Fever and Limp Thinking Outside the Box

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Fever and Limp

Thinking Outside the Box

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Abstract: Fever and limp is a common presentation in the pediatric emergency department. We describe a case of a 21-month-old female patient with prolonged fever and difficulty bearing weight, ultimately diagnosed with a large intracranial abscess. Intracranial abscesses are a rare cause of limp and an uncommon diagnosis in pediatric patients without underlying congenital heart disease. This case highlights the importance of differentiating the features of limp secondary to pain from limp secondary to weakness, which is particularly difficult in the preschool-aged group. It is imperative for practitioners to consider disease of the central nervous system when evaluating acutely nonambulatory children with fevers.

Key Words: brain abscess, leukocytosis, fever

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CASE

A 21-month-old female patient presented to the emergency department (ED) with fever, nasal congestion, and limp. She was seen in the ED 2 weeks before and diagnosed with an upper respiratory tract infection, which had since improved. The mother reported that the child had a temperature of greater than 38.0°C for the past 7 to 8 consecutive days, during which time she had intermittent emesis. On the day of presentation, she had trouble bearing weight and cried with ambulation, hesitating to use the right leg. Her review of systems was otherwise noncontributory. Her medical history was significant for a cleft lip/palate repaired after birth and right congenital anophthalmia. She had no associated cardiac disease and no other structural anomalies. She had mild speech delay but otherwise was developmentally appropriate and walked at 12 months of age.

On physical examination in the ED, she was noted to be alert and nontoxic but fussy with examination. Vital signs were temperature of 38.1°C, pulse rate of 142 beats per minute, respiratory rate of 24 breaths per minute, and oxygen saturation of 99% on room air. She was small for her age, with a weight of 9.30 kg. Mucous membranes were moist. Right anophthalmia was present without prothesis. Tympanic membranes were clear bilaterally. Heart sounds were single S1 and normally split S2 without murmur or gallop. Lungs were clear to auscultation. Abdomen was soft and nontender without masses or organomegaly. There was no lymphadenopathy, and no rashes were present. Her extremities were warm and well perfused. Her spine examination findings were normal, without tenderness over the vertebral bodies. There was no swelling or pain to palpation in her foot, ankle, lower leg, knee, thigh, or hip bilaterally. She had full range of motion in ankles, knees, and hips without pain. Reflexes were 2+ and symmetric in the patella and Achilles. With attempted weight bearing, she could only briefly maintain posture; she cried and was unable to advance a step favoring the right leg.

Laboratory testing was pertinent for a white blood cell count of 20.8×10^6/L with 61% neutrophils and 1% bands, hemoglobin level at 8.6 g/dL, and a C-reactive protein (CRP) of 16.7 mg/dL. Serum chemistries, creatinine, platelets, and creatine kinase were unremarkable. Radiographs of the pelvis and both lower extremities (femur, tibia/fibula, and foot) were negative for fracture or periosteal elevation. The patient was admitted to the floor for presumed osteomyelitis. A magnetic resonance imaging (MRI) of the right lower extremity, however, was negative for bone, joint, and soft tissue disease. Aerobic blood cultures were negative ×3. The patient continued to have fevers and be non–weight bearing. An abdominal ultrasound study was negative for intra-abdominal abscess or mass but was unable to visualize the appendix. An abdominal computed tomography (CT) scan with contrast revealed a normal appendix and was unremarkable for mass, thrombus, or abnormalities of the vertebral bodies. A chest radiograph was negative for acute cardiopulmonary disease. The patient continued to have elevated inflammatory markers and difficult to localize disease. A bone scan result was negative. Serum titers for Lyme disease, human herpesvirus 6, Epstein-Barr virus, cytomegalovirus were negative. A respiratory polymerase chain reaction was negative for common viruses. The patient began to bear weight and had improved gait with physical therapy. The patient was discharged with the diagnosis of a transient synovitis.

The patient returned to the ED 3 days later with worsening gait and persistent fevers. The mother noted that she still had more trouble with the right leg but noticed that she began having decreased movements of her right arm. The mother mentioned that the right arm was the site of her peripheral intravenous catheter during her recent admission. The mother also noted intermittent twitching of her left leg. Physical examination result was unchanged from previous ones, except that strength testing showed slightly decreased strength in right upper and lower extremities. In addition, there was no prolonged clonus, but she had 3+ reflexes in bilateral lower extremities. There was no tenderness or swelling over her vertebral bodies. Laboratory testing revealed a white blood cell count of 22.8×10^6/L and a CRP of 22.0 mg/dL. Computed tomography of the head led to the diagnosis (Fig. 1).

The patient was admitted to the intensive care unit and underwent a left frontal craniotomy to drain the intracranial abscess. She had not received antibiotics before drainage, and the final culture grew multiple organisms including pan-sensitive *Haemophilus parainfluenzae*, pan-sensitive *Streptococcus constellatus*, and several anaerobes. All blood cultures were negative. An echocardiogram showed normal intracardiac anatomy and function. No otic source was identified to signify local spread. It is unclear if her craniofacial defects were contributing factors in

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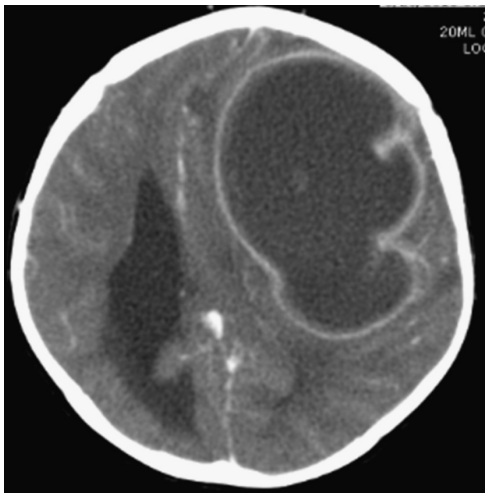

FIGURE 1. Computed tomographic scan (with contrast) demonstrating a large rim-enhancing intracranial abscess causing midline shift, obstructive hydrocephalus, and subfalcine as well as uncal herniation.

the development of this intracranial abscess. She was discharged from the hospital to complete 11 weeks of intravenous ceftriaxone and metronidazole. One year later, the patient had complete neurologic recovery with normal gross and fine motor function in bilateral upper and lower extremities and development as to be expected for her age.

Fever and Limp (Pain vs Weakness)

Fever with limp is a common presentation to the pediatric ED. A thorough history and physical examination is necessary to help narrow a broad differential diagnosis. This can be particularly challenging in the preschool-aged group when it is difficult to localize disease owing to limited communication skills and fussiness with examination.

The etiology for acute limp is usually secondary to pain, but it is important to distinguish the characteristic signs of pain from weakness. Limp from pain occurs secondary to musculoskeletal infections, inflammatory disease, rheumatologic disease, oncologic processes, or intra-abdominal pathology. Limp from weakness, on the other hand, localizes to the muscle, the peripheral nerve, or disease of the central nervous system (brain or spinal cord). Table 1 lists causes of limp with fever. Practitioners should also consider limp from traditional causes (eg, extremity fractures, hemophilia, etc) with a coexisting fever from an intercurrent and unrelated viral infection, especially when rhinorrhea and cough are present.

A complete history should discriminate for recent trauma, duration of fever, localizing signs, and other medical problems that might predispose to a particular disease process. A thorough review of systems can assess for signs or characteristics of systemic illness. Rheumatologic diseases may have associated rash, history of joint effusions, or signs of serositis such as pleuritic chest pain or orthopnea. Oncologic diseases may have associated weight loss, bone pain, bruising, petechiae, mucosal bleeding, hemihypertrophy, or paraneoplastic symptoms such as opsoclonus/myoclonus. Inflammatory processes may reveal recent medication use or recent infections, such as dysentery, streptococcal throat infection, urethritis, or viral syndromes. Abdominal processes may have associated abdominal pain, vomiting, dysuria, or vaginal symptoms. Neurologic causes may have other areas of weakness (eg, upper extremity), slowly progressive presentation, or radiculopathies. Patients with limp and bowel or bladder dysfunction should be assumed to have acute spinal cord pathology until proven otherwise.

The physical examination should evaluate for localizing signs of pain in the soft tissue, bone, or joint in addition to strength, sensation, and reflex testing to exclude neurologic disease. If the patient can bear weight, gait observation is helpful. A child with a limp secondary to pain will spend little time with weight on the affected leg. However, a child with a limp secondary to weakness may spend equal time on both legs, but will shift their weight over the affected leg to keep balance. A careful abdominal examination is necessary because pain on hip flexion and rotation can be a sign of either localized hip disease or a sign of intra-abdominal pathology such as psoas abscess or appendicitis.

Laboratory and radiologic testing should be directed by the results of a focused history and physical examination. Infectious and inflammatory diseases often show an elevated white blood cell count, erythrocyte sedimentation rate, and CRP. Creatine kinase can help differentiate muscle inflammation from diseases of joint or bone. Joint aspiration and synovial analysis are indicated for suspected infectious arthritis of a joint. Patients in Lyme endemic areas with arthritis should prompt serum Lyme titer analysis. Infectious arthritis in a sexually active adolescent should prompt evaluation for acute gonococcal disease

TABLE 1. Differential Diagnosis of Fever and Inability to Bear Weight

Fever/Limp Due to Pain	Fever/Limp Due to Weakness
Infectious (bone/joint/skin/muscle)	Spine
Septic arthritis (eg, *Staphylococcus*, *Streptococcus*)	Spinal cord tumor
Lyme arthritis	Epidural abscess
Gonococcal arthritis	Transverse myelitis
Acute rheumatic fever	Brain
Osteomyelitis	Acute disseminated encephalomyelitis
Soft tissue infection (eg, cellulitis, pyomyositis)	Meningitis
Inflammatory	Intracranial malignancy
Reactive arthritis	Intracranial abscess
Diskitis	Peripheral nerve
Transient synovitis	Peripheral neuropathy
Serum sickness-like reaction	Musculoskeletal
Rheumatologic	Heat stroke/muscle fatigue
Juvenile idiopathic arthritis	Myalgia
Lupus	
Henoch-Schönlein purpura	
Oncologic	
Leukemia	
Musculoskeletal neoplasms	
Retroperitoneal neoplasms	
Intra-abdominal disease	
Appendicitis	
Incarcerated inguinal hernia	
Pelvic inflammatory disease	
Psoas abscess	
Pyelonephritis	

or postinfectious arthritis from chlamydia infection. Radiographs of the pelvis and lower extremities can show signs of subacute osteomyelitis, fractures, or underlying bone disease (eg, malignancy, avascular necrosis, etc). Radiographs can also be helpful to hint at signs of joint effusion by showing widening of the joint spaces, particularly of the knee and hip. Magnetic resonance imaging of the lower extremity is becoming a valuable tool for differentiating acute osteomyelitis from deep soft tissue infection. Computed tomography or ultrasound study of the abdomen can each evaluate for intra-abdominal infections or neoplasms. Ultrasound study of the hip can help verify the presence of a joint effusion.

In the absence of "typical" inflammatory or infectious etiologies of the abdomen and lower extremity, it is necessary to think "outside the box" and consider neurologic etiologies affecting the central nervous system. An MRI of the brain and spinal cord should be considered to evaluate for diskitis, spinal cord tumors, demyelinating diseases, and intracranial pathology. If there are signs of increased intracranial pressure or spinal cord dysfunction, CT or MRI should be performed emergently.

Intracranial Abscess: Epidemiology

In the pediatric population, focal suppurative intracranial abscesses occur most frequently in children 4 to 7 years of age.[1] Intracranial abscesses occur either as a result of paradoxical emboli with hematogenous disease or from direct extension of a local suppurative infection. A summary of the predisposing factors for pediatric brain abscesses is shown in Table 2.

Septic intracranial emboli occur most frequently in children with right-to-left shunting congenital heart disease (CHD) where contaminated venous blood bypasses the reticuloendothelial function of the lung and has direct access to the central nervous system circulation. Approximately 6% of patients with unrepaired cyanotic CHD develop intracranial abscesses,[2] and in select populations, CHD is associated with as many as 26% to 50% of all pediatric intracranial abscesses.[3–5] Tetralogy of Fallot is the most common CHD associated with brain abscesses.[6,7] Septic emboli also occur with infective endocarditis (CHD, artificial valves, or idiopathic). In patients without heart disease, septic emboli can develop from thrombophlebitis of deep neck veins (Lemierre disease), from pyogenic lung disease[8] (bronchiectasis, empyema), or through metastatic bacterial spread from a distant site of infection (bone, skin, teeth, etc).

Spread from a contiguous site of infection occurs not only from the middle ear, sinuses, orbit, face, and scalp, often from a preexisting anatomic opening, but also from bony erosion and local hematogenous dissemination.[2] In developing countries, contiguous spread is more common, such as in China where two thirds of intracranial abscesses occur as a complication from otitis media.[9] In developed countries, the incidence of intracranial abscesses caused by underlying otic and sinus disease is less common and continues to decrease.[4] Young children are more likely to have contiguous spread from the middle ear secondary to Eustachian tube dysfunction. Adolescents are more likely to develop contiguous spread from the paranasal sinuses secondary to the rapid growth of the frontal sinuses in the second decade and the ability for more forceful nose blowing.

Intracranial abscesses can occur with penetrating head injury (intraoral or through skin), after neurosurgery, or as a complication of an intracerebral mass, although these causes are all very rare in developed countries.

Intracranial Abscess: Microbiology

Between 60% and 70% of suppurative intracranial abscesses are caused by the *Streptococcus milleri* group,[10] which consists of 3 species: *S. constellatus*, *Streptococcus intermedius*, and *Streptococcus anginosus*. This group can be either aerobic, anaerobic, or microaerophilic. Staphylococci, enteric bacteria (*Escherichia coli*, *Klebsiella*, *Proteus* spp), and other anaerobic bacteria (*Bacteroides*, *Prevotella* spp) are other commonly implicated microorganisms. Mixed infections occur in 20% to 30% of pediatric intracranial abscesses,[2] and many cases are sterile even in the absence of previous antibiotic treatment. The causative microorganisms of intracranial abscesses differ somewhat by the underlying pathogenesis and patient age group. *Staphylococcus*, for example, is more commonly isolated from abscesses after head trauma and gram-negative species are more commonly found in neonates.

Immunocompromised hosts with brain abscesses, whether from primary immunodeficiency (ie, chronic granulomatous disease, neutrophil dysfunction) or chemotherapy (ie, post-transplant, primary malignancy), should be evaluated for less common organisms such as *Toxoplasma*, fungi, *Nocardia,* and Enterobacteriaceae.

TABLE 2. Predisposing Factors for Pediatric Intracranial Abscesses

Common
Congenital Heart Disease
Otic Infection
Occasional
Meningitis
Penetrating head trauma
Sinusitis
Cystic fibrosis
Unknown/idiopathic
Uncommon
Ventriculoperitoneal shunt infection
Halo device to immobilize cervical spine
Post brain surgery
Lung infections, bronchiectasis
Other site infections (eg, teeth, orbit, bone)
Rare
Esophageal dilatation
Endoscopy
Hereditary hemorrhagic telangiectasia
Pulmonary arteriovenous malformation
Hepatopulmonary syndrome
Septic abortion

Common, greater than 20% of cases; less common, 5% to 15% of cases; occasional, less than 5%.
Adapted from Yogev.[2]

Intracranial Abscess: Diagnostics

The classic presentation is the triad of headache, fever, and focal neurologic deficits, although this combination is found in only 9% to 28% of children with intracranial abscesses.[2,11,12] In addition, generalized seizures occur in fewer than 50% of children with brain abscesses[13]; thus, the clinical presentation is highly variable and may be subtle. Because symptoms may not manifest until there are signs of increased intracranial pressure or significant cortical involvement, delayed diagnosis is commonplace with a mean symptom duration of 2 weeks before diagnosis, often longer with abscesses of the frontal lobe.[2]

Computed tomography is the preferred method of diagnosing brain abscesses in the ED with a sensitivity between 95% and 99%.[14] Computed tomography offers rapid diagnosis of an intracranial lesion and potentially emergent comorbidities such as ventricular obstruction and signs of impending herniation. Intravenous contrast enhances diagnostic ability and should be used if an abscess is visualized on a noncontrast series. Intracranial abscesses classically appear as rim-enhancing lesions with hypodense centers, sometimes with septa or compartments. Other lesions that mimic suppurative intracranial abscesses include neoplasms, neurocysticercosis, and tuberculomas.

After CT establishes the diagnosis, MRI offers additional benefits by showing greater anatomic detail, which often helps better define the lesion and differentiate edema from liquefactive necrosis. Magnetic resonance imaging also offers improved sensitivity for detecting smaller, early satellite lesions and cerebritis.[15] Spectroscopy and diffusion-weighted images can offer additional benefits differentiating pyogenic abscesses from tumors.

Intracranial Abscess: Management

The initial management should focus on patient stabilization being mindful of the ABCs. Patients with altered mental status, pupillary abnormalities, arterial hypertension, and/or bradycardia should be assumed to have intracranial hypertension (ICH) and, potentially, impending herniation. Endotracheal intubation and traditional maneuvers to reduce ICH should be considered (eg, hyperosmolar therapy, seizure prophylaxis, head elevation, sedation/analgesia, hyperventilation, etc). Any sudden deterioration of clinical status suggests either brainstem herniation or rupture of the abscess into the ventricles or subarachnoid space.

Subsequent ED management of intracranial abscesses should be limited. Serum aerobic, anaerobic, and fungal cultures should be obtained along with inflammatory markers (CRP), a complete blood cell count, metabolic panel, and coagulation profile (prothrombin time/partial thromboplastin time). Inflammatory markers, however, have limited diagnostic utility because only 50% of children with intracranial abscesses have a peripheral blood leukocytosis (>10,000 cells/μL).[2] Lumbar puncture offers very little further diagnostic assistance and, furthermore, could pose a risk to the patient in the event of an abscess rupture.[16]

In the absence of clinical septicemia (ie, shock), antibiotics should be deferred until a specific pathogen has been identified. If antibiotics are considered in the setting of clinical sepsis, a broad-spectrum approach should be used to cover for penicillin-resistant *Streptococcus pneumoniae* and methicillin-resistant *Staphylococcus aureus* in addition to common *Streptococcus* species, gram-negative bacteria, and anaerobes. The combination of either vancomycin/meropenem or ceftriaxone/metronidazole is acceptable treatment options. Corticosteroids, as in bacterial meningitis, are controversial and should be reserved for signs of significant mass effect or evidence of cortisol insufficiency.[17]

Further management of intracranial abscesses requires a multidisciplinary approach, which often necessitates care at a tertiary center. Consultancy with the following services should be considered: neurosurgery (for surgical options), critical care (for ICH management), infectious diseases (for antibiotic selection), neurology (for seizure control/prophylaxis), cardiology (for identification or management of right-to-left shunting lesions or endocarditis), and otolaryngology (if signs of otic or sinus disease are present).

The factors influencing treatment options include clinical status, suspected etiology, abscess size/quantity, and abscess location. Surgical drainage reduces intracranial pressure and enables microbiological diagnosis. Computed tomography–guided aspiration allows for a minimally invasive approach to some lesions, particularly to optimize diagnosis in a patient with multiple or deep-seated abscesses. Antibiotic therapy without surgical intervention can be considered if the patient is alert, has no signs of increased intracranial pressure, has an abscess of less than 3 cm in diameter, and has had a relatively short duration of symptoms (<2 weeks).

Intracranial Abscess: Outcomes

Mortality rates for children with intracranial abscesses are 3% to 10%.[12,13,18–21] Mortality rates are higher in patients with rapid onset (<4 days), intraventricular rupture, or altered mental status at initial presentation.[2,22] Long-term outcomes are influenced by the virulence of the pathogen, the location and number of abscesses, the underlying source of infection, and the clinical status at time of diagnosis.[22] Many children with suppurative intracranial abscesses develop long-term sequelae such as motor deficits, seizures, behavior/learning problems, and abscess recurrence. A worse prognosis has been associated with abscesses complicated by multiple lesions, intraventricular rupture, CHD, meningitis, poor neurological status, hydrocephalus, and young age at diagnosis.[22–24]

SUMMARY

Fever and limp is very common in young children, often secondary to transient synovitis and infections of the musculoskeletal system. In the evaluation of fever and limp, however, it is very important to distinguish the etiology of limp between pain and weakness to help target appropriate testing and narrow an otherwise very broad differential diagnosis. Intracranial abscesses are uncommon but should be considered in children with fever and motor deficits especially in the setting of underlying heart disease or intercurrent otic infection.

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