CASE REPORT

Persistent neurogenic bladder dysfunction due to infantile botulism

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SUMMARY

We present a child, 5 months of age, diagnosed with infantile botulism, showing the signs of neurogenic bladder dysfunction. The patient presented with progressive muscle weakness, hypotonia, suckling and swallowing problems and absent peripheral reflexes at clinical examination. Botulinum neurotoxin type A was detected in her serum, confirming the diagnosis. Starting at day 6, the girl presented with a urinary retention initially necessitating free bladder drainage and subsequently intermittent catheterisation. After 6 weeks in intensive care, the patient recovered but the bladder underactivity persisted. Four months following recovery, a urodynamic evaluation was performed, showing a near normal detrusor activity and normal bladder emptying, and the catheterisation was ceased. At 6 months, the girl was diagnosed with a urinary tract infection and bladder emptying problems, which persisted, and clean intermittent catheterisation was started. The final urodynamic evaluation, a year and a half after her initial presentation, revealed a normal detrusor activity and an adequate bladder emptying.

BACKGROUND

Infantile botulism, first described in 1976,^{1 2} is the direct result of colonisation of the gut with *Clostridium botulinum*. The bacteria produce a potent neurotoxin, which targets the presynaptic nerve endings inhibiting the release of acetylcholine.³ It is postulated that the immaturity of the infant's defense mechanisms in the gut allows the colonisation with the *Clostridium*. Interestingly, adult intestinal colonisation has been demonstrated in previous studies.⁴ Although *Clostridium baratii* and *Clostridium butyricum* have also been shown to produce human toxic strains,⁵ but these do not cause botulism. Infant botulism affects infants between 1 week and 12 months of age, the most common onset being between 3 and 4 months.⁶ Infants, who have been breast-fed, appear to have a more favourable prognosis,⁷ and ingestion of honey in the first year of living is a well-known source of infection.⁸ Infant botulism has also been linked to sudden infant death syndrome, and may explain up to 20% of the infants who die without a known diagnosis.⁹ Botulinum toxin is used in the treatment of detrusor overactivity,¹⁰ as it is shown to increase the bladder capacity and decrease detrusor pressure. The toxin is administered through injections directly into the bladder wall and the detrusor muscle at regular intervals.

The main clinical symptoms of infant botulism are difficulty in suckling and swallowing,

constipation, dysphagia, oliguria, general and progressive paralysis and, eventually, failure of the respiratory muscles. Neurological symptoms include ptosis, bad pupillary response to light, ophthalmoplegia, a flaccid look on the face and weak throat reflexes.¹¹ The gradual deterioration of the patient is characteristic of the condition. The disease often demands an intensive supportive care. In the early stages, treatment with a human-derived immunoglobulin, botulinum immunoglobulin, (BIG) seems to shorten the length of admittance to the hospital, and severity of illness through toxin inactivation in the bloodstream.¹²

We report the first case of a child experiencing a neurogenic bladder dysfunction due to infantile botulism.

CASE PRESENTATION

This report concerns a 5-month-old breast-fed girl who presented with clinical signs of dehydration. In the past 4 days prior to admission, she experienced problems of suckling, constipation and dry diapers. The physical examination revealed a generalised hypotonia with weak peripheral reflexes, bilateral ptosis but apyrexia and stable circulation. A nasogastric tube was established at presentation for feeding purposes. On the suspicion of sepsis, broad antibiotic treatment was initiated. In the subsequent hours, the symptoms gradually progressed with the girl losing the ability to suckle, swallow and cough, and signs of respiratory distress necessitated transfer to the intensive care unit (ICU). Lumbar puncture and cerebral ultrasound were unremarkable. On day 4, the diagnosis was confirmed using mouse inoculation¹³ and later botulinum toxin A was detected in her blood and *Clostridium* spores were identified in her faeces. The treatment with BIG started at day 8. During admission, a large bladder was noticed for the first time on day 6. This was confirmed by ultrasound, and the girl was catheterised for more than 250 mL. During the treatment and rehabilitation, she was kept on clean intermittent catheterisation (CIC) due to emptying problems and she experienced 3 urinary tract infection (UTIs). In between CIC, spontaneous voids were noted but with significant residual urine volumes. During this period, the girl recovered with no signs of neurological sequelae apart from the bladder dysfunction. Four months after her diagnosis, she underwent a urodynamic evaluation (figure 1A), showing detrusor activity after infusion of 100 mL saline, with subsequent spontaneous voiding and acceptable residual urine and the regular CIC is stopped. In the next

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Figure 1 The urodynamic evaluations were performed by infusing 37°C saline through a urethral catheter into the empty bladder (15 mL/min), measuring intravesical pressure (Pves). The abdominal pressure (Pabd) was calculated with an anal probe. The detrusor pressure (Pdet) is measured by subtracting Pves with Pabd; in this way, we only get the pressure generated by the detrusor muscle in the bladder wall. Pelvic floor EMG activity was monitored using adhesive electrodes. The first examination (A) showing detrusor contraction after infusion of 100 mL saline. In the following two examinations (B, C), despite the infusion of more than 200 mL saline, no adequate detrusor contraction is seen and the girl had no organised voiding leading to bladder emptying. The final examination (D) showing detrusor contraction with some over-activity up to the voiding and some degree of pelvic floor activity during the voiding which despite that led to the full bladder emptying. EMG, electromyography.

months, occasional measurements of postvoiding residual urine performed by the parents confirmed adequate bladder emptying. However, after 6 months, the girl presented with another UTI, developing bladder retention, and CIC was reestablished. A new urodynamic evaluation after recovery from UTI (figure 1B) shows very little detrusor activity, despite infusion of 200 mL saline. A voiding cystourethrogram was performed, showing no signs of vesicoureteral reflux. The urodynamic evaluation was repeated a month later (figure 1C), and this too showed signs of an underactive detrusor and significant residual. After another 4 months with CIC and almost a year and a half after her diagnosis with infantile botulism, the parents reported consistently full bladder emptying and the girl underwent another urodynamic evaluation showing adequate detrusor activity and normal emptying (figure 1D). After this, CIC was ceased. At 6 months follow-up, the girl was performing well with no UTIs or signs of bladder dysfunction whatsoever.

INVESTIGATIONS

Figure 1 shows cystometries performed before and after resolution of the symptoms.

DIFFERENTIAL DIAGNOSIS

With a diagnosis of infantile botulism, bladder underactivity leading to urine retention seems to be an expectable symptom; however, other conditions leading to neurogenic bladder dysfunction should be considered especially in the light of the persistence of this symptom in the child. Such conditions may include spinal dysraphism and central nervous system lesions. Urine retention and bladder dysfunction are also commonly seen in the ICU patients, and this may have contributed to the patient's bladder dysfunction, although she was not on any point intubated or treated with sedatives.

TREATMENT

Although aetiological treatment with immunoglobulin may improve the clinical course, supportive treatment is still the cornerstone of infantile botulism treatment. A less obvious complication of the condition is bladder dysfunction, which seems to ensue during the acute phase but may persist after discharge necessitating the bladder drainage and/or CIC.

OUTCOME AND FOLLOW-UP

The outcome of the condition is related to the time lapse between disease presentation, diagnosis and treatment. Bladder dysfunction on the basis of infantile botulism seems to have a favourable prognosis if treated appropriately.

DISCUSSION

We present the first case of persistent neurogenic bladder dysfunction related to infantile botulism in a 5-month-old girl. Bladder paralysis due to botulinum toxin has been reported before,^{14 15} but this was in adults with wound-related or food-borne botulism.¹⁵ In both cases, the patients regained the ability to void within 3 months after the initial diagnosis. The bladder recovery period was a lot longer in our patient, affecting bladder emptying for almost 18 months and with significant worsening following a UTI almost a year following the initial presentation. The urodynamic characteristics of the condition were an underactive detrusor and dysfunctional voiding with incomplete bladder emptying. It is of particular interest that the child seemed to recover already 4 months after the presentation, and CIC was stopped, experiencing a relapse of urinary retention following a UTI.

Another explanation for the prolonged detrusor under activity could be the patient's long hospitalisation period and intensive care need. Children in the ICU often have problems of

voiding, thus making it plausible that urine retention could be the result of the patient's poor condition. However, the patient was not intubated or sedated during admission.

One could speculate whether the UTI was responsible for the relapse, as bladder dysfunction and urine retention have been seen in children with UTI. A relapse in infantile botulism has been described before, but the pathophysiology behind the relapse is still unknown, even though three possible mechanisms have been suggested.¹⁶ Glauser *et al* suggest that a subsequent infection, as in this case the UTI, might suppress the immune system to become sensitive to the bacteria again. Furthermore, the immunoglobulin infusion is detectable in the body for at least 6 months,¹² thus making it possible that the immunity against botulinum toxin is lost.

Since *C botulinum* is known to produce a very strong toxin, initial treatment should not involve any antibiotics, due to the risk of bacteria lysis and the chance of increasing toxin levels in the bloodstream. One can therefore postulate that our patient remained colonised with the bacteria for a longer period of

time. A subsequent UTI and the antibiotic treatment use may then exacerbate the symptoms increasing the toxin levels. The duration of latent colonisation in children as well as the age at which a child can withstand colonisation with the clostridia is not clearly elucidated.

Contributors AB drafted, revised and submitted the article. SR and KK revised the draft article.

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Learning points

- Neurogenic bladder dysfunction with detrusor underactivity and urine retention may be a complication of infantile botulism.
- Bladder function can easily be monitored in these children by ultrasound and residual urine measurements and this should be part of the evaluation of a child with infantile botulism.
- Supportive treatment with clean intermittent catheterisation awaiting spontaneous resolution of the symptoms is the treatment of choice but the risk of recurrent urinary tract infection must also be appreciated.
- Bladder dysfunction may persist well beyond recovery of the other neurological symptoms in infantile botulism.

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