Hypermobility in children

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Abstract

Hypermobility can be a normal variant in children but it is also found in a group of children presenting with musculoskeletal pain. A smaller group of children will have hypermobility associated with a more concerning syndrome. The clinical challenge is to differentiate those children who have isolated hypermobility with no other associations from those with syndromes that have potentially life limiting complications. In this review we will discuss the assessment of and provide a framework for classifying those children who are found to be hypermobile. We review the components of connective tissue and describe where known the genetic basis for particular phenotypes. In 2017 the international classification of Ehlers Danlos (EDS) was published which supersedes the Villefranche classification. This review describes the diagnostic criteria for the common subtypes of EDS, provides information on further differentials and discusses the management options.

Keywords ehlers-danlos syndrome; hypermobility; marfans syndrome; musculoskeletal pain

Introduction

In recent years the aetiology, classification, and optimal management of joint hypermobility have been subject to significant uncertainty and confusion. Despite a number of advances in our understanding, notably at the genetic and molecular levels, many important questions remain unanswered. The recently published 2017 EDS International classification and increased emphasis on genetic and molecular diagnosis is welcome but knowledge remains incomplete, particularly for the most common subtypes and further changes are anticipated.

Joint hypermobility is generally regarded to exist when the range of motion in a joint exceeds what would be considered normal. This is itself problematic since age-related normal ranges have not been adequately determined in children. Joint mobility increases up to a maximum in adolescence then falls with increasing age and is greater in girls than boys. Additionally, known ethnic variations further complicate this picture, with people of Indian Subcontinent origin for example, significantly more flexible than Europeans.

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Whilst the terms hypermobility, hyperlaxity and hyperextensibility have been used interchangeably, hypermobility is strictly defined as excessive movement within the normal plane of movement whilst hyperextensibility and hyperlaxity should be reserved for movement in an abnormal plane.

The reported prevalence of joint hypermobility in children varies widely -between 2.3% and 39% depending on the criteria used and the population studied. In a sample of 285 English school children excessive mobility in 4 or more joint pairs was noted in 7%. Although entirely asymptomatic in some children, in many it is associated with significant pain and disability with consequent impact the child, family and health care services. In a minority, hypermobility is present as part of a wider, occasionally life- or limb-threatening syndrome, and identifying these children is an essential but often difficult challenge.

Connective tissue

Abnormalities in connective tissue lead to increased flexibility and tissue fragility. These, in turn, lead to many of the abnormalities found connective tissue disorders. Connective tissues are present in all parts of the body excluding the central nervous system. Therefore many of the disorders discussed have affects beyond the musculoskeletal system. We will briefly summarise the components of connective tissue so as to better understand how specific abnormalities lead to particular disease phenotypes.

Collagen, elastic and reticular fibres

The main components of connective tissue are specialized cells and extracellular matrix. The types of cells in connective tissue vary according to the type of tissue and include fibroblasts, macrophages and plasma cells to name a few. These cells excrete protein and protein-polysaccharide molecules that form the extracellular matrix. There are three main types of fibres within the matrix bridging between the cells. Collagen fibres are strong a resist the pulling forces but allow flexibility. Elastic fibres contain both elastin and fibrillin which both add strength and flexibility, returning to their original length when stretched. The least common are reticular fibres these contain collagen covered in glycoprotein and give support to the walls of blood vessels (see Figure 1). Abnormalities in the genes that code for these structures lead to the disorders discussed during this review.

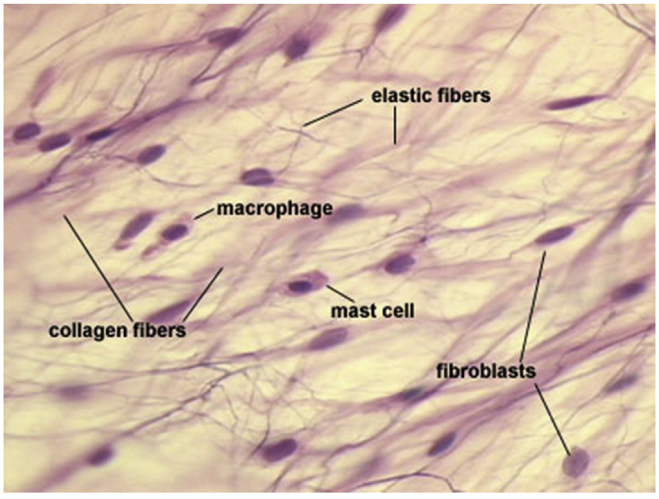

Figure 1 Structure of connective tissue.

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Beighton scoring system (score ≥4 denotes hypermobility)

Scoring 1 point each

1. Passive dorsiflexion of the 5th MCP joint to 90°
2. Apposition of thumb to volar forearm
3. Hyperextension of the elbow >10°
4. Hyperextension of the knees >10°

Scoring 1 point

5. Touch palms to floor with knees straight.

Table 1

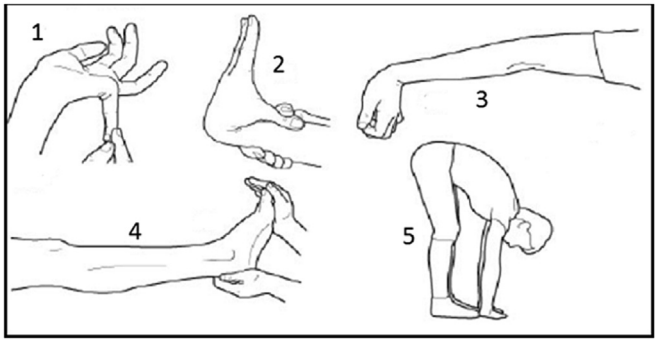

Figure 2 Beighton score.

Classification and assessment of hypermobility

Joint range can be assessed using a goniometer or by comparison with known normal parameters. Several diagnostic scoring systems are used to define hypermobility though none have been validated for use in children. The Beighton score (Table 1, Figure 2) is the most widely used and taught in paediatrics however other scoring systems exist.

Hypermobility can be generalized or localised. Generalised hypermobility occurs when there is hypermobility in multiple joints (usually 5 or more) affecting more than one limb. Localised hypermobility can be inherited or acquired following trauma, joint disease, surgery or training. Generalised hypermobility is more likely to be inherited and is strongly influenced by age, sex and ethnicity.

Peripheral joint hypermobility may be present as a discrete finding in the hands and feet only. It is common in toddlers and usually non-pathological but in the presence of other features may indicate vascular EDS.

Is hypermobility invariably associated with pain in children?

When the Beighton scoring system is applied to a population children a large proportion of those with hypermobility are not hampered by their increased flexibility. A prospective study of 551 Dutch children aged 6–12 years demonstrated that 35% of children scored 5 out of a possible 9 points on the Beighton score when assessed by physiotherapists with the aid of a goniometer. Interestingly 12.3% of the children complained of joint pain, but this was independent of their Beighton score. This finding is reproduced in several other populations including Finnish, Italian and Icelandic school children. Demonstrating that hypermobility itself is not necessarily a contributing factor in the development of musculoskeletal pain.

Kirk and Ansell first described a syndrome of generalized hypermobility in patients presenting with musculoskeletal pain in 1967. Since then our understanding of the impact of hypermobility on the lives of those affected has increased and several different classification systems proposed. There is now consensus regarding how patients with hypermobility are classified:

1. Asymptomatic non-syndromic/isolated localised, peripheral or generalised hypermobility. This may be familial and occur in relatives of patients meeting the diagnostic criteria for EDS
2. Syndromic joint hypermobility
3. Hypermobility Spectrum Disorders (HSDs) - symptomatic hypermobility in individuals not meeting any diagnostic criteria

Hypermobility Spectrum Disorders

Hypermobility spectrum disorders (HSDs) are clinically distinct causes of hypermobility that *result in musculoskeletal symptoms* and *do not fall into a distinct recognizable syndrome*. Their clinical manifestations are generally limited to the musculoskeletal system but some forms may have limited multisystem involvement. There are four subtypes of HSDs.

1. **Generalised HSD (G-HSD)**
   Generalised hypermobility with ≥1 musculoskeletal manifestation(s).
2. **Peripheral HSD (P-HSD)**
   Hypermobility limited to hands/feet with ≥1 musculoskeletal manifestation(s).
3. **Localised HSD (L-HSD)**
   Hypermobility at single/group of joints in one limb with ≥1 musculoskeletal manifestation(s).
4. **Historical HSD (H-HSD)**
   Self-reported historical generalised hypermobility with negative current Beighton score and ≥1 musculoskeletal manifestation(s).

The secondary manifestations of hypermobility are trauma, chronic pain, and disturbed proprioception. Hypermobile joints are prone to both macro and microtrauma from dislocations, subluxations and soft tissue injury which can lead to pain which may become chronic. Impaired proprioception coupled with reduced muscle strength can lead to a cycle of limited activity. This association is not fully understood with evidence suggesting an associated between generalised hypermobility and developmental co-ordination disorders in children.

The prevalence and genetic basis of HSD is not known. Pain in the presence of generalized hypermobility appears to commonly occur within families with a first-degree relative often being affected. However, this may be an illness model rather than simple autosomal dominant genetic inheritance.

The interaction between hypermobility and pain is complex and may be due to poor proprioception, autonomic dysfunction and fatigue. Several factors impact whether young people with hypermobility experience pain including, psychological factors such as anxiety and depression, physical fitness, biomechanical factors including joint instability and neurological factors that are thought to lead to up regulation of pain signals. Many other associations have been suggested though there is limited reproducible data. Some studies have suggested an increase in the incidence of

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