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CLUSTER OF TWO CASES OF BOTULISM DUE TO *CLOSTRIDIUM BARATII* TYPE F IN FRANCE, NOVEMBER 2014

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The first two cases in France of botulism due to *Clostridium baratii* type F were identified in November 2014, in the same family. Both cases required prolonged respiratory assistance. One of the cases had extremely high toxin serum levels and remained paralysed for two weeks. Investigations strongly supported the hypothesis of a common exposure during a family meal with high level contamination of the source. However, all analyses of leftover food remained negative.

On 12 November 2014, two cases of botulism were notified to the regional health agency (ARS) in France. The cases were two women in the same family. They were hospitalised in intensive care where they received respiratory assistance and could therefore not be interviewed. Epidemiological and microbiological investigations were conducted by the regional office of the French Institute of Public Health Surveillance (InVS) and the national reference centre (NRC) for botulism in order to confirm the outbreak and to determine the source of exposure.

Case descriptions

Case 1 was a woman in her 60s with symptom onset on 10 November 2014 around 8 pm (20 h after the family meal) including hypercapnia, gradually descending flaccid paralysis, complete respiratory muscular paralysis and bilateral non-reactive mydriasis. She was immediately admitted to intensive care requiring mechanical ventilation. Case 1 remained completely paralysed (limbs, ocular and respiratory muscles) for two weeks. She needed respiratory assistance for 46 days. On 6 January 2015, she was discharged from hospital with a persisting flaccid paraparesis of lower limbs.

Case 2 was a woman in her late 20s with symptom onset on 11 November 2014 around 8 pm (44 h after the meal), gradually developing diplopia, ptosis, dysphonia, dysphagia and respiratory distress. She was admitted to intensive care on 12 November with flaccid paraparesis and respiratory paralysis. She needed respiratory assistance for 11 days. On 1 December she had fully recovered and was discharged from hospital.

No predisposing factors for intestinal and wound botulism such as antibiotic treatment or gastrointestinal illness during the preceding weeks or a skin lesion were identified for either case.

On 13 November, and before identification of the type of neurotoxin, both cases received intravenous botulinum antitoxin type ABE, which was inadequate for treatment of botulinum neurotoxin type F (BoNT/F) [1].

Epidemiological investigation

Both women had participated in a meal together with six other family members on 9 November 2014. Telephone interviews with family members were conducted to identify epidemiological links between the cases. The two patients also had had lunch together on 6 November in a cafeteria but eaten different meals. They live in different towns and had not met on any other occasion during the two weeks before symptom onset.

The only common exposure consistent with the usual incubation period of botulism (12–36 h [2]) was the family meal at the home of a family member. The food list included industrially processed food (potato chips, drinks, pre-packaged grated carrots and raw beets, country pâté and cheese) except for two artisanal fruit tarts, raw tomatoes, roast beef and pork and home-made mayonnaise. Beef and pork roasts were cooked by Case 1 without additional ingredients. The two cases had shared the same bottle of alcopop (a flavoured alcoholic beverage with an alcohol concentration of 5%), the only common exposure not shared with any other person. One person drank another bottle of the same type. The patients had no other common consumption. No food classically at risk of botulism such as home-made cured meat

products or canned food was identified.

Laboratory investigation

The NRC confirmed the diagnosis of botulism on 17 November with an extremely high BoNT/F serum level for Case 1 (ca 400 mouse lethal doses (MLD)/mL) and a lower level for Case 2 (1–2 MLD/mL). BoNT/F was identified in a stool sample of Case 1 (160 MLD/g), whereas no toxin was detected at the limit of detection (20 MLD/g) for Case 2.

Clostridium baratii was isolated from stool samples of both patients.

Several food leftovers (pâté, roast beef, mayonnaise and apple tart) were analysed by the NRC. Two empty and one full alcopop bottles were tested. All food and drink samples tested negative for toxin (mouse bioassay) and for the presence of neurotoxicogenic *Clostridium* (PCR and culture).

Discussion

Investigations confirmed two cases of botulism type F due to *C. baratii*. The very high BoNT/F level in the serum of Case 1 suggests a high level of toxin contamination of the source, yet the analyses of the food items remained negative. However, the family meal was the only plausible common exposure. Repeated interviews of the family and of Case 2, after recovery, were not conclusive. As the only item exclusively consumed by the cases, the shared alcopop bottle was highly suspected. However, all microbiological analyses were negative. Furthermore, the acidity of the drink (pH = 3.5) was not compatible with *C. botulinum* growth and toxin production [3].

Not all food items eaten during the meal of 9 November could be tested, but the ones consumed by the two patients, with the exception of potato chips and roast pork that were fully consumed, were all tested and were negative.

Other possible routes of *C. baratii* infection include skin lesions or intestinal colonisation [1,2,4]. Neither skin lesions nor intestinal disorders nor predisposing gastrointestinal factors were identified in either case, making those routes of infection improbable.

Active case search has been carried out by interviewing family members and through the mandatory botulism notification system. No other case was identified locally or elsewhere in France.

Botulism type F is extremely unusual in France (no case reported up to now) and across the world. The few documented cases of botulism type F were mostly reported in the United States (US) [1,4-11]. Between 1981 and 2002, 13 cases of adult botulism type F were notified to the US surveillance system. All cases were sporadic; no clustering was described [4].

Characteristic early symptoms of foodborne botulism type A, B and E are blurred vision, dysphagia, dysphonia, marked fatigue and vertigo. Neurological symptoms are always descending the body [2]. Botulism type F, due to *C. botulinum* or *C. baratii*, commonly causes severe illness with tetraplegia and respiratory distress [4,6-10,12] often preceding the neurological symptoms. The presentation of Case 1 with rapidly progressing severe respiratory distress as first symptom was consistent with the case series described in the US, where mean duration of respiratory support was reported to be 24 days (10–84 days) and duration of neuromuscular impairment eight days [4].

BoNT/F is usually detected in serum and gastric liquid but irregularly found in stool samples. *C. botulinum* F and *C. baratii* F are usually isolated from stools [6,7,9,12-14]. Here, BoNT/F was detected in serum and in stool samples. The bacteria were isolated from stools.

Food items most often associated with botulism type F are canned tuna or home-made meat preparations (dried, canned or fresh) such as liver pâté, dried meat or raw-dried game [5,7,15,16]. However, for most cases documented in the literature, the source of contamination is not reported [1,4,13,14]. For the present cluster, the food items consumed at the suspected meal were not ones typically incriminated for botulism. Indeed, most food items eaten by the cases were industrial products. It is thus important to widen the scope of the investigation into food items but also other possible sources of contamination. Continuous mandatory notification of botulism cases will help identify other toxin F cases and direct future investigations.

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Conflicts of interest

None declared.

Authors' contributions

Christine Castor: Study conduct, collecting and validating data, wrote the first draft of the paper and reviewed the manuscript critically. Christelle Mazuet: Microbiological analysis, literature review and reviewed the manuscript critically. Mélanie Saint-Leger: Clinical management of patients and reviewed the manuscript critically. Sabine Vygen: Wrote the first draft of the paper, collecting data and reviewed the manuscript critically. Juliette Coutureau: Literature review and reviewed the manuscript critically. Marion Durand: Clinical management of patients and reviewed the manuscript critically. Michel-Robert Popoff: Microbiological analysis, literature review and reviewed the manuscript critically. Nathalie Jourdan Da Silva: Study conduct, wrote the first draft of the paper and reviewed the manuscript critically.

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