Jpn. J. Infect. Dis., 59, 126-128, 2006

Short Communication

An Unusual Case of Brain Abscess by *Gemella morbillorum*

Maria Carla Liberto*, Giovanni Matera, Rossana Puccio, Vincenzo Barbieri, Angela Quirino, Renata Capicotto, Vincenzo Guadagnino[1], Kurt Pardatscher[2] and Alfredo Focà

Department of Medical Sciences, Institute of Microbiology, [1]Department of Experimental and Clinical Medicine, Institute of Infectious Diseases, and [2]Department of Medical Sciences, Institute of Neuroradiology, University of Catanzaro, Catanzaro, Italy

(Received August 11, 2005. Accepted February 3, 2006)

SUMMARY: A case of deep brain abscess by *Gemella morbillorum* is described. Due to high fever, lethargy, severe headache, and the risk of intraventricular rupture of the suppurative lesion, a CT-guided stereotactic aspiration of the abscess was successfully performed. The patient responded well to a 6-week course of meropenem, metronidazole, and fluconazole. *Gemella* spp. should not be considered as trivial commensals of the mucous membranes, but appear as emerging pathogens involved in endocarditis, septic shock, and necrotizing pneumonia, as well as in serious intracranial infections.

Gemella morbillorum is an anaerobic-to-aerotollerant, Gram-positive, no motile, and non-spore-forming coccus that can be observed in singles, pairs, and short chains. It has been grouped with viridans streptococci, from which it can be distinguished by biochemical activities and molecular tests (1). *G. morbillorum* is a normal resident microbiota of several mucosal surfaces, including the oropharynx and the gastrointestinal and female genital tract, and its clinical significance is unclear. Infections by *G. morbillorum* of the central nervous system (CNS) are unusual, and brain abscesses reported in the literature include description of only four clinical cases (1-3). Endocarditis, septic shock, and other cardiovascular infections (4) are the most frequently reported diseases caused by such organisms; however, sinusitis, pneumonia, gynecological infections, empyema, septic arthritis, and infections of the eye can also be found in the literature (3).

A 75-year-old white woman presented to a primary care clinic with a 7-day history of headache, fever, nausea, and vomiting. A first cranial CT showed a minimally contrast-enhancing right frontal round mass (diameter, 4 cm), adjacent to the anterior horn of the lateral ventricle. Such a lesion was surrounded by a hypodense halo consistent with oedema and produced a shift of the brain midline to the left. The initial suspicion based on this first imaging approach was an astrocytoma. Corticosteroid therapy was started.

One month after the beginning of the illness, the patient was referred to our institution for neurosurgical consultation.

Upon admission, neurological evaluation revealed progressive ideomotor impairment and speech and gait disturbances, without clinical signs of meningitis. Laboratory analysis showed a peripheral leukocyte count of 12,000 cells/mm^3, an increased erythrocyte sedimentation rate of 60 mm/h and a CD4 lymphocyte count within the normal range. A cranial CT study in our institution confirmed the features already exhibited by the previous CT examination (Fig. 1), and magnetic resonance imaging (MRI) showed the right frontal mass as well as an enhancement of the ependymal surface of the frontal and occipital horn of the lateral ventricles. Lumbar puncture in order to sample cerebrospinal fluid (CSF) was not carried out in our patient because it could be associated with increased morbidity and lethality due to intraventricular rupture or leakage of the brain abscess (1).

Following the CT-guided stereotactic aspiration, the purulent material obtained was microscopically evaluated by a pathologist, and brain tissue debris, including a relevant number of neutrophils, macrophages, and other inflammatory cells, was observed.

Aerobic as well as anaerobic cultures of the purulent sample were carried out on Columbia sheep blood agar and on Schaedler agar base supplemented with 5% sheep blood and vitamin K. A nonhemolytic Gram-positive coccus grew within 48 h. The biochemical identification system Rapid ID 32A (bioMerieux, Marcy l'Etoile, France) allowed us to identify the bacterium as a *G. morbillorum* strain, due to the typical reaction pattern ("excellent identification") for such a species.

The strain under investigation was sensitive to penicillin, amoxicillin/clavulanic acid, piperacillin/tazobactam, ticarcillin/clavulanic acid, cefoxitin, cefotetan, imipenem, clindamicin, chloramphenicol, and amoxicillin, but was resistant to metronidazole. Based on the data obtained from the susceptibility test, empiric therapy started at the time of the stereotactic aspiration was not changed. Such an antibiotic regimen included a 6-week course of intravenous meropenem (1 g every 12 h), metronidazole (100 ml every 8 h) and diflucan (100 mg every 24 h). Steroid therapy was maintained for 2 weeks after microbiological diagnosis to reduce perilesional oedema and inflammation. A present source of infection from the cardiovascular and gastrointestinal districts was evaluated, and no pathological features were found. However orodental procedures were found in the patient history, as well as an infectious pleural disease that had occurred several months earlier. Since *G. morbillorum* has been reported as a cause of pleural infectious exudates (5), there could have been a primary diffusion from the oral district to pleural tissues. Then, metastatic diffusion to the brain might have derived from an old primary oral infectious site, or from the more recent pleurisy.

Ten days after the abscess aspiration, the patient became conscious, her headache became mild, and she began to walk

*Corresponding author: Mailing address: Institute of Microbiology, Department of Medical Sciences, University of Catanzaro, Via T. Campanella, 115, I-88100 Catanzaro, Italy. Tel: +39-0961-712427, Fax: +39-0961-770403, E-mail: mliberto@unicz.it

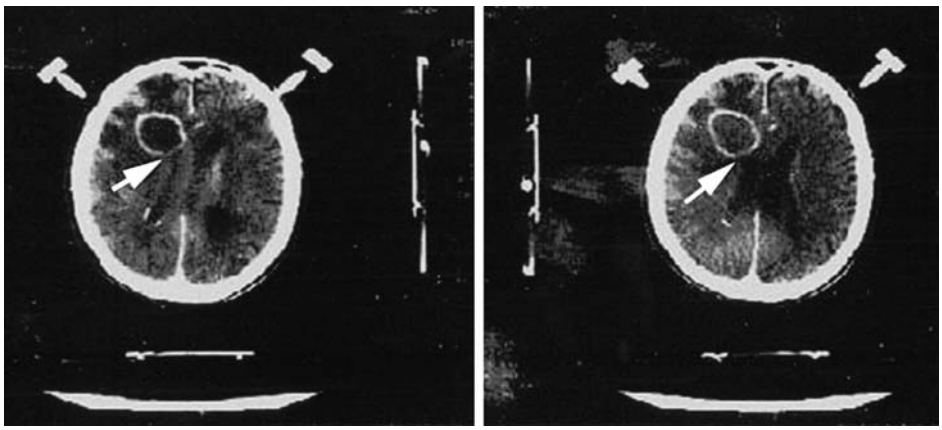

Fig. 1. Coronal slices from post-contrast brain CT showing a minimally contrast-enhancing right frontal round mass (diameter, 4 cm), adjacent to the anterior horn of the lateral ventricle (arrow). The lesion was surrounded by a hypodense halo consistent with oedema and produced a shift of the brain midline to the left.

without obvious disturbances. A CT scan carried out 2 weeks after the surgery revealed that the mass effect began to decrease significantly and the frontal right horn of the lateral ventricle began to expand, while the volume delimiting the brain inflammatory region began to narrow. After 2 months, the patient was reevaluated. She had resumed her previous daily activities. The CT scan showed no evidence of persistent infection with a fair gliotic reaction and absence of the hypodense center in the place of the original lesion.

Mortality from brain abscess (regardless the etiology) ranged from 30 to 60% until the late 1970s, when the availability of more effective antibiotics (particularly metronidazole), novel surgical procedures, and CT scan caused a reduction to 10%. The empiric medical therapy for brain abscess usually includes a β-lactam plus metronidazole (6).

G. morbillorum was isolated for the first time by Tunnicliff from the blood of a subject with measles (7). Such bacterium was then named *Diplococcus morbillorum*, *Streptococcus morbillorum*, and was finally included in the genus *Gemella* with its present name in 1988 (8). Until now, only four cases of *G. morbillorum* brain abscess have appeared in the literature. The first report by Murray et al. dealt with a case presenting as meningitis (1). Two other publications appeared more recently in 2002 and in 2003 (2,3). Messori et al. have reported a young male without previous clinical records, with the exception of canine avulsion and chronic sinusitis; this subject presented with fever, headache, lethargy, nausea, and vomiting and underwent a stereotactic, medical imaging approach with a successful outcome (2). Spagnoli et al. have published the most recent study on *G. morbillorum* brain abscess presenting with hemiparesis and seizures (3).

CNS infections due to *G. morbillorum* are a diagnostic and therapeutic challenge for the physician because of the insidious presentation and evolution, the difficulty of making a connection with the primary septic site, and the need for a long course of antibiotic association (3). Indeed, the clinical presentation of cerebral abscess includes nonspecific signs and symptoms (e.g., headache, fever, nausea, vomiting, and lethargy) that may be seen with many other syndromes (1). However, the only four cases of brain abscess due to *G. morbillorum* reported in the literature have been associated with more specific clinical features such as neck stiffness (1,2), hemiparesis, or seizures (3), which could suggest a neurological disease. In contrast, our case presentation, more insidiously, included all of the above reported nonspecific signs and symptoms, without any neck stiffness, hemiparesis, seizures, or other clinical features, which could draw the physician's attention to a primary neurological impairment. Based on the CD4 lymphocyte count, our patient was immunocompetent. However, previous cases of brain abscess due to *Gemella* have been reported in immunocompetent patients (2,9).

Published hypotheses regarding pathogenetic mechanisms of *Gemella* infections include downregulation of IL-12 and IFN-γ, which are well known to play a crucial role in the eradication of many different pathogens (10). Also, stimulation of antineutrophil antibodies has been reported to be caused by the presence of *G. morbillorum* in blood and CSF of a 17-year-old girl (11). Both mechanisms may account for the possibility of a very late metastasis from an original primary infectious site. Indeed, our patient had orodental procedures some years ago and an infectious pleural disease several months earlier. Since *G. morbillorum* has been reported as a cause of pleural infectious exudates (5), it is possible that in the present case it spread to the brain from the more recent pleural infection or from an old primary oral infectious site, as reported previously for another *G. morbillorum* brain abscess, which presented 7 years after the avulsion of both canines (2). Indeed *Gemella* spp. are part of the commensal bacteria of the oral cavity (1,2).

Metronidazole susceptibility is a controversial issue in therapy for *Gemella* infections.

Some isolates of *G. morbillorum* are metronidazole sensitive (12). In contrast, the strain of the present study and other isolates reported in the literature (3) are resistant to such an important antibiotic, which is often used in the abscess therapy, due to its broad antimicrobial activity, rapid bacterial killing, good tissue penetration, moderate adverse effects, low cost, and the possibility of sequential parenteral and oral administration (13). Kuriyama et al. have shown that the frequency of metronidazole resistance among *G. morbillorum* strains isolated from cranial infections is 10% (12).

G. morbillorum brain abscess requires a subtle clinical interpretation, a fine radiological follow-up, and a careful microbiological diagnosis in order to avoid lethal complications. However, based on the above reported microbiological results, which were supported by the biochemical pattern of our strain and by data from the literature, we are confident of this isolate speciation, which contributed significantly to the successful outcome of this case.

Based on our experience and on scientific literature (2,6,9), a possible regimen for *Gemella* brain abscess should include a broad spectrum β-lactam (e.g., meropenem or amoxicillin) plus an anti-anaerobic drug (e.g., metronidazole or clindamycin) at full dosage for at least 6 weeks.

Gemella organisms are very often isolated in mixed infection (9,14). Therefore, we strongly believe that the lack of organisms other than *Gemella* in the culture of our clinical sample could be easily explained by the previous empiric treatment, which would control possible co-pathogens (fungi, Gram-negative anaerobic rods). Withdrawal of either metronidazole or fluconazole would allow one or more previously controlled, but not eradicated, potential pathogens to grow again. When planning a long therapeutic schedule, such a risk should be taken into account, particularly after the surgical procedure, due to the possibility of the spread of infectious exudates to other brain districts, as reported by other authors (2).

In order to reduce oedema around an abscess, our patient received steroids for several weeks before and for 2 weeks after the microbiological diagnosis (15). Many antibiotics, including β-lactams, cannot reach adequate concentrations in brain tissue due to steroid administration (16). However, dexamethasone does not have deleterious effects on fluconazole pharmacokinetics in the brain (17); moreover fluconazole has been successfully used in a case of frontal lobe brain abscess in a patient with normal immunity (18).

In conclusion *G. morbillorum* should not be considered a simple commensal of the mucous membranes, but an emerging pathogen involved in severe diseases, including brain abscess.

REFERENCES

1. Murray, C. K., Hospenthal, D. R., Grimberg, B. T. and Gasser, R. A. (1998): *Gemella morbillorum* brain abscess presenting as acute meningitis. Infect. Dis. Clin. Pract., 7, 477-480.
2. Messori, A., Bartolucci, F., Dini, M., Paggi, A. M., Ricciuti, R. A., Rychlicki, F. and Salvolini, U. (2002): *Gemella morbillorum* deep brain abscess successfully treated with combined stereotactic, medical and imaging approach. Eur. J. Radiol., 44, 143-151.
3. Spagnoli, D., Innocenti, L., Ranzi, M. L., Tomei, G. and Villani, R. M. (2003): Cerebral abscess due to *Gemella morbillorum*. Eur. J. Clin. Microbiol. Infect. Dis., 22, 515-517.
4. La Scola, B. and Raoult, D. (1998): Molecular identification of *Gemella* species from three patients with endocarditis. J. Clin. Mirobiol., 36, 866-871.
5. Poulose, V. (2002): Gemella empyema cured without antibiotics: a case report. Ann. Acad. Med. Singapore, 31, 802-804.
6. Mathisen, G. E. and Johnson, J. P. (1997): Brain abscess. Clin. Infect. Dis., 25, 763-781.
7. Tunnicliff, R. (1917): The cultivation of a micrococcus from blood in pre-eruptive and eruptive stages of measles. JAMA, 68, 1028-1030.
8. Kilpper-Balz, R. and Schleifer, K. H. (1988): Transfer of *Streptococcus morbillorum* to the genus *Gemella* as *Gemella morbillorum* comb. nov. Int. J. Syst. Bacteriol., 38, 442-443.
9. Lee, M. R., Lee, O., Kim, Y., Yang, S. M., Seo, H. and Cho, Y. K. (2004): Brain abscess due to *Gemella haemolysans*. J. Clin. Microbiol., 42, 2338-2340.
10. Ribeiro Sobrinho, A. P., de Melo Maltos, S. M., Farias, L. M., de Carvalho, M. A., Nicoli, J. R., de Uzeda, M. and Vieira, L. Q. (2002): Cytokine production in response to endodontic infection in germ-free mice. Oral Microbiol. Immunol., 17, 344-353.
11. Nagashima, T., Hirata, D., Yamamoto, H., Okazaki, H. and Minota, S. (2001): Antineutrophil cytoplasmic autoantibody specific for proteinase 3 in a patient with shunt nephritis induced by *Gemella morbillorum*. Am. J. Kidney Dis., 37, E38.
12. Kuriyama, T., Karasawa, T., Nakagawa, K., Yamamoto, E. and Nakamura, S. (2002): Bacteriology and antimicrobial susceptibility of gram-positive cocci isolated from pus specimens of orofacial odontogenic infections. Oral Microbiol. Immunol., 17, 132-135.
13. Rafii, F., Wynne, R., Heinze, T. M. and Paine, D. D. (2003): Mechanism of metronidazole-resistance by isolates of nitroreductase-producing *Enterococcus gallinarum* and *Enterococcus casseliflavus* from the human intestinal tract. FEMS Microbiol. Lett., 225, 195-200.
14. Kao, P. T., Tseng, H. K., Liu, C. P., Su, S. C. and Lee, C. M. (2003): Brain abscess: clinical analysis of 53 cases. J. Microbiol. Immunol. Infect., 36, 129-136.
15. Pandian, J. D., Moosa, N. V., Cherian, P. J. and Radhakrishnan, K. (2000): Brainstem abscess complicating tetralogy of Fallot successfully treated with antibiotics alone. Neurol. India, 48, 272-275.
16. Kourtopoulos, H., Holm, S. E. and Norrby, S. R. (1983): The influence of steroids on the penetration of antibiotics into brain tissue and brain abscesses. An experimental study in rats. J. Antimicrob. Chemother., 11, 245-249.
17. Lortholary, O., Nicolas, M., Soreda, S., Improvisi, L., Ronin, O., Petitjean, O., Dupont, B., Tod, M. and Dromer, F. (1999): Fluconazole, with or without dexamethasone for experimental cryptococcosis: impact of treatment timing. J. Antimicrob. Chemoter., 43, 817-824.
18. Kawakami, N., Nishizaki, T., Sugiyama, S. and Ito, H. (1994): Aspergillus brain abscess in a patient with normal immunity - case report. Neurol. Med. Chir. (Tokyo), 34, 237-240.