JOURNAL OF CLINICAL MICROBIOLOGY, July 2006, p. 2655–2656 Vol. 44, No. 7
0095-1137/06/$08.00+0 doi:10.1128/JCM.00467-06

Sepsis Caused by *Veillonella parvula* Infection in a 17-Year-Old Patient with X-Linked Agammaglobulinemia (Bruton's Disease)

Magdalena Strach,[1] Maciej Siedlar,[2]* Danuta Kowalczyk,[2] Marek Zembala,[2] and Tomasz Grodzicki[1]

Department of Internal Diseases and Gerontology[1] and Department of Clinical Immunology, Polish-American Children's Hospital,[2] Jagiellonian University Medical College, Krakow, Poland

Received 3 March 2006/Returned for modification 4 April 2006/Accepted 26 April 2006

A case of a male, 17-year-old, X-linked agammaglobulinemia patient with bacteremia caused by *Veillonella parvula*, without a defined primary site of infection, is presented. The report demonstrates that *V. parvula* should not be regarded as a nonpathogenic microorganism, at least not in patients with certain forms of immunodeficiency disease.

CASE REPORT

We present the case of a 17-year-old boy with X-linked agammaglobulinemia (XLA). XLA was diagnosed in the second year of life, with no detectable B lymphocytes in the peripheral blood and serum immunoglobulin G (IgG), IgA, and IgM levels of <0.04 g/liter at the time of diagnosis. Since the 10th month of life, he has suffered from recurrent pharyngitis, tracheitis, and bronchitis. At the age of 22 months, he developed purulent bilateral otitis media. Because treatment with antibiotics was ineffective, radical tympanoatriomastoidectomy was performed. At that time, XLA was recognized and he was placed on substitution with intravenous (i.v.) Ig infusions every 4 weeks. At the age of 10 years, a cochlear prosthesis was implanted in the left ear. In the 17th year of life, he had a blunt trauma of the left leg. After 4 days he developed fever (37.5 to 39.5°C), pain, skin edema, and a flare of the left shank. Upon hospital admission, local dermatitis and panniculitis were noted. His electrolyte levels and liver function tests were normal, and his white blood cell count was within the normal range, with a predominance of granulocytes. Intravenous lincomycin and vancomycin, oral paracetamol, metamizole, and i.v. Ig (0.6 g/kg of body weight) were administrated. Over the next 5 days, no improvement was seen and additional otorrhea appeared on the left side. Blood, urine, and otorrheal swab cultures were negative on several occasions. A chest X-ray was normal, but shading of the entire right maxillary sinus was noted. An abdominal ultrasound scan revealed only slight splenomegaly, gastroscopy revealed esophagitis and hiatus hernia, and echocardiography showed no pathological changes. An ultrasound scan of the left shank showed local inflammation without signs of abscess. Computed tomography of the head showed a solid structure in the left and back side of the middle ear and in the remaining parts of the mastoid bone.

To distinguish between inflammatory granuloma and an acute inflammatory process, a skin biopsy of the left shank was performed. The pathologist reported panniculitis with possible erythema nodosum. Lincomycin was replaced by ciprofloxacin, vancomycin was continued, and ketoconazole and lanzoprazol were added. Improvement was noted, the temperature went down to a range of 37.0 to 37.5°C, and inflammatory infiltration and pain of the left shank diminished. Because of computed tomography changes, the patient was examined several times by otolaryngologists to exclude the middle ear as a potential site of infection. The patient was discharged after 24 days of hospitalization and admitted to a laryngology reference center. He was treated conservatively (without antibiotics given) for 5 days and then was discharged with no signs of inflammation in the mastoid and middle ear region. During a 32-day stay at home, the patient had a temperature of 37.0 to 37.5°C every evening and four episodes of temperature of 39.0°C. Inflammation of the left shank worsened simultaneously with temperature rise. Following the fifth episode of 39.0°C temperature, the patient was again admitted to the hospital. Upon admission, the patient's condition was severe, with a temperature of 40.0°C. Clinical examination revealed inguinal lymph node enlargement and tachycardia of 110 beats/min. Upon hematological examination, leucocytosis of $17 \times 10^3/\mu l$ with 61% neutrophils was observed. Wound swab cultures (from a left shank biopsy), taken three times, were negative. Blood samples taken several times after 7 days of incubation under aerobic and anaerobic conditions were negative. Intravenous ciprofloxacin and i.v. Ig were administered. A radioactive gallium scan showed a slightly increased uptake in the left shank, right sacroiliac, and right brachial joints. During the 7 days, no improvement was seen and doxycycline with ciprofloxacin were given. During the second day of doxycycline administration, the temperature decreased to the normal level. The patient's condition improved, the flare and inflammation of the left shank receded, and inguinal lymph node swelling decreased.

On the 10th day of hospitalization, the bacteriology laboratory reported growth in one of the blood samples (taken on the third day of hospitalization), cultured at an increased CO_2 concentration, of an undetermined gram-negative strain. It was sensitive to doxycycline, tetracyclines, gentamicin, cefepime, meropenem, imipenem, and trimethoprim-sulfamethoxazole and was resistant to vancomycin, chinolones, lincomycin, amoxicillin, and amoxicillin-clavulanic acid. The bacterial sample

* Corresponding author. Mailing address: Department of Clinical Immunology, Polish-American Children's Hospital, Jagiellonian University Medical College, Wielicka 265 Str., 30-663 Krakow, Poland. Phone: (48-12) 658 24 86. Fax: (48-12) 658 17 56. E-mail: misiedla@cyf-kr.edu.pl.

was sent to the microbiology reference center for precise identification. The patient was discharged in very good condition after 22 days of hospitalization. Oral doxycycline was prescribed for the next 10 days as a continuation of 15 days of i.v. administration of this antibiotic. The patient is undergoing regular control; after 2 years he is in good health and takes no drugs except regular i.v. Ig substitution and occasional antibiotics.

XLA is the primary humoral immunodeficiency caused by mutation of the Bruton's tyrosine kinase (*Btk*) gene, located on the X chromosome. This leads to a block in B-cell maturation, resulting in an almost total absence of B cells in the peripheral blood and panhypogammaglobulinemia. Cellular immunity is intact. Clinical manifestations of XLA include recurrent sinopulmonary bacterial infections, otitis media (usually in early childhood), and hepatosplenomegaly. The most common infections are due to pyogenic bacteria (*Streptococcus pneumoniae*, *Haemophilus influenzae*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*). Untreated infections may lead to bronchiectases, pulmonary fibrosis, and death, even in childhood. The basic therapy for XLA includes substitution with i.v. Ig and aggressive treatment of infections with broad-spectrum antibiotics (7).

Two months after the patient's discharge, the microbiology reference center reported that the microorganism had been identified as *Veillonella parvula*. No antibiogram was made, because *V. parvula* is usually sensitive to clindamycin, metronidazole, imipenem, meropenem, and chloramphenicol, and 70 to 80% of strains are sensitive to penicillin. This microorganism, a nonfermentative anaerobic gram-negative coccus, can be isolated from healthy persons and is usually present in the normal oral, intestinal, and vaginal microflora. When isolated from clinical specimens, it is often regarded as a contaminating or commensal microorganism. *Veillonella* spp. have been reported to be important pathogens involved in periodontitis (10) and a rare cause of chronic tonsillitis (6), chronic sinusitis (16), endocarditis (12, 4), obstructive pneumonitis (11), meningitis (14, 2), and lung (13) and pelvic (17) abscesses. The most frequently reported *V. parvula* infection is osteomyelitis; *V. parvula* as the only microorganism causing infection has been identified in two such cases (3, 15). Among cases of gram-negative sepsis, *V. parvula* has usually been associated with localized anaerobic infections, e.g., osteomyelitis (5), and has often been reported to be part of a polymicrobial process (18, 1). Bacteremia caused by *V. parvula* as the only microorganism and without a defined site of primary infection is extremely rare and, to our knowledge, has been described just twice: in a patient with posthepatic cirrhosis (9) and in a 5-year-old boy with stage IV neuroblastoma treated with chemoradiotherapy (8). In the case presented, *V. parvula* was the only microorganism isolated from the peripheral blood specimen taken during hospitalization, and no primary site of infection was defined. Therefore, *V. parvula* should not be regarded as a nonpathogenic microorganism, as it may be the cause of life-threatening bacteremia, at least in patients undergoing immunosuppressive therapy (8) or in patients with primary humoral immunodeficiency diseases (as in this report).

All authors have read and approved the manuscript and have no conflicts of interest related to this research.

REFERENCES

1. **Arrosagaray, P. M., C. Salas, M. Morales, M. Correas, J. M. Barros, and M. L. Cordon.** 1987. Bilateral abscessed orchiepididymitis associated with sepsis caused by *Veillonella parvula* and *Clostridium perfringens*: case report and review of the literature. J. Clin. Microbiol. **25:**1579–1580.
2. **Bhatti, M. A., and M. O. Frank.** 2000. *Veillonella parvula* meningitis: case report and review of *Veillonella* infections. Clin. Infect. Dis. **31:**839–840.
3. **Bongaerts, G. P., B. W. Schreurs, F. V. Lunel, J. A. Lemmens, M. Pruszczynski, and M. A. Merkx.** 2004. Was isolation of *Veillonella* from spinal osteomyelitis possible due to poor tissue perfusion? Med. Hypotheses **63:** 659–661.
4. **Boo, T. W., B. Cryan, A. O'Donnell, and G. Fahy.** 2005. Prosthetic valve endocarditis caused by *Veillonella parvula*. J. Infect. **50:**81–83.
5. **Borchardt, K. A., M. Baker, and R. Gelber.** 1977. *Veillonella parvula* septicemia and osteomyelitis. Ann. Intern. Med. **86:**63–64.
6. **Chaturvedi, V. N., A. Methwani, P. Chaturvedi, and P. Narang.** 1989. Bacterial flora in chronic tonsillitis. Indian Pediatr. **26:**52–56.
7. **Conley, M. E., A. Broides, V. Hernandez-Trujillo, V. Howard, H. Kanegane, T. Miyawaki, and S. A. Shurtleff.** 2005. Genetic analysis of patients with defects in early B-cell development. Immunol. Rev. **203:**216–234.
8. **Fisher, R. G., and M. R. Denison.** 1996. *Veillonella parvula* bacteremia without an underlying source. J. Clin. Microbiol. **34:**3235–3236.
9. **Gessoni, G., N. Sacchetto, S. Gelmi, O. Portesan, A. Imperato, C. Barotti, G. Simonato, and F. Callegari.** 1989. *Veillonellae*: personal observation of a fatal bacteremia. Boll. Ist. Sieroter. Milan. **68:**193–196.
10. **Hughes, C. V., P. E. Kolenbrander, R. N. Andersen, and L. V. Moore.** 1988. Coaggregation properties of human oral *Veillonella* spp.: relationship to colonization site and oral ecology. Appl. Environ. Microbiol. **54:**1957–1963.
11. **Liaw, Y. S., P. C. Yang, Z. G. Wu, C. J. Yu, D. B. Chang, L. N. Lee, S. H. Kuo, and K. T. Luh.** 1994. The bacteriology of obstructive pneumonitis. A prospective study using ultrasound-guided transthoracic needle aspiration. Am. J. Respir. Crit. Care Med. **149:**1648–1653.
12. **Loughrey, A. C., and E. W. Chew.** 1990. Endocarditis caused by *Veillonella dispar*. J. Infect. **21:**319–321.
13. **Mori, T., T. Ebe, M. Takahashi, H. Isonuma, H. Ikemoto, and T. Oguri.** 1993. Lung abscess: analysis of 66 cases from 1979 to 1991. Intern. Med. **32:**278–284.
14. **Nukina, S., A. Hibi, and K. Nishida.** 1989. Bacterial meningitis caused by *Veillonella parvula*. Acta Paediatr. Jpn. **31:**609–614.
15. **Singh, N., and V. L. Yu.** 1992. Osteomyelitis due to *Veillonella parvula*: case report and review. Clin. Infect. Dis. **14:**361–363.
16. **Su, W. Y., C. Liu, S. Y. Hung, and W. F. Tsai.** 1983. Bacteriological study in chronic maxillary sinusitis. Laryngoscope **93:**931–934.
17. **Williams, B. T.** 1977. Pelvic abscess associated with repeated recovery of *Veillonella*. Am. J. Obstet. Gynecol. **129:**342–343.
18. **Wilson, W. R., W. J. Martin, C. J. Wilkowske, and J. A. Washington II.** 1972. Anaerobic bacteremia. Mayo Clin. Proc. **47:**639–646.