We report a clinical case of meningoencephalitis with subdural empyema in an immunocompromised farmer caused by toxigenic Clostridium perfringens type A, which was identified by 16S RNA gene analysis of cerebrospinal fluid and subdural empyema. In immunocompromised patients, C. perfringens should be considered a potential pathogen of sepsis.
were not possible. According to MIC data for incubation. Therefore, biochemical tests and susceptibility testing with different antibiotics are needed. The patient was treated with voriconazole. The patient could be discharged from the ICU after 1 month of intensive care treatment. Subdural empyema and diffuse encephalitis with or without pneumocephalus has been presented (23).

The most frequent clinical manifestation of *C. perfringens* infection is myonecrosis, or gas gangrene. If only minor amounts of toxins are produced, infections may present as a mild, self-limiting disease. If local infections spread via hematogenous dissemination, every organ might be involved, including the brain. Central nervous system manifestation of *C. perfringens* infection in humans is rare (9). Most commonly, the meninges are affected (1, 2, 3, 6, 7, 10–14, 16–19, 21, 22, 23–25, 29, 30) after clinical manifestation of sepsis (31). Rarely, focal or diffuse encephalitis with or without pneumocephalus has been presented (2, 13, 22, 27, 29), and only a single case of subdural empyema has been reported in the current literature (23). In our patient due to the clinical findings of generalized epileptic seizure, radiological evidence of progressive brain edema, and detection of *C. perfringens* type A by molecular analysis of CSF and subdural empyema, we diagnosed a meningoencephalitis and subdural empyema with *C. perfringens*. We were unable to cultivate *C. perfringens*, probably due to the antibiotic treatment started 3 days before sampling. However, the diagnosis was unambiguous according to (i) direct microscopic detection of plump Gram-positive, rod-shaped bacteria in large quantities in two independent samples of the subdural lesion and (ii) 100% identification of the 16S rRNA gene PCR amplicon with *C. perfringens* in both clinical samples (cerebrospinal fluid and subdural empyema). In addition, the *cpa* gene, which codes for the virulence factor alpha-toxin of *C. perfringens* type A, was amplified and confirmed by sequence analysis.

Usually, infections with *C. perfringens* start from a recent surgical wound, trauma, or intra-abdominal disease, such as infections of the biliary tract or other gastrointestinal infections (26). However, in most of the cases of *C. perfringens* meningitis, the site of infectious origin remains unidentified (6, 11, 13, 14, 18, 21, 23, 24, 28), as in our patient. *C. perfringens* is a common part of the intestinal flora of domestic animals, such as cattle, and the bacteria are spread into the environment by feces (33). In our case, gastrointestinal disease caused by a food-borne infection was ruled out. There was a history of minor trauma caused by a strike of a cow’s hoof 3 weeks before onset of symptoms. Possibly, *C. perfringens* type A was carried on the cow’s hoof and transmitted into the wound. Due to the preexisting coagulopathy and the history of trauma, we assume a chronic subdural hematoma as the site of onset for the CNS manifestation. Although repeated normal aerobic and anaerobic blood cultures remained negative, a transient bacteremia with *C. perfringens* type A is likely to have happened in a chronically exposed and immunocompromised farmer.

Subdural empyema and diffuse encephalitis with *C. perfringens* are reported to be fulminating and have a fatal outcome in 30 to 60% of patients (33).
100% of untreated patients (9). The functional recovery in our patient might be explained by the early targeted therapy with penicillin and metronidazole. There are expert recommendations but no in vivo data regarding the treatment of C. perfringens CNS manifestations (21). In vitro, antibiotic drugs with activity against Gram-positive anaerobic bacteria (penicillin, clindamycin, and metronidazole) reportedly show low MICs (32). To date, no C. perfringens isolates resistant to penicillin, clindamycin, or metronidazole according to EUCAST clinical breakpoints for anaerobic Gram-positive rods (20) have been described. In the treatment of a brain abscess with C. perfringens, a favorable outcome after immediate surgical debridement or drainage was reported (5, 8).

In conclusion, we report the first case of cerebral infection due to C. perfringens type A manifested with subdural empyema and diffuse meningoencephalitis, which was diagnosed by 16S rRNA sequencing and a multiplex PCR approach. The patient was successfully treated with targeted antibiotic therapy and surgical removal of subdural empyma. Even though rarely reported, C. perfringens type A should be considered a differential pathogen in a patient with immunosuppression. If no pathogen can be cultivated due to ongoing antibiotic treatment, molecular analysis such as broad-range 16S RNA PCR is a valuable and rapid tool leading to an accurate diagnosis.

Nucleotide sequence accession number. The 16S sequence of the patient’s isolate has been submitted to GenBank under accession no. JQ782390.

REFERENCES