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Meningitis Caused by *Gordona aurantiaca* (*Rhodococcus aurantiacus*)

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In a case of hairy cell leukemia, *Gordona aurantiaca* (*Rhodococcus aurantiacus*) was isolated from cerebrospinal fluid as the pathogen responsible for lethal infection of the central nervous system. The pathogen had been isolated previously from one case of pulmonary infection process only.

Isolation of *Gordona aurantiaca* (*Rhodococcus aurantiacus*) from humans has been confined until recently to sputum. Attention to its etiologic role in pulmonary infections was first drawn by Tsukamura and Kawakami in 1982 (10). In the case to be reported here, *G. aurantiaca* was isolated from the cerebrospinal fluid (CSF) of a patient with hairy cell leukemia (HCL). The bacterium is regarded as the infective agent responsible for the meningitis which caused the death of the patient.

The patient was a 43-year-old male, a sewage worker by occupation. HCL was discovered in May 1981 when he was treated for a generalized herpes simplex virus infection which raised the suspicion of a primary disease of hematological nature. The diagnosis of HCL was based on the finding of typical cells in the blood and bone marrow and confirmed by their electron microscopic features as well as by their tartrate-resistant acid-phosphatase positivity. A conventional splenectomy could not be performed because of bacterial superinfection (*Staphylococcus aureus*) of the cutaneous lesions. The patient was started on lithium and maintained on it until death. His cutaneous process continued for another six months. In the meantime, he experienced recurrent febrile episodes, the first caused by otitis media. Subsequently, in July 1981, a pulmonary infiltrate made up of minute patchy densities was found. No pathogen was demonstrable either by repeated blood cultures or by routine sputum studies. After treatment with various antibacterial agents, regression eventually was attained with cotrimoxazole. The patient was fairly well for the next four months. In January 1982, high temperatures, vomiting, mental confusion, and signs of meningeal irritation appeared. The high cell count and low glucose concentration in the CSF pointed to a bacterial process, and lack of neutrophils was consistent with granulocytopenia in the peripheral blood. In view of the prevalence of atypical mycobacterial infections in HCL, the patients was started on isoniazid, rifampin, ethambutol, and, later, streptomycin. A transitory improvement, reflected in a decrease in the cell count in the CSF, was followed four weeks later by steadily progressing mental confusion and increasing signs of cerebral pressure until death occurred. From the CSF drawn 10 days after the appearance of signs of meningeal irritation and before the start of antituberculosis treatment, *G. aurantiaca* had been cultured, but the patient died before it was finally identified.

The brain, weighing 1,320 g, revealed leptomeningeal hyperemia. On gross examination, sporadic greenish-yellow nodules, approximately 3 mm in diameter, were seen on its surface. Histological study revealed specific granulomatous tissue with giant cells of the Langhans type. No pathogens were demonstrable by Ziehl-Neelsen or Gram staining. Liver, spleen, lymph node, and bone marrow abnormalities were consistent with HCL. There was no evidence of any infective dissemination, even in the lungs.

The first CSF specimen, drawn on day 2 of hospitalization, contained 1,400 white cells per mm^3, of which 100% were lymphocytes. The protein and glucose levels were 228 mg/100 ml and 1.37 mmol/liter, respectively. (Blood glucose measured concomitantly was 7.4 mmol/liter.) In the five CSF specimens taken subsequently until day 37 of hospitalization, the cell count ranged between 220 and 1,300 cells per mm^3, the protein level ranged between 129 and 288 mg/100 ml, and the glucose concentration ranged between 0.82 and 2.20 mmol/liter. Microscopic examination of stained sediments of the first and subsequent five CSFs revealed no acid-fast bacilli or other microorganisms, including fungi. All six CSF specimens were cultured in aerobic and anaerobic broth and on blood and chocolate agar and incubated for 3 days. The specimen drawn 10 days after the appearance of signs of meningeal irritation, however, was inoculated also on Löwenstein-Jensen agar and incubated for a prolonged time. Neither the aerobic and anaerobic broth nor the blood and chocolate agar cultures revealed any growth, but on both Löwenstein-Jensen agar slants inoculated in parallel, slightly brownish-yellow, rough, dry *Mycobacterium*-like scotochromogenic colonies appeared on day 7 of incubation.

The isolate was a gram-positive short bacillus with some branching filaments. It proved to be slightly acid fast when stained by the method of Gordon and Smith (3) but was not acid fast when stained with the Kinyouns stain. When subcultured aerobically, it grew on simple media after three days of incubation at 28°C and 37°C but not at 42°C or above. No growth was observed anaerobically. The organism was catalase positive and oxidase negative. Glucose was utilized oxidatively on Hugh Leifson medium. It produced acid from lactose, mannitol, sucrose, maltose, salicin, glycerol, trehalose, and sorbitol, but no reaction was observed with starch, arabinose, xylose, inositol, and raffinose. The β-galactosidase test, performed by the method of Tsukamura (8), was negative. Motility was not detected, urease and niacin were not produced, and nitrate was not reduced to nitrite. Aerial mycelium was not formed. An iron uptake test, performed as described by Wayne and Doubek (13), was positive.

The properties found suggested an organism with charac-

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TABLE 1. MICs for *G. aurantiaca* isolate by the agar dilution method

Drug (source)	MIC (μg/ml)
Penicillin (Biogal)	12.5
Ampicillin (Chinoin)	1.56
Cephalothin (Ely Lilly & Co.)	400.00
Cefoxitin (Merck Sharpe & Dohme)	25.0
Cefamandole (Lilly)	50.0
Streptomycin (EGYT)	12.5
Gentamicin (The Upjohn Co.)	0.4
Kanamycin (Sigma Chemical Co.)	1.6
Tobramycin (Biogal)	1.6
Tetracycline (Chinoin)	50.0
Doxycycline (Pfizer Inc.)	6.25
Chloramphenicol (EGYT)	12.5
Erythromycin (Sigma)	25.0
Sulfadimidine (Alkaloida)	800.0
Trimethoprim (EGYT)	6.25
Co-trimoxazole (Wellcome Research Laboratories)	6.25
p-Aminosalicylic acid (E. R. Squibb & Sons)	250.0
Ethambutol (Chinoin)	250.0
Isoniazid (Gedeon Richter)	30.0
Rifampin (Pharmachim)	3.1

ters intermediate between the *Nocardia*, rapidly growing *Mycobacterium*, and *Rhodococcus* genera. The isolate differed from any of the *Nocardia* spp. first of all by the absence of aerial mycelium, from rapidly growing *Mycobacterium* spp. by the absence of acid fastness with Kinyouns stain, and from *Rhodococcus* spp. by β-galactosidase activity and inability to reduce nitrate (12).

The organism was sent to the Centers for Disease Control, Atlanta, Ga., for proper identification. They confirmed our results and completed the tests with those for xanthine and hypoxanthine hydrolysis. The organism, which hydrolyzed xanthine and hypoxanthine, was identified as *G. aurantiaca* by June M. Brown (Reference and Investigative Branch, Division of Mycotic Diseases), to whom we are much indebted.

To determine the in vitro susceptibility of the isolate to several antimicrobial agents, a method described for preparing uniformly dispersed cultures of *Nocardia asteroides* was used (1). The MICs obtained by the agar dilution method are given in Table 1.

The genus *Gordona*, as an intermediate between the genera *Mycobacterium* and *Nocardia*, consists of slightly acid-fast organisms found in soil and associated with pulmonary disease (7). *G. aurantiaca* was described by Tsukamura and Mizuno as a new species of the genus *Gordona* (11). In 1974, Tsukamura proposed the generic name *Rhodococcus* for organisms of the genus *Gordona* and so-called rhodochrous organisms, and included *G. aurantiaca* in the genus *Rhodococcus* as *R. aurantiacus* (9). Goodfellow et al., however, assigned this organism to a new genus in 1978 (2). Later (in 1979), Tsukamura et al. also considered it to be outside the genus *Rhodococcus* (12). Tsukamura and Kawakami isolated 14 strains of *G. aurantiaca* (*R. aurantiacus*) in their laboratory from the sputa of patients with tuberculosis or tuberculosislike lung disease. A case of pulmonary infection, the first human infection in which this organism had been regarded as the responsible pathogen, was reported by the same authors (10).

The attempts to identify our isolate resulted in only approximating its proper taxonomic position. Tsukamura and Kawakami provide a chart for the differentiation of *G. aurantiaca* from other rhodococci and nocardiae and some rapidly growing mycobacteria (10). The reactions presented in their work have to be supplemented by the results of the xanthine and hypoxanthine hydrolysis tests, which are useful characteristics for the differentiation of *G. aurantiaca* from *Rhodococcus* and from rapidly growing *Mycobacterium*. Because the taxonomic position of this organism is still uncertain, only a few strains had been isolated until recently, and the strain isolated by us seems to be the second to cause disease in humans, we suggest that all strains showing characters intermediate between the genera *Nocardia*, *Rhodococcus*, and *Mycobacterium* be sent to some reference laboratory for proper identification.

The etiology of the present case of meningitis may be ascribed to *G. aurantiaca* (*R. aurantiacus*) on the following grounds. (i) The clinical course pointed to a bacterial process, and only this organism was isolated. This isolate in a compromised host may be interpreted in our view as being indicative of an active infection, similar to organisms belonging to the rhodochrous complex isolated from sputum (4). (ii) Atypical mycobacteria (possibly nocardiae) closely related to *G. aurantiaca* (*R. aurantiacus*) may produce cerebral processes consistent in pathology with the present observations (6). The same pathogen accounts in all probability for the earlier pulmonary process. Our failure to isolate it may have been due to the fact that study of the sputum was confined to routine tests. Likewise, the isolation of the organism from only one CSF specimen can be explained by the fact that only this specimen underwent prolonged incubation on Löwenstein-Jensen medium. Its absence from the histological preparation may be connected with the combined antibacterial medication.

In HCL, cell-mediated immunity is impaired. Patients with HCL are susceptible to a wide range of infecting organisms (5, 6, 14), including nontuberculous (atypical) mycobacteria which have become important pathogens for compromised hosts (14). It should, however, be noted that published cases of meningitis caused by nontuberculous mycobacteria, even as part of a generalized infection, are very rare (15). It was nevertheless suspicion of an atypical mycobacterial infection which prompted us to change over from ampicillin and penicillin to a combined antibacterial medication active also against mycobacteria. The death of the patient precluded any evaluation of the therapeutic attempt.

The results of the sensitivity tests, which were unknown until after the death of the patient, failed to justify the use of isoniazid and ethambutol as the medication of first choice in this infection.

We intend by the present report to draw attention to the necessity for considering the possible involvement of opportunistic pathogens, even those as rare as *G. aurantiaca* (*R. aurantiacus*) in infection, including that of the brain, in immunologically compromised patients.

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