CASE REPORT

Multidisciplinary approach to the management of a case of classical respiratory diphtheria requiring percutaneous endoscopic gastrostomy feeding

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SUMMARY

We present a case of a Caucasian woman aged 67 years referred with a 4-day history of sore throat, dysphagia, fever and nasal blockage. Examination revealed a swollen neck and pharyngeal pseudomembrane. A throat swab was positive on culture for *Corynebacterium ulcerans*, with toxin expression confirmed on PCR and Elek testing. A diagnosis of classical respiratory diphtheria was made, with subsequent confirmation of the patient's domesticated dog as the source of infection. The dog had recently been attacked by a wild badger and was being treated for an ear infection. The patient made a good recovery with intravenous antimicrobial and supportive therapy; however, she subsequently developed a diphtheritic polyneuropathy in the form of a severe bulbar palsy with frank aspiration necessitating percutaneous endoscopic gastrostomy feeding. A mild sensorimotor peripheral neuropathy was also diagnosed. The patient eventually made an almost complete recovery.

BACKGROUND

Classical respiratory diphtheria consists of the triad of membranous pharyngitis, fever and neck swelling secondary to lymphadenopathy and soft tissue oedema ('bull neck').¹ This department of health notifiable disease is now rare in the UK due to immunisation and most cases occur in those with partial or waning immunity.² Routine paediatric diphtheria vaccination has ensured that most cases are now mild and are unknowingly treated as streptococcal pharyngitis in the primary care setting. The rarity of this condition means that many clinicians have not encountered a case and are unlikely to consider it among their differential diagnoses for a sore throat.

Most cases of respiratory diphtheria are attributed to toxigenic strains of either *Corynebacterium diphtheriae* or *Corynebacterium ulcerans* and are clinically indistinguishable. Both produce an exotoxin causing local tissue necrosis and systemic complications such as myocarditis and neuritis.³ Until the 1990s, symptomatic infections in the UK were more common due to *C. diphtheriae*; however, since then *C. ulcerans* has become the predominant pathogen.¹ *Corynebacterium ulcerans* was formerly associated with consumption of unpasteurised dairy products; however, contact with domesticated and wild animals harbouring the organism is now the more important risk factor.^{4 5}

Diagnosis is by culture of *Corynebacterium* isolate and detection of *tox* gene is by PCR.⁶ Isolates positive for the presence of *tox* gene must then undergo Elek virulence testing to determine if the toxin is being actively expressed.

Laboratory surveillance in England and Wales between 1986 and 2013 detected 66 toxigenic isolates of *C. ulcerans*. Clinically, these manifested mostly as nasal, laryngeal and cutaneous forms of diphtheria; only four fatalities and seven cases of the classical respiratory diphtheria were recorded.⁷ In the USA, the last reported cases of toxigenic *C. ulcerans* occurred in 2005 and 2010.^{8 9}

Here, we discuss a case of classical respiratory diphtheria with progressive neurological deficit. This is not only uncommon but can be easily missed with serious morbidity if the diagnosis of diphtheria is not made.

CASE PRESENTATION

A British Caucasian woman aged 67 years with a background of asthma, hypothyroidism and an unclear immunisation history was admitted with a 4-day history of sore throat, dysphagia, fever, nasal blockage and passing loose stools. Clinical examination demonstrated a swollen soft palate which was occluding the posterior oropharyngeal wall and tender, firm neck lymphadenopathy. The patient was feverish at 38.7°C. Examination by flexible nasendoscopy (FNE) was limited by copious nasopharyngeal secretions and swelling.

INVESTIGATIONS

Routine haematology and biochemistry revealed a marked neutrophilia and raised C reactive protein plus acute kidney injury. Lateral neck X-ray was consistent with swelling of the prevertebral soft tissues. Stool, urine, blood and throat cultures were negative throughout her first admission.

DIFFERENTIAL DIAGNOSIS

- ▶ Streptococcal pharyngitis
- ▶ Epiglottitis
- ▶ Infectious mononucleosis
- ▶ Deep space neck abscess
- ▶ Oropharyngeal malignancy
- ▶ Measles
- ▶ Acute necrotising ulcerative gingivitis (Vincent's angina)
- ▶ Behcet's syndrome
- ▶ Stevens-Johnson syndrome

CrossMark

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TREATMENT

The patient's condition improved with intravenous coamoxiclav and metronidazole antibiotics, fluids, dexamethasone, analgesia and benzydamine hydrochloride throat spray. Three days later, she was tolerating soft diet and free fluids and was discharged. One day later, *C. ulcerans* was isolated from the admission throat swab and the patient was readmitted urgently to a side room with barrier precautions. Management with intravenous steroid and benzylpenicillin and clarithromycin antibiotics was instigated as per culture sensitivities and empirical therapy recommendations.^{10 11} The soft tissue swelling had reduced sufficiently to permit posterior pharyngeal wall examination and a fibrinous, adherent, thick yellow pseudomembrane was noted. The *C. ulcerans* isolate was subsequently found to be toxin gene positive on PCR. On revisiting the patient's history in more detail, it was discovered that she kept four horses and a dog. The dog had recently been attacked by a wild badger and she had been treating it for an ear infection.

An emergency meeting between Public Health England and our hospital's own microbiology, infection control, nursing and medical teams was convened. It was decided to treat the patient with equine antitoxin, which was administered uneventfully. Elek testing 4 days later confirmed active expression of diphtheria toxin. Serial ECGs throughout the patient's admission demonstrated normal sinus rhythm without any concerning features. Screening of relevant healthcare staff deemed to be at risk was performed by occupational health, and the patient's husband was swabbed and given a course of prophylactic antibiotics. The patient's dog subsequently tested positive for toxigenic *C. ulcerans* with active toxin expression as per Elek testing. The patient was fit for discharge 1 week later with 14 days of oral antibiotics.

OUTCOME AND FOLLOW-UP

At outpatient review 8 days later, the patient reported worsening dysphagia for solids and liquids. FNE revealed a generally inflamed supraglottic area with significant secretions. Dietary supplement drinks were prescribed and a barium swallow ordered in addition to making an outpatient referral to dietetics. Over the course of the next 3 weeks, the patient was reviewed regularly in clinic and noted to be struggling with oral intake. Repeat throat swab was negative. Eventually, the patient was readmitted and a water contrast swallow demonstrated gross aspiration. A nil by mouth order was instigated and nasogastric tube feeding was started. Videofluoroscopy 9 days later demonstrated persistent frank aspiration and a percutaneous endoscopic gastrostomy (PEG) tube was inserted. Neurology review concluded that the patient most likely had dysphagia secondary to diphtheria. Over the following 2 months, the PEG feed was slowly weaned in the community as the patient regained the ability to tolerate oral intake. Four weeks after establishing oral diet, the patient could tolerate all solids except for those with a thicker consistency such as cake and bread crusts.

Neurology follow-up 6 weeks after discharge made note of a new progressive, bilateral paraesthesia of the lower limbs and hands which had been present during the patient's second admission and had been worsening since discharge. On examination, there was subtle weakness of finger extension in the right hand and big toe bilaterally on dorsiflexion, with altered pin prick sensation in the lower legs and hands. Reflexes were absent in the lower limbs with withdrawing plantar responses. This picture was attributed to a diphtheritic polyneuropathy (DP) and slowly

improved with conservative management. At 6 months from the initial illness, the patient was able to tolerate most foods but interestingly still struggled with cheese and bread crusts. Her peripheral neuropathy had also mostly resolved; however, she does occasionally drop objects and periods of heightened emotion seem to exacerbate her symptoms.

DISCUSSION

Although the symptom of a sore throat is usually a benign and self-limiting condition, it is critical that a thorough assessment is made in order to rule out unusual and potentially serious causes. The presence of a pharyngeal membrane should alert the clinician to the possibility of diphtheria infection and may necessitate immediate barrier nursing of the patient and documentation of a detailed history including immunisation status, foreign travel, animal contact and dairy product consumption. Throat swabs must be obtained and accompany a request form that specifically highlights the possibility of diphtheria infection. The local microbiology department must be informed as soon as a case of diphtheria is suspected. A multidisciplinary team (MDT) meeting involving representatives from a number of relevant groups (box 1) should be convened and contact tracing in the community and the hospital setting performed, with treatment or prophylaxis administered where indicated.

The medical team should ensure that this organism has been actively ruled out on culture before discharge is planned. The decision to give antitoxin should be sanctioned by the MDT, given its expense and scarcity as a resource. The patient must be properly consented regarding the risks of antitoxin administration, including life-threatening anaphylaxis. Critical care staff with airway management expertise should be involved in the patient's treatment, particularly during the administration of the test dose of antitoxin. A cardiac arrest trolley should be placed in close proximity to the patient for the duration of the infusion.

Following the acute illness, the patient must be followed up closely in clinic to monitor for the development of DP-associated signs and symptoms. DP is a common and potentially severe complication occurring in ~20% of diphtheria patients, although recovery is possible.¹² Dysphagia and dysphonia secondary to hypopharyngeal and palatal muscle weakness tend to have an onset in the order of days to weeks, with segmental demyelination of peripheral nerves resulting in limb weakness, loss of tendon reflexes and sensory disturbance developing weeks to months after the initial infection.^{13–16} Death generally occurs from myocarditis, autonomic dysfunction

Box 1

Members present at our multidisciplinary meeting

- ▶ Consultant microbiologist
- ▶ Infection Control Nurse Specialist
- ▶ Head of Risk and Governance
- ▶ Senior Occupational Health Advisor
- ▶ Charge nurse of relevant ward, matron of surgery, chief nurse
- ▶ Consultant Ear, Nose and Throat Surgeon
- ▶ Communications representative
- ▶ Public Health England representative
- ▶ Reference Laboratory representative

resulting in cardiac arrhythmias or respiratory failure caused by diaphragmatic or laryngeal involvement.¹²

In the case presented above, it became clear after several outpatient appointments that the patient was not able to maintain adequate oral intake and that dietician input and supplementary enteral feeding were required. Early review by a neurologist and a speech and language therapist ensures that gold-standard treatment and rehabilitation is provided, although this is largely supportive. Feeding PEG tube insertion may be required. The patient only reported several weeks after her second discharge that she had been suffering for some time with worsening paraesthesia in her hands and legs, since she had initially attributed this to being immobile in hospital. The authors believe that cases of diphtheria should be regularly reviewed to actively exclude the development of DP complications through a combination of history (are you experiencing any tingling or weakness in your limbs?), examination (reduced power, sensation and deep tendon reflexes) and investigations (serial ECGs to monitor for prolonged QT interval suggestive of impending arrhythmia). The findings of these assessments should be documented clearly in the case notes.

Although rare in the UK, cases of diphtheria do still occur and can have a significant impact on patients. It is therefore important that doctors exclude this diagnosis at least clinically in anyone presenting with a sore throat. For example, a recent culture-proven case of *C. ulcerans* infection suspected to have been transmitted by a pet dog was reported in 2013 in a middle-aged woman in Scotland.¹⁷ Serious complications can develop and may require aggressive management strategies, and to the authors' knowledge, this is the first published case of diphtheria requiring PEG feeding. In 2014, a Nigerian child suffering from DP was managed with nasogastric tube feeding; however, he also made a good recovery.¹⁸ Given the potential for transmission to close contacts and the lack of relevant experience of most clinicians, an MDT approach should be adopted in order to comprehensively manage this disease.

Patient's perspective

- ▶ Being moved to an isolation room on a different ward and being looked after by a nursing team which was not dedicated to ENT patients was worse than hell.
- ▶ The percutaneous endoscopic gastrostomy feeding felt quite alien and shocking and I could not lead my life and yet I knew it was a necessity.
- ▶ The fact I was fit and healthy beforehand helped a terrific amount in my recovery.
- ▶ I had to shut myself off to the risks of equine antitoxin when they were being told to me, or else I never would have accepted the treatment.
- ▶ I read a book every day to distract me from the situation or else I would have gone mad.
- ▶ The contact at Public Health England was like a fairy godmother to me, coordinating the swabbing of the grandchildren, treating the dog and checking on my recovery.
- ▶ My follow-up was essentially coordinated by the speech and language therapist and she was super.
- ▶ I am glad to have recovered as well as I have. If I do not recover anymore I am happy. I did not realise how serious it was at the time.

Learning points

- ▶ Classical respiratory diphtheria is now extremely rare in the UK as a result of routine childhood vaccination.
- ▶ It is now usually attributable to toxigenic strains of either *Corynebacterium diphtheriae* or *Corynebacterium ulcerans* harboured by wild or domesticated animals.
- ▶ Diphtheritic polyneuropathy is a potentially severe complication with variable onset occurring in ~20% of diphtheria patients. Bulbar palsy may be severe and persistent enough to warrant percutaneous endoscopic gastrostomy feeding.
- ▶ As diphtheria is a reportable disease, a multidisciplinary approach is mandated in order to optimally manage these complex patients and coordinate contact tracing efforts.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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