EASILY MISSED?

Perthes' disease

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This is one of a series of occasional articles highlighting conditions that may be more common than many doctors realise or may be missed at first presentation. The series advisers are Anthony Harnden, professor of primary care, Nuffield Department of Primary Care Health Sciences, University of Oxford, and Richard Lehman, general practitioner, Banbury. To suggest a topic, please email us at practice@thebmj.com

A mother took her 8 year old son, who had been limping and complaining of occasional leg pain, to see their general practitioner. The boy was otherwise healthy. He walked with a limp, was afebrile, and had painful, reduced internal rotation and abduction of his right hip. Plain radiographs confirmed the diagnosis of Perthes' disease, prompting paediatric orthopaedic referral, followed by an osteotomy.

What is Perthes' disease?

Perthes' disease is the clinical manifestation of idiopathic femoral capital epiphysis vascular compromise, affecting children aged between 4 and 12 years when the epiphyseal blood supply is solely from the lateral epiphyseal vessels.[1] The annual incidence of Perthes' disease among children under the age of 15 ranges from 0.2 to 19.1 per 100 000.[2] Bilateral involvement occurs in approximately 15% of cases and is usually asymmetric. Perthes' disease affects boys three to four times more frequently than girls and is more common in children of low birth weight, children exposed to maternal smoking during pregnancy, those from lower socioeconomic groups, and children of white ethnicity.[2-5] Affected children tend to be shorter than controls and have delayed bone age.[6] Whether Perthes' disease is a single disease or the result of different pathogenetic mechanisms remains a question. A long term natural history study found that the entire clinical course of Perthes' disease lasted, on average, approximately 34 months during childhood, with long term sequelae affecting patients later in adult life.[7]

Why is Perthes' disease missed?

Musculoskeletal complaints are common in children; most are related to self resolving trauma.[8] Most have a benign clinical course requiring no specific treatment. Among many children with a painful or painless limp, however, will be a few boys and girls affected by Perthes' disease. Doctors encountering children with musculoskeletal complaints report a low confidence in their clinical skills in comparison with other body systems.[9] The medical literature suggests that just under half of cases of Perthes' disease in children are diagnosed in the advanced stages of the disease, despite pain or a limping gait being present for several months.

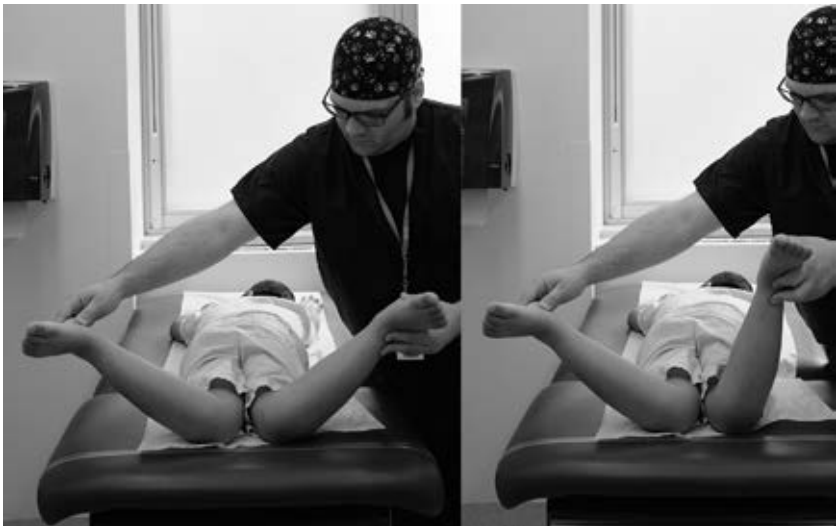

Fig 1 | Examining the hips. Left: patient is prone on examining table with hips in extension; here we see symmetrical maximum internal rotation of hips. Right: a common early finding in Perthes' disease is restriction of internal rotation range, as shown on right hip here

KEY POINTS

- Children presenting with a limp, with or without groin pain or knee pain, should be evaluated for Perthes' disease
- Physical findings include decreased hip abduction and decreased hip internal rotation compared with the unaffected side
- The diagnosis is confirmed on plain radiographs
- Early diagnosis, referral, and operative management can improve the shape of the femoral head and delay the onset of degenerative arthritis

Why does this matter?

Untreated Perthes' disease may cause permanent femoral head deformity, followed by early onset arthritis requiring hip replacement in young adult life. Surgical treatment in early disease has been shown to improve the outcome and delay or prevent osteoarthritis for well defined subgroups of children.[10]

How is Perthes' disease diagnosed?

Clinical

Perthes' disease is diagnosed by characteristic changes on plain radiographs in the context of a corresponding clinical presentation. An affected child may present because of an insidious onset of a limp with or without pain. Pain may be felt at the hip (groin) but is commonly referred to the knee at this age. The child may walk with a limp. Muscle wasting in the thigh or buttock may accompany decreased abduction and internal rotation of the affected hip. We examine hip abduction with the child supine and the hips in extension, making sure the pelvis is stabilised to isolate true hip joint motion and compare one side with the other. Lying the child prone with extended hips and flexed knees allows easy comparison of internal rotation range (fig 1, left). A loss of internal rotation with or without pain at the end range is often the most sensitive clinical finding (fig 1, right).

Investigations

A full blood count together with either a C reactive protein concentration or an erythrocyte sedimentation rate is useful in excluding an inflammatory condition such as septic arthritis. A transient synovitis of the hip secondary to an intercurrent viral illness is common in children of this age group and may mimic Perthes' disease. Because the natural history of a transient synovitis is one of complete improvement over time, a child who continues to limp on follow-up

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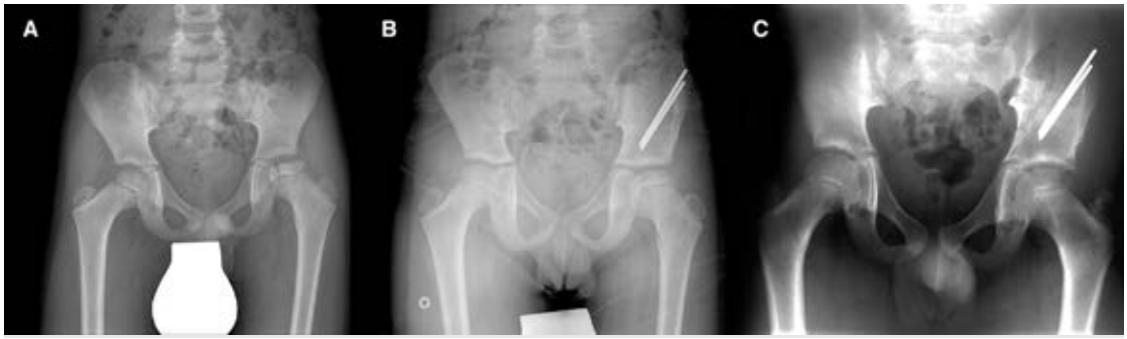

Fig 2 | Radiographic findings and course of treatment. Left: radiograph of 7 year old boy with Perthes' disease showing increased density of left femoral head, with early collapse and fragmentation (right side is normal). Centre: same boy at age 9, following surgical treatment with pelvic osteotomy; femoral head is reossifying and restoring its shape. Right: the same boy at age 12, with nearly full anatomic restoration of shape of femoral head

should undergo repeat plain film imaging of the hips after 8-12 weeks. Anteroposterior and frog lateral radiographs of both hips are sufficient to confirm the diagnosis in most cases but occasionally may be normal in the early stages of disease. The characteristic radiological changes occur first in the femoral epiphysis and metaphysis and later in the acetabulum (fig 2, left). Plain film radiology is used to divide disease progression into four stages, each lasting several months. The first radiological stage is recognised as a dense and sclerotic femoral epiphysis. Next, the epiphysis loses height and fragments, followed by a regeneration stage and, finally, a stage of repair.

How is Perthes' disease treated?

The mainstay of management of Perthes' disease is to minimise pain, maximise motion, and avoid an irreversible femoral head deformity. Prognosis differs according to the patient's age and the stage and extent of disease. Extrusion of the femoral head occurs during the fragmentation stage of active disease and is a recognised risk factor for development of early osteoarthritis. Younger children (5-7 years old) identified at an earlier disease stage are generally treated non-operatively,[11] with range of motion exercises or activity modification encouraging swimming or cycling and discouraging vigorous jumping and landing activities. The choice of either surgical or non-surgical treatment is difficult. Experts recommend surgical treatment for children over the age of 8 and radiological staging of more advanced disease, because a prospective multicentre cohort study (with each centre applying its preferred treatment) found that operative management (osteotomy of the femur or pelvis) improved the sphericity of the femoral head at maturity compared with non-operative management with physiotherapy and/or abduction bracing.[12] Other consecutive case series have found that the use of an A-frame orthosis resulted in a high proportion of spherically congruent hips for children of all ages irrespective of the extent of disease.[13] Pain, arthritis, and ongoing hip dysfunction remain common long term sequelae in patients who are older at disease onset or who present with a poorer prognosis on the basis of radiological staging (fig 3). Studies are in progress to compare the outcomes of non-surgical and surgical treatments in 6-8 year olds and of differential surgical procedures for children over 11 years, as well as evaluating the role of drugs that limit bone resorption and potentially preserve femoral head shape.

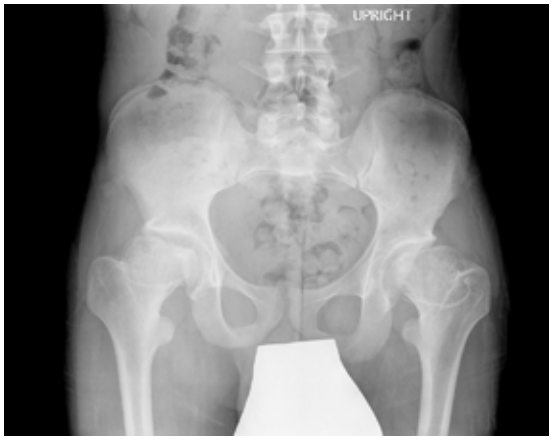

Fig 3 | Radiograph of 15 year old patient who had bilateral Perthes' disease in late childhood. Femoral heads remain flattened and aspherical. Early osteoarthritis may result

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UNCERTAINTIES PAGE

Are mood stabilisers helpful in treatment of borderline personality disorder?

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This is one of a series of occasional articles that highlight areas of practice where management lacks convincing supporting evidence. The series adviser is David Tovey, editor in chief, the *Cochrane Library*. This paper is based on a research priority identified and commissioned by the National Institute for Health Research's Health Technology Assessment programme on an important clinical uncertainty. To suggest a topic for this series, please email us at uncertainties@thebmj.com

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- What is the optimal pharmacological management of retained placenta? (*BMJ* 2014;349:g4778)
- Should we advise patients with sutures not to swim? (*BMJ* 2014;348:g3171)
- Whom should we "test and treat" for *Helicobacter pylori*? (*BMJ* 2014;348:g3320)
- Should doctors prescribe cannabinoids? (*BMJ* 2014;348:g2737)

Borderline personality disorder is a severe mental health problem that affects around 1% of people.[1] It is characterised by intense unstable relationships, impulsivity, and chronic feelings of emptiness.[2] Affective instability is also a core symptom, with marked fluctuations in mood, which may switch rapidly from hopelessness and despair to feeling irritable, angry, and out of control. People with this condition have high rates of deliberate self harm and a rate of suicide that is 20 times that of the general population.[3] Although psychological treatments have been shown to improve the mental health of people with borderline personality disorder,[4] many people do not engage with such treatments, and as many as half of those who do engage drop out before treatment has been completed.[5]

People with borderline personality disorder are more likely to experience mood disorders, including bipolar affective disorder.[6 7] Differentiating between borderline personality disorder and bipolar affective disorder can be difficult. Changes in mood are much more frequent among people with borderline personality disorder, and such patients are more likely to report feelings of anger, in contrast to elated mood reported by people with bipolar disorder.[8]

Affective instability among people with borderline personality disorder has led to interest in the role of mood stabilisers (sodium valproate, lamotrigine, topiramate, carbamazepine, and lithium) as a potential treatment. However, the evidence base for the use of these drugs in people with this condition is poor, and considerable uncertainty exists about whether they should be used in clinical practice. Current guidance from the National Institute for Health and Care Excellence (NICE) states that drug treatments should "not be used for borderline personality disorder or for the individual symptoms or behaviour associated with the disorder."[9] By contrast, American guidelines state that mood stabilisers should be considered as a second line treatment for affective dysregulation in patients with borderline personality disorder.[10]

What is the evidence of uncertainty?

In the United Kingdom, no drugs are licensed for the treatment of borderline personality disorder. Despite this, people with this condition are often prescribed large amounts of psychotropic medication.[11] A recent national audit of prescribing for people with personality disorder, which involved collecting data on more than 1700 patients from 41 trusts in England, found that nine out of 10 people with borderline personality disorder were being prescribed at least one drug for their mental health. Three quarters of patients were receiving antidepressant drugs despite good evidence that these are of very little if any benefit.[12] By contrast, only one in five patients were being prescribed a mood stabiliser. When interviewed about their experience of medication, people with borderline personality disorder report confusion among prescribers about what if any drugs they should take.[13]

A Cochrane systematic review that was completed in 2009 reported the results of eight randomised trials of mood stabilisers for people with borderline personality disorder.[14] These trials were small, with between 19 and 56 participants (median 29), and had relatively short follow-up (range 1-6 months, median 3 months). A diverse range of outcome measures were used, limiting the scope for meta-analysis. Most studies relied partly or exclusively on recruiting members of the public by advertising in local media. As a result, study participants had less severe problems than are generally seen among people using secondary care mental health services. The authors reported clinically significant reductions in interpersonal problems with valproate and topiramate, in impulsivity with lamotrigine and topiramate, and in anger with lamotrigine and topiramate compared with placebo. They concluded that mood stabilisers are potentially effective in treating several symptoms of borderline personality disorder but not the overall severity of the condition. In a disorder that persists over time, knowing whether any positive effects are sustained in the longer term is critical. This is particularly so for drugs that carry a significant adverse effect and toxicity burden. Known risks of severe toxicity in overdose (tremor, ataxia, seizures, and coma with lithium; respiratory depression, tachycardia, and seizures with carbamazepine; respiratory depression, metabolic acidosis, and coma with valproate; and seizures and coma with lamotrigine) or congenital abnormality and cognitive impairment (most prominently for valproate) may be outweighed by the benefits of these agents for indications that are evidence based, such as bipolar disorder or epilepsy. This may not be so in borderline personality disorder, in which benefit is uncertain.

We searched PubMed, Medline, and the Cochrane Library to identify any additional published trials of mood stabilisers for borderline personality disorder. We found no new published trials, but open label follow-up of studies of people participating in trials of lamotrigine and topiramate reported continuing reductions in anger and aggression 18 months after randomisation.[15 16] Limitations of these studies are that they were small (mean 30 participants), patients and researchers were not blinded, and the dropout rate among those who had taken the placebo was high (45%) in one study.[16]

Is ongoing research likely to provide relevant evidence?

NICE guidelines on the management of borderline personality disorder recognised the need for better evidence on the role of mood stabilisers for this condition,[9]

Box 1 | Recommendations for further research[9]

Population: Adults who meet diagnostic criteria for borderline personality disorder, excluding those who have comorbid bipolar affective disorder

Intervention: Addition of a mood stabiliser that has been demonstrated to improve the mental health of people with bipolar affective disorder (lithium, carbamazepine, valproate, topiramate, lamotrigine) to standard care

Control: An inert placebo in addition to standard care

Outcome: Mental health and social functioning assessed using measures used in previous trials (severity of symptoms of borderline personality disorder, interpersonal problems, suicidal behaviour) and over a period of at least one year after randomisation

Box 2 | Strategies to help patients requesting medication for their distress

Provide patients with information about personality disorder, including best available evidence that medication has little role in helping people to cope better with their problems (for example, www.mind.org.uk and www.emergenceplus.org.uk)

Keep patients actively involved in their own management—for instance, by asking: "How did you get through other crises in the past?" "What helped then, and could you try this now?"

Provide information about local and national help lines

Try to ensure that consistent advice is delivered by everybody working in the service

and box 1 outlines their recommendations for further research. A search of the metaRegister of Controlled Trials in February 2014 identified only one ongoing trial of mood stabilisers for people with borderline personality disorder. The LABILE study (ISRCTN90916365) is a randomised controlled trial of the clinical and cost effectiveness of lamotrigine versus placebo over a 52 week period in adults with borderline personality disorder. This study is due to report its findings in 2017.

What should we do in the light of the uncertainty?

Concerns have repeatedly been expressed about the quality of care that people with borderline personality disorder receive. Problems in coping with interpersonal relationships that are at the heart of this condition can also affect therapeutic relationships. Patients may present to services in a state of high emotional distress demanding that something be done to help them. At such times, clinicians may feel under pressure to prescribe drugs, but this should generally be avoided. Instead, general principles for working with people with personality disorder should be followed: maintaining a calm and empathic stance, exploring reasons for distress, and actively involving patients in their own management by asking questions about how they have coped with difficult experiences in the past.[9] Information about help lines and crisis support and offering follow-up may also help to contain the patient's anxiety.

If medication is prescribed during a crisis, consideration should be given to using a drug with few side effects and low toxicity. On the basis of expert opinion, NICE guidelines suggest using a short term sedative antihistamine for people experiencing sleep problems secondary to emotional distress.[9] Although randomised trials examining the use of these drugs for people with borderline personality disorder have not been conducted, they do not have the same potential for abuse as benzodiazepines and some other types of hypnotics.

Patients who experience repeated crises, have poor social functioning, or are at risk of harming themselves or others should be referred to secondary care mental health services. Patients should be encouraged to reflect on whether particular aspects of the way they get on with others might be perpetuating their problems. Those who are willing to consider exploring this further and would like help with trying to do things differently should be referred for assessment for an evidence based psychological therapy.

We do not recommend the routine use of mood stabilisers for the treatment of borderline personality disorder. These agents have potential, but evidence from pragmatic trials among people using secondary care services is lacking and no data on long term clinical and cost effectiveness exist. Furthermore, the adverse effects and potential for toxicity of these agents must be weighed against this uncertain benefit. In making a decision about treatment with a mood stabiliser, the prescriber must consider the side effect profile of the individual drug, interactions with other drugs, previous history of adherence and self harm using prescribed drugs, and, among women of childbearing age, their psychosexual history and use of contraception. Any decision to start a mood stabiliser should be made by a psychiatrist as part of a general assessment of mental health and development of an agreed treatment plan. People with borderline personality disorder who are offered mood stabilisers as a treatment should be told about the uncertain benefit and risks of these drugs, so that they are in a position to make an informed decision. If mood stabilisers are prescribed, the prescriber should explain that they are being used "off-licence" and will be discontinued after a trial period of three to six months if symptoms do not improve. A decision to stop medication may trigger feelings of fear and abandonment, but this is not a sound basis for continuing treatments that are ineffective. Instead, changes should be planned in advance and discussed fully with the patient, and alternative strategies to help people attain better mental health should be explored (see box 2).

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