Late Type Vitamin K Deficiency Related with Prolonged Antibiotic Therapy in a 7-month-old Infant

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ABSTRACT

We herein report a case of intracranial hemorrhage due to late-type vitamin K deficiency during antibiotic therapy. A 7-month-old male infant was hospitalized for convulsion. He was diagnosed as bacterial meningitis, and treatment with ceftriaxone and vancomycine was administered. On the 16th day of therapy, a subdural hemorrhage occurred. Protrombin time and partial thromboplastin time were found to be prolonged. Platelet count, fibrinogen and D-Dimer levels were all normal. The patient was diagnosed as "Vitamin K Deficiency Bleeding". He was treated with 3 mg vitamin K intravenously and the subdural hematoma was drained. His follow up was uneventful. We suggest that patients especially who receive antibiotic treatment for more than two weeks should be followed for late-type vitamin K deficiency.

Keywords: Intracranial hemorrhage, Vitamin K deficiency, Antibiotic therapy

ÖZET

Yedi Aylık bir Olguda UzamışAntibiyotik Tedavisi ile İlişkili Geç Tip K Vitamini Eksikliği

Biz burada antibiyotik tedavisi esnasında gelişmiş, geç tip K vitamini eksikliğine bağlı bir intrakranial kanama olgusunu sunuyoruz. Konvülziyon şikayeti ile başvuran 7 aylık bir erkek hastaya, bakteriyel menenjit tanısı konularak seftriakson ve vankomisin tedavileri başlandı. Tedavinin 16. gününde subdural hemoraji ortaya çıktı. Protrombin zamanı ve parsiyel tromboplastin zamanında uzama saptanırken platelet sayısı, fibrinojen ve D-Dimer düzeyleri normaldi. Hastaya K vitamini eksikliğine bağlı kanama teşhisi konuldu. Tedavisi için 3 mg K vitamini intravenöz olarak verildi ve subdural hematom boşaltıldı. Daha sonraki takiplerinde herhangi bir sorun yaşanmadı.
Biz özellikle 2 haftadan daha uzun bir süre antibiyotik tedavisi almakta olan hastaların geç tip K vitamini eksikliği bakımından yakından takip edilmesi gerektiğini düşünüyoruz.

Anahtar Kelimeler: İntrakraniyal kanama, Vitamin K eksikliği, Antibiyotik tedavisi

INTRODUCTION

Vitamin K deficiency bleeding (VKDB) is a clinical picture characterized by bleedings due to insufficient levels of vitamin K dependent homeostatic factors (II, VII, IX, X) correctable by vitamin K replacement. It was formerly called as Hemorrhagic Disease of the Newborn (HDN), but this term has been discarded as this disorder can also be observed after the neonatal period.[1,2] Vitamin K level in newborns is usually low due to insufficient storage, and low placental transfer.[3] VKDB can be classified into three groups according to the time of occurrence; early type, (within the first 24 hours), classic type (between the 1st and 7th days) and late type (between the 7th day and 6th month).[4] In cooperative studies, the upper limit was set arbitrarily at the end of week 12, but infants presenting with VKDB between weeks 13 and 26 were be reported.[5,6] Late type VKDB can be classified as idiopathic or secondary, depending on the etiology. The cause of secondary VKDB is malabsorption of vitamin K. This situation is usually a result of hepatic and intestinal diseases.[3] VKDB usually manifests as 'warning bleeds' such as mild bruises, epistaxis or umbilical oozing, and rarely is followed by intracranial hemorrhage. Late-type VKDB has particular importance owing to frequent intracranial hemorrhages with high mortality and morbidity. In previously studies, intracranial hemorrhage (ICH) was reported as 65-100% due to vitamin K deficiency.[7]

Vitamin K deficiency is known to cause coagulopathy and bleeding in patients receiving antibiotic therapy. Herein, we report a case of intracranial hemorrhage due to vitamin K deficiency related with prolonged antibiotic therapy.

CASE REPORT

A 7-month-old male infant was hospitalized for convulsions. The convulsions stopped after intravenous diazepam (0.3 mg/kg/dose). He did not have abnormal prenatal, natal and postnatal history, physical and neurological development was normal. He had been given prophylactic intramuscular vitamin K (1 mg) just after birth. He had not been fed with mixed nutrients, but had been breastfed. The family history was noncontributory. In physical examination, his weight, height and head circumference were within 25-50th percentile, and body temperature was >39.5^{0}C rectal. An intracranial pathology was not detected in computed tomography. Lumbar puncture was performed for meningitis and he was diagnosed to have meningitis according to the findings of the cerebrospinal fluid (80 neutrophil/mm^3, protein: 74 mg/dl, glucose: 50 mg/dl). Intravenous ceftriaxone (100 mg/kg/day), and fluid replacement (100 ml/kg/day) was administrated. On the 4th day of therapy, his body temperature was still high (>39.5^{0}C rectal) and control lumbar puncture was normal except polymorphonuclear leukocytes. Accordingly, vancomycine was added to the treatment. In the meantime, initial cerebrospinal fluid cultures were positive for group A beta hemolytic streptococcus. Antibiotic therapy was changed to cefotaxime (100 mg/kg/day) and vancomycine (60 mg/kg/day) according to the antibiogram results. There was no change of head circumference during the therapy. On the 13th day of therapy, body temperature was normal and a control lumbar puncture revealed normal cerebrospinal fluid. On the 16th day of therapy, emesis occurred, and bleeding started from the vascular catheter on his arm. Prothrombin time (PT) and partial thromboplastin time (PTT) were found to be prolonged. Thrombocyte count, fibrinogen and D-Dimer levels were normal. The patient was diagnosed as VKDB and intravenous vitamin K (3 mg) was given. After three hours, PT and PTT values normalized. After coagulation tests became normal, computed tomography was performed and it uncovered a subdural hemorrhage (Figure 1). Since his hemoglobin was 5.8 g/dl, erythrocyte suspension was transfused and then he was transferred to the neurosurgery department. After drainage of the subdural hematoma, antibiotic therapy was continued until the 21st day. One day later, he had bleeding from the vascular catheter again; repeat PT and PTT were prolonged but thrombocyte count, fibrinogen and D-Dimer levels were normal. The patient was treated with intravenous vitamin K (3 mg) again. After 3 hours, PT and PTT values normalized. He was discharged on the 24th day and the follow up was uneventful thereafter.

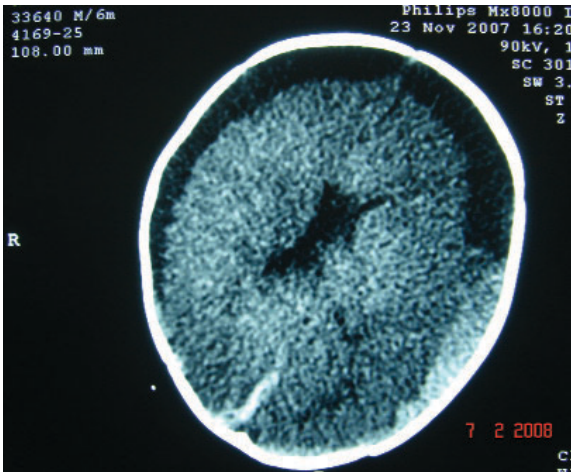

Figure 1. Subdural hemorrhage on computed tomography

DISCUSSION

In 1961, the American Academy of Pediatrics (AAP) stated that all newborns should receive vitamin K prophylaxis to prevent VKDB. In 1993, the AAP has declared that oral or parenteral neonatal vitamin K prophylaxis is safe and effective in preventing classic VKDB.[8] Subsequent assessments have also confirmed the need of oral and parenteral vitamin K prophylaxis for all newborns and showed no evidence of deleterious effect of this treatment.[8] Vitamin K deficiency is a worldwide problem in the newborn infant, particularly for those who are being breastfed. The breast milk of mothers whose babies suffer from late VKDB contains lower levels of vitamin K than controls. VKDB is uncommon in countries where nearly all newborn infants receive prophylactic intramuscular vitamin K at birth.[8]

In a bleeding infant with prolonged PT but without any findings pertaining to other bleeding disorders is almost diagnostic for VKDB. Rapid correction of PT and/or cessation of bleeding after vitamin K administration are also confirmative.[7] Late type VKDB is usually observed in breastfed infants who do not take vitamin K at birth. Nevertheless VKDB has also been reported in infants who received oral and, more rarely, intramuscular vitamin K at birth.[8] Late type VKDB leads to significant morbidity and mortality due to high incidence of intracranial hemorrhages.[7] Our case had received vitamin K prophylaxis (1 mg) after birth and he had also been breastfed. He had had no bleeding problems until his admission to the hospital.

Several studies revealed that vitamin K deficiency was seen following prolonged antibiotic therapy, during the course of severe diseases especially infectious ones, and in malnutrition.[9] The exact role of antibiotics in the pathogenesis of vitamin K deficiency and the mechanism of hypoprothrombinemia continues to be poorly understood. Detection of vitamin K deficiency in hospitalized children shows that physician's still lack information about this important cause of bleeding that can easily be prevented.[9] Although the incidence of actual bleeding is low, most of the studies have shown a significant incidence of hypoprothrombinemia. Hypoprothrombinemia is to be considered in children on prolonged antibiotics especially in those who are severely ill. Mechanisms causing vitamin K deficiency include combined effects of low vitamin K intake and loss of normal bowel flora synthesizing vitamin K.[10] Antibiotic usage and infections before the onset of bleeding were not reported in the literature including large series of patients with VDKB.[11] Suzuki et al. reported a case with intracranial hemorrhage due to vitamin K deficiency related to oral antibiotic use.[12] Firkin et al have stressed the importance of vitamin K prophylaxis in patients whose nutrition is inadequate, who are treated with intravenous antibiotics and who are on intravenous fluids for prolonged periods of time.[10] Our patient had been breastfed, his body weight and length were within normal limits. He was diagnosed as bacterial meningitis; antibiotic therapy and intravenous fluid were started. On the 16th day of therapy, he was diagnosed as VKDB and intravenous vitamin K (3 mg) was given. After three hours, PT and PTT values normalized.

As for conclusion, we imply that prophylactic vitamin K might be given to decrease the morbidity and mortality due to late type VKDB in patients with severe illnesses especially if they receive intravenous antibiotic therapy for more than two weeks.

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