warrell MJ, Warrell DA. Rabies and other Lyssavirus diseases. Lancet 2004;363:959-69.
3. Geçer S. Kuduz ve tetanoz profilaksisi. Cerrahpaşa Tıp dergisi 2008;61:223-34.
4. Masthi NRR, Raviprakash D, Gangasagara SB, Sriprakash KS, Ashwin BY, Ullas PT. Rabies in a blind patient confusion after corneal transplantation. Nati Med J India 2012;25(2):83-4.
5. Maier T, Schwarting A, Mauer D, Ross RS, Martens A, Kliem V. Management and outcomes after multipl corneal and solid organ transplantations from a donor infected with rabies virus. Clin Infect Dis 2010;50(8):1112-9.
6. Mani CS, Murray DL. Rabies. Pediatr Rev 2006;27:129-35.
7. World Health Organization. WHO expert consultation on rabies. WHO Tech Rep Ser 2005;931:1-88.
8. Hemachudha T, Ugolini G, Wacharapluesadee S, Sungkarat W, Shuangshoti S, Laothamatas J. Human rabies: neuropathogenesis, diagnosis, and management. Lancet Neurol 2013;12 (5):498-513.
9. Madhusunada SN, Sukumaran SM. Antemortem diagnosis and prevention of human rabies. Ann Indian Acad Neurol 2008;11(1):3-12.

2016;23(3):302-5
DOI:10.5455/jtomc.2016.03.035

10. Sheikh KA, Alverez MR, Jackson AC, Li CY, Asbury AK, Griffin JW. Overlap of pathology in paralytic rabies and axonal Guillain-Barre Syndrome. Ann Neurol 2005;57:768-72.
11. Schupbach A, Zbang L, Thomas B, Ellerbroek J, Leone D. Fatal human rabies infection confirmed with skin biopsy specimen. J Am Acad Dermatol 2012;67(2):321-3.
12. Dacheux L, Revnes JM, Buchy P. A reliable diagnosis of human rabies based on analysis of skin biopsy specimens. Clin Infect Dis 2008;47(11):1410-17.
13. Hemachudha T, Wacharapluesadee S. Antemortem diagnosis of humanrabies. Clin Infect Dis 2004;39:1085-86.
14. Merigan TC, Baer GM, Winkler WG. Human interferon administration to patients with symptomatic and suspected rabies. Ann Neurol 1984;16(1):82-7.