Case report

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Guillain-Barré Syndrome presenting as unilateral hip pain in a child

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Objective. The aim of this report is to highlight the importance of close observation and follow-up in children who present with an acutely irritable hip. This is because hip pain is a symptom of not only benign but also severe conditions. Thus, at the time of the initial presentation, hip pain can be misdiagnosed. This report serves as an example for a wide range of doctors such as orthopaedic surgeons, paediatricians, emergency room physicians or primary care physicians, because these are the first-line doctors who treat patients with a painful hip. **Case report.** We herein present a three-year-old child who was admitted to our hospital with pain in the right leg and initially diagnosed with transient synovitis of the hip. An additional examination two days later, after severe deterioration of the clinical picture, revealed that our patient was actually suffering from Guillain-Barré syndrome. Failure to diagnose Guillain-Barré syndrome and initiating prompt treatment is potentially life-threatening. **Conclusion.** Clinicians should be aware that hip pain could be the presenting complaint of Guillain-Barré syndrome, a syndrome that has many clinical features. Even when all the clinical and laboratory findings indicate a benign condition, Guillain-Barré syndrome should still be considered. Therefore, close observation and follow-up in children who present with an acutely irritable hip is highly recommended. In this way, the potentially catastrophic consequences of more severe conditions can be avoided.

Introduction

Guillain-Barré syndrome (GBS) is an acute, immune-mediated peripheral neuropathy. This is generally characterized by fast progressive muscle weakness and paraesthesia (1, 2). Although GBS is a relatively uncommon condition, the consequences of a missed or delayed diagnosis and delayed treatment can lead to progression of muscle weakness and a worse outcome (3). Hip pain is a symptom of both benign and severe conditions. It is suggested to be a primary complaint in paediatric GBS commonly preceding the onset of motor paralysis (4-11). The aim of this report is to highlight the importance of close observation and follow-up in children who present with an acutely irritable hip, as hip pain may be the presenting complaint in both benign and severe conditions. Thus, at the time of the initial presentation, hip pain can be misdiagnosed, resulting in potentially severe consequences.

Case report

A three-year-old girl was admitted to our hospital with pain in the right leg. The pain had started the previous day. At the time of her admission, she limped and was reluctant to walk. The pain was precipitated by walking and was vaguely localized to the right hip. In the preceding five days, the patient suffered a three-day fever that was accompanied by flu-like symptoms (e.g., coryza, headache, sore throat and productive cough). The child received symptomatic treatment at home with antipyretics. She was apyrexial for 48 hours prior to her admission. On examination, she was also apyrexial but irritable. She refused to stand or bear weight and preferred to lie down with her right hip flexed and mildly rotated externally. The child was distressed on flexion, extension and internal rotation of the right hip. The joint had a full range of movement with no swelling or tenderness. There were no signs of trauma, rashes, oedema or warmth to the limbs. A physical examination revealed normal muscle power, muscle tone and strength in the lower and upper extremities. The tendon reflexes were interpreted as normal in the extremities. Sensation was bilaterally normal. Furthermore, the cranial nerves were intact. The rest of the physical examination revealed no pathological findings. Her personal and family history revealed no specific information. Her neurological development was compatible with her age and all of her immunizations were on schedule. She had had no recent immunizations and had not been exposed to neurological agents.

Laboratory tests revealed negative inflammatory markers (CRP and leukocyte count). The X-ray of the right hip joint showed no pathological findings. The ultrasound of the right hip revealed a small amount of effusion without synovial thickening. The more severe causes of hip symptoms, such as septic arthritis, osteomyelitis, Legg-Calve-Perthes disease, juvenile idiopathic arthritis, fractures and tumours, were excluded from the diagnosis with imaging and laboratory investigations. Normal neurological examination excluded neurological conditions such as GBS. The most likely diagnosis was transient synovitis of the hip. The treatment consisted of rest and anti-inflammatory agents. A follow-up examination was arranged for three days later.

However, two days after the first admission, the child presented a clinical deterioration with ataxic walking and inability to walk independently. This resulted in her re-admission to our hospital. On examination, lower limb weakness and hypotonia were found, as well as minimal antigravity movements in the lower limbs. A neurological examination revealed isochoric pupils, papillary light reflexes bilaterally positive, muscle strength 5/5 at neck flexor muscles, 5/5 at distal and proximal muscles of the upper extremities and 3/5 at distal and proximal muscles of the lower extremities. There were no clonuses or tremors. An examination of the upper limbs revealed normal tone and power. Reflexes of the biceps, triceps and supinator were interpreted as normal. On the other hand, the tendon reflexes were bilaterally reduced in the lower extremities. The patella and ankle reflexes were diminished bilaterally. Plantar reflex response was flexion. The intestine and bladder sphincters were intact. Autonomic functions were normal. There was no loss of touch or pins-and-needles sensation. There was coughing. Examinations of the lungs and rest systems were normal. Biochemical laboratory tests with ammonia and lactate, as well as haematological tests, showed no pathological findings. A retinal examination revealed no specific findings. In the MRI of the brain, no pathology was observed at the brain stem. Furthermore, the whole spine MRI after a gadolinium injection showed no pathological findings. There were no microbial proliferations in cultures of blood, urine, stool

Table 1 Nerve conduction studies

Type of nerve	Name of nerve	Latency	CMAPs	NCV
		R/L, ms; (Range)	R/L; ms (Range)	R/L; ms (Range)
Motor	Median	2.5/2.6; (1.7-3)	4.8/4.9; (4-12)	49.5/49.6 (49-73)
	Ulnar	2.1/2; (1.3-2.4)	5.2/5.4; (5-18)	49.7/49.9; (49-65)
	Peroneal	2.4/2.5; (2.2-4)	1.2/1.1; (2-12)	41.2/41.4; (40-60)
	Tibial	2.5/2.6; (2-4)	1/1.1; (2-12)	43.8/43.9; (43-57)
Sensory	Median	2/2.1; (1.8-2.5)	38.4/38.6; (17-85)	55.2/56.3; (53-75)
	Ulnar	1.9/2.1; (1.7-2.4)	53.8/53.9; (15-62)	56/56.7; (53-79)
	Sural	1.9 /1.8; (1.7-2.4)	26.0 /47.6; (8-47)	44.5/45; (44-59)

R/L= Right/Left; CMAPs=Compound muscle action potentials; NCV=Nerve conduction velocity.

and cerebrospinal fluid. There were no leukocytes in the cerebrospinal fluid and protein as well as glucose were in the laboratory reference range. The results of the serum immunoglobulins were normal. The neostigmine test was negative. The serologic tests were negative for the herpes virus, Epstein-Barr virus, cytomegalovirus, rubella, rubeola, toxoplasmosis, enteroviruses, respiratory viruses, Lyme disease and *Mycoplasma pneumoniae*. There were no microbial proliferations in the culture for *Salmonella*, *Shigella* and *Campylobacter jejuni*. The child finally underwent nerve conduction studies (NCSs). The findings of motor NCSs in the lower limbs showed markedly reduced amplitude of compound muscle action potentials (CMAPs), whereas distal latencies and motor conduction velocities were normal. The findings in the upper limbs were interpreted as normal, as were the findings of sensory NCSs (Table 1). Unfortunately, anti-ganglioside antibodies, which could be informative, were not possible to be tested in our laboratory.

Based on clinical features with motor involvement, electrophysiological investigation, as well as the normal laboratory findings, this patient was diagnosed with acute motor axonal neuropathy (AMAN) subtype of GBS or paraparetic GBS according to the Wakerley et al. classification (9). Lee et al. reported the first case of AMAN confirmed by electrophysiological studies that was accompanied by severe pain of the entire body (8). They suggested that clinician should be on the alert to atypical sensory symptoms from the classical presentation of AMAN even if the patient is diagnosed with AMAN electrophysiologically and should consider proper treatment options based on clinical presentations (8). Our diagnosis was strengthened according to this report and the patient was treated with 0.4 g/kg/day of intravenous immunoglobulin for five days. She did not require respiratory support and recovered slowly. Three months later, at the outpatients' follow-up, she had fully recovered.

Discussion

As hip pain is the presenting complaint in many conditions, it is important that it is recognized and diagnosed in childhood. The initial presentation of an acutely irritable hip in a child can pose a diagnostic challenge to an orthopaedic surgeon, paediatrician, emergency-room physician or primary-care physician. The differential diagnosis includes both benign and severe conditions such as transient synovitis of the hip, Legg-Calve-Perthes disease, osteomyelitis, septic arthritis, trauma and neurological conditions such as GBS (3). At the presentation time, our patient's clinical examination,

imaging tests and blood tests excluded the more serious clinical conditions and the diagnosis of transient synovitis of the hip was established. As a result, our patient was treated in an outpatient setting with oral analgesics and rest.

Transient synovitis of the hip is the most common cause of hip pain in children. Since transient synovitis has been associated with the risk of subsequent Perthes disease, clinical and a possible radiological or laboratory review were recommended to our patient three days after the first admission (12, 13). However, our patient's clinical condition deteriorated two days later. Our neurological examination at that time and the normal laboratory tests contributed to our differential diagnosis of GBS. GBS and more specifically the AMAN subtype was finally established, taking into account our neurological examination, the normal laboratory and imaging investigation and the findings of the NCSs. It was suggested that in approximately 40% of patients, NCSs performed within the first week can suggest a diagnosis of neuropathy without fulfilling the criteria for one of the specific electrophysiological subtypes (9, 14). Furthermore, although albuminocytologic dissociation in cerebrospinal fluid is a typical finding in GBS, elevations of protein usually occur in the second or third week of illness in AMAN and, as with our patient, patients with AMAN may have normal cerebrospinal fluid protein in the first week (8, 15). Hence, the appropriate treatment for GBS was started.

GBS is considered to be an acute immune-mediated neuropathy with several variations: a classic demyelinating form, acute inflammatory demyelization polyneuropathy (AIDP), acute motor–sensory axonal neuropathy (AMSAN), acute motor axonal neuropathy (AMAN) and Miller–Fisher syndrome (8, 16). Wakerley et al. from the GBS Classification Group presented clinical criteria to enable neurologists and non-neurologists to diagnose GBS and all its variants using a simple yet all-inclusive classification system (9). GBS is characterized by autoimmune attack on the peripheral myelin proteins of nerve roots and peripheral nerves. It is a relatively uncommon condition. Nevertheless, it is the most common cause of acute general paralysis in developed countries (3). In AMAN subtype, the pathological features differ from the features of AIDP in that macrophages invade the space between the Schwann cell and axon, leaving the myelin sheath intact (17, 18). Griffin et al. proposed the attractive hypothesis that AMAN and AMSAN are part of the spectrum of a single type of immune attack on the axon (18, 19). Among several variations, AMAN is characterized clinically by nearly pure motor syndrome without sensory involvement and final diagnosis of AMAN, as in our patient, is based on electrophysiological findings such as decreased CMAPs without any evidence of demyelination or change in sensory nerve action potential (SNAP). Despite the fact that AMAN has not been reported on atypical symptoms, Lee et al. described the first case of AMAN with sensory symptoms. More specifically, a 3-year-old male who was admitted with bilateral leg weakness and severe lower back and leg pain was finally diagnosed with AMAN (8). AMAN is reported more commonly in China than western countries and the majority of northern Chinese patients with GBS were classified as having AMAN (8, 20). Although most children with GBS usually have a benign and relatively limited clinical illness, failure to diagnose GBS and to initiate prompt treatment with plasmapheresis or intravenous immunoglobulin could lead to progression of muscle weakness and a worse outcome.

It is suggested that pain constitutes a common and often severe symptom in the whole spectrum of GBS (including MFS, mildly affected, and pure motor patients (11). Similar to our case, it has been also

reported as an atypical sensory symptom of AMAN subtype of GBS (8). Furthermore it has been suggested that, as it frequently occurs as the first symptom, before the onset of motor paralysis, pain in GBS requires full attention (11). It is likely that sensory nerve fibre involvement results in more severe pain (11). However, in daily clinical practice it is still considered to be an uncommon presenting symptom of GBS. This can lead to misdiagnosis or delayed diagnosis of this variant of GBS. Similarly to our case, many children who presented with pain as an early symptom of GBS were initially diagnosed with a musculoskeletal disease (4). Mahmoud et al. investigated the role of clinical presentation scaling in GBS to predict patients' short-term outcome. They found that all children experienced some degree of pain, which was mild to severe (5). Nguyen et al. retrospectively reported on a series of children under the age of six years with GBS (6). They found that pain was a symptom in all of the children at some time during their hospital stay. In their study, on admission, pain was present in 23 out of 29 patients (79%). Pain was often the most important symptom and led to misdiagnosis in 20 patients (69%). Linden et al. analysed the epidemiologic, clinical, laboratory and development profile of GBS series studied at a Child Institute, between 1989 and 2000. They found that pain was present in 62.3% (38/61) of the patients, more frequently occurring in the inferior members. They stated that it was an important cause of irritability in the smaller children. In some cases, this led to a delay in diagnosis (7).

On the other hand, despite the fact that we considered the pain as the presenting symptom of GBS that preceded the onset of motor paralysis, it cannot be denied that the hip pain in our patient may have occurred because of the preceding viral infection. However, according to strong evidences in the literature, pain could be the presenting complaint of GBS. Additionally, as previously stated, Lee et al. described the first case report of AMAN confirmed by electrophysiological studies that was accompanied by severe pain of the entire body. They concluded that clinician should be on the alert to atypical sensory symptoms from the classical presentation of AMAN even if the patient is diagnosed with AMAN electrophysiologically (8).

Furthermore, the AMSAN subtype of GBS was excluded because of a number of reasons. Firstly, in our case the findings of sensory NCSs were without pathological findings and except from the presenting symptom of pain there were no other sensory symptoms or sensory clinical findings which could indicated AMSAN subtype of GBS. Additionally, similar to our case, AMAN is characterized by rapidly progressive weakness, and usually good and full recovery, (our patient three months after the presentation, at the outpatients' follow-up, she had fully recovered) while AMSAN is generally associated with slow and incomplete recovery (21, 22). Because of these reasons as also the fact that the number of GBS-subtype AMSAN cases is very small (< 10% of AMAN cases) and in children even smaller the most likely diagnosis in our case was AMAN subtype (23). Therefore, we considered that our patient was presented with atypical sensory symptoms (hip pain) and we strongly believed that hip pain was the presenting symptom of the AMAN subtype of GBS.

Therefore, our case demonstrates that children with painful hips should be under observation. Taking into account that the common symptom could also be part of an uncommon syndrome, a follow-up a few days later should always be recommended. It is important that all clinicians recognize the value of both serial physical examinations and ongoing critical interpretations of the acquired clinical and laboratory data.

In this way, they can adjust a tentative diagnosis towards a potentially life-threatening disease.

Conclusion

Pain of the lower limb can be a predominant symptom in both benign and severe conditions. Thus, misdiagnosis at the time of initial presentation can occur. Clinicians should be aware that hip pain could be the presenting complaint of GBS, a syndrome that has many clinical features. Even when all the clinical and laboratory findings indicate a benign condition, GBS should be considered. Therefore, close observation and follow-up in children who present with an acutely irritable hip are highly recommended. In this way, the potentially catastrophic consequences can be avoided.

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