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Sphingobacterium multivorum septicemia in an infant: Report of a case and review of the literature

Bir infantta Sphingobacterium multivorum sepsisi: Olgu sunumu ve literatür taraması

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SUMMARY

Sphingobacterium multivorum has been reported as a rare microorganism causes diseases in patients with predisposing conditions. We describe the first case of invasive disease caused by S.multivorum in a patient without an underlying disorder. A 73-day-old boy with a fever to 39°C, lethargy, vomiting, hypotonia and convulsion was admitted to Kocaeli University Faculty of Medicine Hospital on November 21st, 1999. The 15-year-old mother and baby were living in a tent-city in Izmit where an earthquake of 7.4 Richter scale centered on August 17th, 1999. S.multivorum was isolated from blood cultures. The infant received a 10-day course of ampicillin and cefotaxime and was discharged with and uneventful recovery. Both mother and patient were seronegative for HIV. At follow-up studies eight month later immune profile was normal. The evidence in the present case suggests that under certain circumstances S.multivorum may cause invasive disease in an otherwise normal host.

Key words: *Sphingobacterium multivorum, septicemia*

ÖZET

Sphingobacterium multivorum altta yatan bir nedene bağlı olarak nadiren insanda hastalık oluşturan bir bakteridir. İlk defa bu olguyla altta yatan bir hastalığa bağlı olmaksızın bir hastada S.multivorum infeksiyonu gösterilmiştir. Kocaeli Üniversitesi Tıp Fakültesi Hastanesi'ne 73 günlük bir erkek çocuk 39°C ateş, letarji, kusma, hipotoni ve konvulizyon şikayetleriyle 21 Kasım 1999 yılında başvurdu. Bebek, 15 yaşında ki annesiyle birlikte 17 Ağustos 1999 yılında Richter ölçeğine gore 7,4 şiddettinde depremle yıkılmış İzmit'te bir çadır kentte yaşamaktaydı. Bebeğin kan kültürlerinden S.multivorum izole edildi, bunun üzerine tedavide 10 gün süreyle ampisilin ve sefotaksim verildi ve hasta beklenmedik bir şekilde iyileşerek taburcu edildi. Anne ve bebekte HIV negative bulundu. Sekiz ay süren takip sonucunda yapılan immune profile normal bulundu. Bu olgudan bazı durumlarda S.multivorum'un sağlıklı bir kişide invazif bir hastalığa neden olabileceği sonucu elde edildi.

Anahtar kelimeler: *Sphingobacterium multivorum, sepsis*

INTRODUCTION

The genus *Sphingobacterium* is composed of Gram-negative, nonmotile, oxidase- and catalase-positive bacilli and includes organisms previously classified as Flavobacterium species. Of the five *Sphingobacterium* species, most isolates from humans are *Sphingobacterium multivorum* and *Sphingobacterium spiritivorum* (1). *S. multivorum* has been reported as a rare but serious cause of respiratory disease, peritonitis and septicemia in patients have several predisposing conditions (2-6). We describe the first case to our knowledge of invasive disease caused by *S. mul-*

tivorum in a patient without a predisposing underlying disease. In addition we review the literature concerning invasive disease produced by this organism.

CASE REPORT

A 73-day-old male was admitted to Kocaeli University Faculty of Medicine Hospital on November 21st, 1999 with a 12-hour history of lethargy, unwillingness to breast-feed, vomiting, convulsion and a fever to 39°C. He was transferred for further management from a "tent-city health center" in Izmit, about 100 km east of Istanbul, where an earthquake of 7.4 Richter scale centered on August 17th, 1999. The family was living in a tent set on the ground after the earthquake. The hygiene conditions of the tent-city were sub-optimal at and after birth which it occurred three weeks after the earthquake. Water supply was insufficient for bathing and washing the clothes. The patient was the first child of a 15-year-old mother. He was a fullterm infant with no perinatal problems. One week before admission, a 5 mm diameter pustular lesion with an erythematous border developed on his right buttock after an accidental scratch by a fingernail of the mother and then healed in a few days. Any history of insect bite, trauma or laceration was not revealed for this lesion. There were no any unusual alternative medicine treatments or ointments applied to the infant's skin or fed to the infant. The infant was strictly breast fed and the mother did not have any mastitis or skin wounds. None of the other family members and tent-mates had any open wounds or infections.

Physical examination upon admission revealed a well-developed, unconscious and hypotonic infant with a rectal temperature of 41.2°C, heart rate of 144/minute and respiratory rate of 48/minute. The patient was unresponsive to painful stimuli. Abdomen was slightly distended and hepatomegaly was palpated 3 cm below the costal margin. The remainder of the examination was unremarkable.

Initial laboratory studies included a WBC count of 19100/mm_ with 82% neutrophils, 8% band forms and 10% lymphocytes and a platelet count of 506 000/mm_. Polymorphonuclear leukocytes had marked toxic granulations on peripheral blood smear. Blood urea nitrogen was 23 mg/dL and aspartate aminotransferase was 107 IU/L. Serum electrolytes, glucose, calcium, creatinine and alanine aminotransferase concentrations were within normal limits. Findings on a chest radiograph did not reveal any abnormalities, and the result of a urinalysis was normal. A noncontrasted head CT scan was normal. A lumbar puncture yielded clear, colorless CSF with no cells. The glucose level was 72 mg/dL and protein level was 43 mg/dL. No organisms were seen on Gram-stained, acridine-orange and acid-fast smears or an India ink preparation. A blood buffy-coat smear stained with acridine-orange was negative. CSF, urine, stool and two consecutive blood cultures were obtained on the day of admission.

The patient was hospitalized with a diagnosis of suspected sepsis. Intravenous ampicillin in a dosage of 200 mg/(kg•d) and cefotaxime 200 mg/(kg•d) were administered. He had no convulsions at the hospital and emesis was no longer noted. On the second hospital day he became responsive to stimuli and started to have spontaneous extremity movements. On the third day he was afebrile and the next day he was taking oral feedings well. At that time blood culture obtained upon admission was reported positive for *S. multivorum*. Cultures of CSF, stool and urine revealed no pathogens.

The serum Ig profile was normal with IgG of 431 mg/dL, IgA of 26 mg/dL and IgM of 69 mg/dL. C3 and C4 concentrations were 111 mg/dL and 35 mg/dL, respectively. Circulating lymphocyte surface marker profile also was normal with the results of CD3 75%, CD4 45%, CD8 38%, CD19 12%, CD20 14% and CD56 10%. Both mother and patient were seronegative for HIV.

S. multivorum was eventually isolated from the cultures of two blood samples drawn on the day of admission after an incubation of 48 hours at BACTEC 9050 (Becton Dickinson Diagnostic Instrument Systems). Cultures of blood obtained on the second hospital day remained negative. The organism grew low convex, smooth and opaque, nonhemolytic, light yellow pigmented 1 mm diameter colonies on blood

agar after 24-hour incubation. The isolates were Gram-negative bacilli, oxidase- and catalase-positive and nonmotile. Biochemical identification of the isolates was accomplished by using the Sceptor® (Becton Dickinson Diagnostic Instrument Systems, Sparks, MD 21152) Gram-Negative Breakpoint/ID Panel (Cat. No. 4480430) with the results of profile number: 2304040, validity: 12 and confidence: 95.01. The definitive identification was reached by means of the set of tests described in the Manual of Clinical Microbiology (7). The strain showed positive reactions in the following tests: catalase, oxidase, growth on MacConkey agar, growth at 37°C and room temperature (22°C), urease, esculin hydrolysis and acidification of glucose, lactose, maltose, sucrose and xylose, and negative for motility at room temperature and 37∞C, indole production, hydrogen sulfide production and assimilation of citrate. Antibiotic susceptibility tests were performed by the same Sceptor® panel and confirmed by the Kirby-Bauer single disk diffusion method according to National Committee on Clinical Laboratory Standards (NCCLS) guidelines (8). The isolates were susceptible to cefotetan, cefuroxime, cefotaxime, ampicillin/sulbactam, amoxicillin/ clavulanate, amikacin, gentamicin, ticarcillin, ticarcillin/clavunate, ciprofloxacin, tetracycline and imipenem; intermediate susceptible to ampicillin, ceftriaxone, cefoperazone and piperacillin, and resistant to trimethoprim-sulfomethoxazole (TMP-SMZ), aztreonam, cefazolin, ceftazidime, cephalotin and tobramycin.

The infant eventually received a 10-day course of antibiotics and was discharged with no medication. At follow-up visits two, five and eight months later, findings on physical examinations were normal.

An epidemiological search for a possible source of the infection could not be performed because of the extraordinary conditions in the region after the earthquake which most of the medical facilities were destroyed or badly damaged including ours, making the remaining medical team ineffective.

The serum Ig and circulating lymphocyte surface marker profiles, and C3 and C4 concentrations were retested on July 12, 2000. The Ig profile was normal with IgG of 640 mg/dL, IgA of 48 mg/dL, IgM of 117 mg/dL, IgG1 of 540 mg/dL, IgG2 of 45 mg/dL, IgG3 of 42mg/dL and IgG4 of 14 mg/dL. Circulating lymphocyte surface marker profile also was normal with the results of CD2 68%, CD3 61%, CD4 31%, CD8 32%, CD19 27%, CD20 25%, CD22 23% and CD56 11%. C3 and C4 concentrations were 120 mg/dL and 44 mg/dL, respectively.

DISCUSSION

The genus *Sphingobacterium* was created to classify the organisms contain large amounts of sphingophospholipid compounds in their cell membranes and have other taxonomic features that distinguish them from flavobacteria (1). The natural habitats of these organisms are soil, plants, foodstuffs, and water sources, including those in hospitals (7). Although most isolates from humans are *S. multivorum* and *S. spiritivorum* of the five Sphingobacterium species currently named (1,7), a review of the literature has shown S. multivorum to be a rare cause of invasive disease in humans (Table 1) (2-6). However, all five previously reported cases have underlying diseases and/or immunocompromised. One patient each had alcoholic liver disease (2), hemodialysis (3), lymphoma and chemotherapy (4), cystic fibrosis (5) and diabetes mellitus and HIV infection (6) as predisposing conditions. Of the total cases one had a fulminant course ending in the death of the patient (6). Of the total six patients including the present case four had septicemia, one each had spontaneous peritonitis and an acute respiratory disease.

To our knowledge the patient described here is the first reported case of invasive disease caused by *S. multivorum* in the literature who did not have a predisposing underlying disease and/or immune deficiency. However, the sub-optimal living conditions of a tent-city environment, especially with a 15-year-old mother, must have severely compromised hygiene and predisposed the infant to septicemia. The source of the septicemia in this patient remains obscure. It is possible that infection occurred because of the sub optimal living conditions in a tent on the ground and close contact with the natural habitats of this organism.

Table 1. Summary of reported cases of *Sphingobacterium multivorum* disease in humans

Case (Reference) no.	Sex	Age	İllness	Source	Predisposition	Therapy (duration)	Outcome
1 (1)	M	60 y	Peritonitis	Peritoneal fluid	Alcoholic liver disease	Ampicillin and gentamicin (4 d), carbenicillin and gentamicin (12 d)	Recovered
2 (3)	M	43 y	Septicemia	Blood	Hemodialysis	Ampicillin (10 d) and tobramycin (one dose)	Recovered
3 (4)	M	57 y	Septicemia	Blood	Non-Hodgkin's lymphoma,	Pefloxacin and TMP-SMZ (duration not reported)	Recovered
4 (5)	F	20 mo	Respiratory disease	Bronchoaspirate	Cystic fibrosis	Ceftazidime and amikacin	Recovered
5 (6)	M	47 y	Septicemia	Blood, sputum	Diabetes mellitus, HIV positive	Ampicillin and gentamicin, ceftriaxone and TMP-SMZ; (total 6 d)	Died
6 (PR)	M	73 d	Septicemia	Blood	-	Ampicillin and cefotaxime (10 d)	Recovered

NOTE. TMP-SMZ = trimethoprim-sulfametoxazole; HIV = human immunodeficiency virus; PR = present report.

Whether the previous pustular lesion predisposed to septicemia as an entry or a primary focus for *S. multivorum* in this patient was unclear.

Sphingobacterium species are known intrinsically resistant to many commonly employed antibiotics. S. multivorum can produce an extended-spectrum β-lactamase and a metallo-β-lactamase conferring resistance to third generation cephalosporins and carbapenems, respectively (1,7). However, the antimicrobial susceptibility noted in the previous reports (2-6) and in the present case varied widely among the isolates. The isolates aforementioned did not show a common susceptibility pattern. The response to therapy in two patients also varied independently from the antimicrobial susceptibilities of isolates. A patient with septicemia improved clinically after receiving ampicillin and one dose tobramicin, despite in vitro testing showing ampicillin resistance (3). The other patient was treated with a combination of ceftriaxone and TMP-SMZ for septicemia but developed meningitis and died although the isolate was susceptible to these antibiotics (5). In other cases including the present case the patients were treated with the antibiotics that the isolates were susceptible and had uneventful recovery.

The isolation of *S. multivorum* from clinical specimens has been considered as an opportunistic pathogen, probably acquired nosocomially, appears to affect patients with predisposing conditions (1-7). The evidence in the present case, however, demonstrates the pathogenic potentialities of this organism and strongly suggests that under certain circumstances *S. multivorum* should be added to the list of microorganisms that may cause invasive disease in an otherwise normal host.

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