INTRODUCTION

Guillain-Barré syndrome (GBS) is an acute or subacute inflammatory demyelinating polyradiculoneuropathy (AIDP) characterized by progressive symptoms of distal numbness and paresthesias, ascending weakness and gradual loss of reflexes. The sensory symptoms affect the limbs and spread proximally, and the weakness can be distributed variably at onset but is typically ascending (1). Adults present with sensory abnormalities, ascending flaccid paralysis and areflexia, but in children this classic triad is typically not predominant. Instead, pain, gait unsteadiness and refusal to walk are the most common presenting symptoms, whereas frequent findings on examination are dysautonomia, meningismus and ataxia (2–5).

We present a case of GBS that was not diagnosed until late in the disease process, in part because the presenting symptoms were not attributed to a neurological disorder. In addition, the patient’s neurological exam was limited, and newly acquired clinical and laboratory data were not put in the appropriate clinical context, leading to failure to adjust the tentative diagnosis.

CASE REPORT

An almost 4-year-old healthy boy presented with a 4-day history of sore throat, non-productive cough, decreased oral intake, decreased activity and worsening diffuse pain. Four days prior, he had reported pain in the knees and both arms. Later, he reported diffuse pain throughout his body, and he refused to walk even though he was able to. Next, it prevented him from walking up stairs. In the Emergency Room, he was afebrile and non-toxic appearing, and general paediatric exam was remarkable only for hoarseness and mild tachycardia. Generalized weakness and diffuse pain were noted but not specified further, neurological examination reported as ‘non-focal’ whereas gait and deep tendon reflexes were not assessed. He was admitted to the general paediatrics floor with a working diagnosis of a viral infection with myalgia and dehydration.

On hospital day (HD) 2, meningismus was suspected and cerebrospinal fluid (CSF) examination revealed two WBC/mm³, 298 RBC/mm³, total protein of 117 mg/dL (range 15–45) and a glucose level of 75 mg/dL (range 60–80). Extensive laboratory studies including an infectious workup were negative (data not shown).

From HD 3 to 4, progressive weakness developed with worsening head control and reduced truncal strength, accompanied by weakness of arms and legs. His limb pain was minimally responsive to non-steroidal anti-inflammatory drugs. Next, he was intubated for 3 days (HD 5–7) because of progressive respiratory failure. Just prior, a neurology consultation was obtained, revealing an alert patient with bilateral facial weakness and symmetrically flaccid
limbs with strength less than antigravity. Deep tendon reflexes were absent, and there was no Babinski sign.

In the intensive care unit (ICU), he developed mild dysautonomia including intermittent tachycardia, bradycardia and hypertension that self-resolved without intervention. His pain was controlled with gabapentin and opioids. Imaging studies (Fig. 1) and electromyography (not shown) confirmed the clinical diagnosis, and he was treated with 2 g/kg of intravenous immunoglobulin (IVIg) over 2 days.

He was discharged home after 3 weeks in a rehabilitation hospital. At his 1-month follow-up appointment, he was back to his playful and active self, and his exam had almost returned to baseline, with residual diminished reflexes.

DISCUSSION

Our patient had a classic paediatric presentation, with ascending weakness and progressive pain as prominent features. The initial neurological examination was challenging and his weakness and neuropathic pain were attributed to myalgia secondary to a viral illness. Neither gait nor deep tendon reflexes were assessed and a neurological disorder was not considered. Ideally, the diagnosis of GBS should be made clinically.

Guillain-Barré syndrome is a post-infectious or post-vaccination autoimmune attack on peripheral myelin proteins of nerve roots and peripheral nerves. The presumed pathophysiological mechanism is referred to as ‘molecular mimicry’, in which protein epitopes of several different infectious agents strongly resemble those of specific peripheral myelin proteins, although in classic GBS there is no antibody that can be tested for (1,6). The disorder is not common with an estimated incidence of 1–4 cases/100 000/year in adults and more rare in children (0.3–1.3/100 000/year) (1,7). There are several well-described variants, depending on the predominant site of inflammation (myelin in ~95%, axon in ~5% of cases), nerves affected (motor or sensory) and distribution pattern (ascending or descending, peripheral or cranial nerves) (1). Full overviews can be found elsewhere, including known associated antibodies in various subtypes (1,2,6). About two-thirds of patients have a history of an immunization or infection within the previous 6 weeks, most commonly a flu-like viral illness or a gastroenteritis, although in more than 85% is the specific culprit that is never identified (1). Common infections include cytomegalovirus, Epstein-Barr virus, varicella, other herpes viruses and hepatitis. Campylobacter jejuni and to a lesser extent Mycoplasma pneumoniae and Hemophilus influenzae antecedent infections are associated with acute motor axonal neuropathy (AMAN) (6), a pure motor GBS variant with axonal injury rather than demyelination, a more severe disease course and sometimes worse clinical outcome (8). Our patient had a non-specific concurrent upper respiratory tract infection.

Confirmatory tests in all GBS rely on inflammation and demyelination, however, not all studies are needed in every case. Well-defined clinical and auxiliary test criteria in adults and children can be found on the website of the international Brighton Collaboration on immunization safety data (9). CSF examination is usually performed and may show albuminocytologic dissociation, signifying an increased total protein level occurring in the absence of an elevated white blood cell count. In our case, the elevated protein in the CSF was initially incorrectly attributed to the elevated (and lysed) red blood cells in the CSF, contributing to a delay of the diagnosis. In practice, for every 1000 RBC/mm$^3$ CSF, the total protein is raised by 1 mg/dL, i.e. raising the total CSF protein only by ~0.5 mg/dL in our patient (10).

Figure 1: Post-contrast sagittal (A) and axial (B) T1-weighted spinal magnetic resonance images. The white bar in (A) indicates the level of the axial image (B). In (A), the spinal canal is in the back (to the right) of the vertebral column. In (B), the smaller round structure below the dark large intervertebral disk is the spinal canal. In both (A) and (B), the nerve roots of the cauda equina stand out from the darker cerebrospinal fluid as the inflammation results in gadolinium uptake, in (B) seen as bright round dots (white arrow).
Nerve conduction studies (NCS) can be supportive but can be technically challenging early in the disease and in young children (4). In our patient, multiple motor and sensory NCS showed either absent or severely reduced amplitude of the response to nerve stimulation (‘conduction block’), slowed nerve conduction velocities or non-simultaneous arrival of electric pulses through the nerve fibres in the muscle (‘temporal dispersion’), indicating diffuse demyelination (data not shown). Needle electromyography (EMG) 2–3 weeks after symptom onset may reveal muscle denervation, as in our patient (data not shown), indicating (secondary) injury to the axon (4). Spinal magnetic resonance imaging (MRI) is not carried out routinely, but may reveal post-contrast enhancement of inflamed cauda equina nerve roots – also in our case (Fig. 1), however, neither the sensitivity nor specificity is known in children (11). In our patient, the ongoing neurological deterioration and the CSF desorption imaging (MRI) is not carried out routinely, but may reveal post-contrast enhancement of inflamed cauda equina nerve roots – also in our case (Fig. 1), however, neither the sensitivity nor specificity is known in children (11). In our patient, the ongoing neurological deterioration and the MRI and EMG/NCS studies confirmed the clinical suspicion.

The clinical course is typically monophasic, with the onset and progression of symptoms over 2–4 weeks. This is followed by a plateau phase and finally a recovery phase, which can take weeks to months with a tendency to be shorter and more complete in children than adults (12,13). Complications arise from respiratory failure with ventilator support (15% of affected children), refractory pain, malnutrition, profound dysautonomia and hospital acquired infections (2,12). Treatment for GBS consists of immunomodulation with IVlg or plasma exchange (PE), both of which can speed recovery time and increase the chance of a full recovery (7). Well-designed clinical trials have shown that IVlg and PE are equally effective in treating GBS (7,13), however in paediatric cases IVlg is preferable due to its safety profile and ease of administration. Of importance, steroids are contraindicated in the treatment of GBS as they have been shown to be ineffective and increase the risk of nosocomial infection while hospitalized (14).

Paediatric long-term outcome is generally excellent, with 96% of cases experiencing either full recovery or subtle residual symptoms with no functional impact, only in part dependent on GBS subtype (3,4,8). Our patient had a short but dramatic hospital course, an excellent response to IVlg and a near-complete recovery at follow-up.

CONCLUSION

There are three interesting points to this case: 1. Pain is a common and often prominent presenting sign in paediatric GBS. 2. It should be reinforced that the neurological exam (strength, gait, deep tendon reflexes, plantar responses) should not only be part of the basic skill set of the (resident) paediatrician, but also performed routinely in patients in whom weakness is considered, regardless of suspected aetiology. 3. It underlines the importance of serial physical exams and ongoing critical interpretation of acquired clinical and laboratory data to adjust a tentative diagnosis towards a potentially life-threatening disease.

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AUTHOR CONTRIBUTIONS

Danielle Pier is a medical student who followed the patient during the ICU course. She did the first drafting and several major edits of the manuscript. Dr. Hallbergson is a supervising resident on the General Pediatrics Service, has presented the case for the Medicine Department and tailored the manuscript to the general paediatrician. Dr. Peters, Chief Resident in Pediatric Neurology, is the senior author. He edited and oversaw Ms. Pier’s and Dr. Hallbergson’s work.

References