CASE REPORT

Lightning can strike twice: an unlucky patient of neurological interest

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SUMMARY

Poliomyelitis, once a worldwide epidemic, is becoming increasingly rare owing to the introduction of the polio vaccine in the 1950s. It is estimated that the number of cases of polio has reduced by 99% since the Global Polio Eradication Initiative (GPEI) started in 1988. Amyotrophic lateral sclerosis (ALS) is another relatively uncommon condition which also affects anterior horn cells with debilitating neurological, and deadly, consequences. An unusual case of an aggressive form of ALS developing in a 72-year-old patient with paralytic poliomyelitis in childhood is presented. Her initial presentation was puzzling, and our approach to the diagnostic dilemma is discussed.

BACKGROUND

Diseases which most commonly affect anterior horn cells include motor neurone disease (MND), poliomyelitis, spinal muscle atrophy, progressive muscle atrophy and West Nile virus.¹

ALS is the most common form of MND.² It classically presents with upper and lower motor neurone signs, including weakness (owing to muscle atrophy), fasciculations, spasticity, hyper-reflexia and sparing of the sensory system. Despite ALS receiving much research attention over many years, its pathogenesis is still not fully understood, and cure remains elusive, making it a terminal diagnosis.^{3–4} ALS has rarely been reported in patients with antecedent poliomyelitis infection.⁵

CASE PRESENTATION

A 72-year-old woman of Italian descent was referred to the neurology outpatient clinic of a large community hospital for investigation of increasing left leg weakness. Her medical history included hypertension, osteoporosis, gastroesophageal reflux disease and chronic backpain secondary to osteoarthritis. She was also diagnosed with poliomyelitis at the age of 9 months, with isolated right lower limb involvement, for which she underwent two tendon lengthening operations in childhood, and was prescribed a right ankle-foot-orthosis. There were no diagnosed neurological problems within the family.

She first presented in June 2012, with a 6-month history of left lower limb weakness. She was systemically well and denied any visual, speech, swallowing, bowel or bladder problems. On examination, the residual postpolio paralysis was apparent in her right leg and only mild proximal lower limb weakness was demonstrated in the left leg. Blood tests were unremarkable (including

creatinine kinase, serum protein electrophoresis, thyroid function and vitamin B₁₂) and her medication list did not include statins. In the setting of chronic spine degenerative changes, and in the absence of other neurological signs, the impression was that she was suffering from a polyradiculopathy, or myopathy.

One month later she represented with increasing lower backpain and associated functional decline. Her pain was located in the lumbosacral area, and was exacerbated by movement. She denied any recent illness, fever, trauma, weight loss and she maintained control of bladder and bowels. This was diagnosed as 'acute on chronic backpain secondary to osteoarthritis'. She was later transferred to a subacute facility for rehabilitation.

On admission, she had a fall which she attributed to her legs 'giving way'. An MRI scan failed to demonstrate any evidence of disc protrusion, neural compression or significant spinal stenosis to account for the patient's subjective reports of increasing left lower limb weakness in the setting of slow worsening of her backpain. She also began to complain of overwhelming fatigue.

She was referred for electromyography and nerve conduction studies, which were suggestive of a disorder affecting anterior horn cells. These tests, however, were limited in their ability to reliably distinguish between stable postpolio patients and those with a superimposed neuropathic process.

DIFFERENTIAL DIAGNOSIS

The two most probable diagnoses included postpolio syndrome (PPS) and ALS. Debate among her treating physicians ensued. Some believed PPS was more probable; she had proven previous polio infection, and it is much more common, affecting 25–40% of polio sufferers,⁶ as opposed to ALS with an incidence of only 2/100 000.⁷ In addition, she was complaining of fatigue, and demonstrating slowly progressive muscle weakness in keeping with PPS. Others argued that ALS was the more likely explanation as PPS usually affects the previously affected area, not new areas, and although it would be unlikely (and incredibly unfortunate) to develop ALS in addition to prior polio, this was not impossible; a small handful of cases of possible ALS postpolio had been reported.^{8–9}

Unfortunately the disease process began to rapidly progress. Prior to her first presentation in June, she was completely independent with tasks of daily living, and mobilised independently. By mid-September she was essentially bed-bound,

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requiring hoist transfers and began to complain of mild upper limb weakness bilaterally.

She developed generalised fatigue, severe exertional dyspnoea in the absence of any known cardiopulmonary disease, and her bed mobility continued to deteriorate secondary to increasing weakness in her upper limbs. She then developed widespread fasciculations, increased tone and diminished reflexes. She became increasingly emotional (suggestive of a pseudobulbar affect), and reported hoarseness of voice. Clinically it became apparent that she had a very rapidly progressive form of ALS.

TREATMENT

The patient was started on riluzole 50 mg twice daily once the diagnosis was confirmed in September. Respiratory function tests revealed a moderately severe restrictive ventilatory defect with a forced vital capacity of only 49% of predicted. A percutaneous endoscopic gastrostomy was inserted. She required intensive occupational therapy, dietetic and physiotherapy input.

OUTCOME AND FOLLOW-UP

Tragically, she developed severe hospital acquired pneumonia which failed to respond to intravenous antibiotics. She died in October, less than 5 months from her initial presentation.

A postmortem examination was not performed.

DISCUSSION

Previous studies have failed to convincingly demonstrate a relationship between polio and ALS.^{10–12} In fact, one study has even suggested a potentially protective effect of poliomyelitis in later developing ALS based on the rarity of ALS among postpolio survivors.¹³

Given that only 0.5% of people with polio develop paralysis and 0.02% develop MND, our patient was incredibly unlucky, and this low probability may have biased how we originally interpreted her early presentation.

There are a number of differential diagnoses to be considered in this case. While it is beyond the scope of the present article to discuss them all, a few important differentials will be discussed.

Multifocal motor neuropathy (MMN) with conduction block is a condition causing demyelination of peripheral nerves, mainly motor nerves, likely autoimmune in origin.¹⁴ Like ALS, MMN leads to cramping, fasciculations, fatigue and weakness (often beginning in hands or feet), with a sparing of sensory signs and symptoms. It differs from ALS however in that it tends to be slower in progression, is usually asymmetrical, exhibits minimal/no atrophy and lacks upper motor neurone signs.¹⁵ It is important to differentiate MMN from ALS as MMN has been shown to respond to immunomodulating and immunosuppressive treatments.^{14 16}

The European Federation of Neurological Societies/Peripheral Nerve Society has put forward the following guidelines¹⁷ to aid the diagnosis of MMN:

Definite MMN:

- ▶ Weakness without objective sensory loss in the distribution of two or more nerves is present for more than 1 month.
- ▶ Definite motor conduction block is present in at least one motor nerve with normal sensory nerve conduction studies.
- ▶ Exclusion criteria not present.

Probable MMN:

- ▶ Weakness without objective sensory loss in the distribution of two or more nerves.
- ▶ The presence of probable motor conduction block in two or more motor nerve segments with normal sensory nerve conduction studies.

- ▶ Exclusion criteria not present.

OR:

- ▶ Weakness without objective sensory loss in the distribution of one nerve.
- ▶ The presence of probable motor conduction block in one motor nerve segments with normal sensory nerve conduction studies.
- ▶ Exclusion criteria are not present.
- ▶ At least two supportive criteria met.

Supportive criteria:

- ▶ Elevated titres of serum IgM anti-GM1 antibodies.
- ▶ Increased cerebrospinal fluid (CSF) protein (< 1 g/L)
- ▶ MRI shows increased signal on T2-weighted imaging of brachial plexus with diffuse nerve swelling.
- ▶ Objective clinical improvement following intravenous immunoglobulin treatment.

Exclusion criteria:

- ▶ Upper motor neuron signs, such as spasticity, clonus, extensor plantar response.
- ▶ Marked bulbar involvement.
- ▶ Sensory involvement more marked than minor vibration loss in the lower limbs.
- ▶ Diffuse symmetric weakness during initial weeks.

These criteria highlight the overlap between the two conditions; for example, if it were not for the 'exclusion criteria' our patient could have qualified as having 'definite' MMN.

Another possible diagnosis that could have been entertained is chronic inflammatory demyelinating polyneuropathy (CIDP). This widely varying clinical entity is also immunologically driven, with recruitment of T and B cells demyelinating proximal segments of the peripheral nervous system.¹⁸ It too can present with symmetrical weakness, hypotonia, atrophy, fatigue and fasciculations; however, it is often characterised by periods of relapse, occasionally with complete recovery,¹⁹ and is more likely to have a sensory component compared with ALS. Again, it is important to differentiate these two conditions as CIDP has been shown to be successfully treated with corticosteroids, intravenous immunoglobulins and plasma exchange, with immunomodulating therapies being successful to a lesser degree.²⁰

Plasma cell dyscrasias should also be considered as they have been implicated in the development of neuropathies.²¹ These disorders include multiple myeloma, extramedullary plasmacytoma, monoclonal gammopathy of unknown significance (MGUS), 'POEMS' syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy and skin changes), amyloidosis and cryoglobulinaemia. These conditions bring about their neurological signs and symptoms, including neuropathy, through compression, infiltration, metabolic and autoimmune (cytokine or vasculitic) mechanisms.²² It is important for risk stratification purposes to identify those patients with plasma cell dyscrasias owing to the implications for their treatment, as well as prognosis and monitoring requirements.²³

In retrospect, our diagnosis may have been assisted by some further testing, including antibody testing (ie, anti-GM1) and CSF analysis. Despite these omissions, in hindsight the diagnosis of ALS appears to have been an easy one to make. A combination of factors may have been involved in our failure to make the correct diagnosis more promptly, and reflection of these aspects provides a number of learning points.

Diseases do not always present 'classically'. In fact, as a junior doctor it is important to remember that textbook definitions of disease entities are not the norm in clinical practice.

Perhaps not all the signs and symptoms of a disease will develop, or perhaps they are just yet to develop in the time

frame in which you see the patient. Furthermore, there may be distracting, pre-existing or unrelated signs and symptoms which add to the diagnostic challenge. For example, in this case, we were initially misled by the pre-existing lower backpain and prior polio infection.

When a diagnostic challenge exists, it is important to constantly re-evaluate the evidence. Getting opinions from colleagues may also be helpful to provide a new perspective, and may ensure you do not become 'invested' in a particular diagnosis. When weighing up differential diagnoses we must also remember that having one terrible illness does not protect you from having another one. 'Fairness' does not feature in clinical medicine.

Learning points

- ▶ Diseases do not always present 'typically'.
- ▶ In formulating differential diagnoses we must remember that having one terrible illness does not protect you from having another one.
- ▶ When a diagnostic challenge is presented, constant re-evaluation and second opinions are crucial.
- ▶ Despite the multitude of advanced diagnostic aids at our disposal, often it is only time which will reveal the true nature of a clinical problem.

Competing interests None.

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