

## Childhood bone tumours in primary care:

helping GPs to identify 'the needle in the haystack'

**D Shanmugavadivel** (ORCID: 0000-0002-1912-4543), BMedSci, MRCPCH, PGDipMedEd, PGDipPublicHealth, NIHR doctoral research fellow; **J-F Liu** (ORCID: 0000-0001-5796-7878), MSc, research assistant; **K Vedhara** (ORCID: 0000-0002-9940-7534), BA Hons, PhD, FAcSS, professor of health psychology, Academic Unit of Population and Lifespan Sciences, School of Medicine, University of Nottingham, Nottingham. **A Ball-Gamble** (ORCID: 0000-0002-0708-0918), FRSA, Chief Executive; **A Polanco** (ORCID: 0000-0002-4619-0773), BSc, MRes, PhD, national head of PPIE for NIHR CRNCC, Children's Cancer and Leukaemia Group, Leicester. **P Nathan**, BMedSci, MSc, FRCGP, DCH, GP, RCGP Innovation Fellow, Hollybrook Medical Centre, Parkfields Surgery, Littleover, Derby. **D Walker**, BMedSci, FRCP, FRCPC, emeritus professor of paediatric oncology, Children's Brain Tumour Research Centre, School of Medicine, University of Nottingham, Nottingham. **S Ojha** (ORCID: 0000-0001-5668-4227), MD, PhD, MRCPCH, clinical associate professor in neonatal medicine, Academic Unit of Population and Lifespan Sciences, School of Health Sciences, University of Nottingham, Nottingham, and Children's Hospital, University Hospitals of Derby and Burton NHS Trust, Derby.

### Address for correspondence

Dhurgshaarna Shanmugavadivel, Population and Lifespan Sciences, University of Nottingham, E/E2066 Queen's Medical Centre, Derby Road, Nottingham NG7 2UH, UK.

Email: shaarnashan@doctors.org.uk

Submitted: 7 July 2023; Editor's response: 10 July 2023; final acceptance: 10 July 2023.

©The Authors 2023; 73: 377-379.

DOI: <https://doi.org/10.3399/bjgp23X734673>

### INTRODUCTION

In 2018, the World Health Organization declared childhood cancer as a global disease burden, launching a Global Initiative to improve survival to 60% worldwide by 2030.<sup>1</sup> If achieved, it is estimated that an extra 1 million children's lives will be saved. In the UK, childhood cancer is the largest illness cause of death in childhood in 1-19-year-olds and the incidence continues to rise.<sup>2</sup> Unlike in adult cancers, there are no modifiable risk factors or cost-effective screening options and so early diagnosis is key to reducing morbidity, mortality, and late effects from treatment burden.

### THE DIAGNOSTIC JOURNEY

The adult cancer diagnostic journey has been defined in the literature as a combination of many time intervals including the time from the first symptoms to presentation and then from presentation to diagnosis.<sup>3</sup> Children and young people (CYP) with cancer experience prolonged and clinically significant intervals throughout the health service both at primary and secondary care level. In bone tumours, the time to diagnosis can be life and limb saving, reducing the need for amputation.

The national HeadSmart campaign aimed to address diagnostic delay for childhood brain tumours in the UK by developing gold-standard clinical guidance and disseminating it through a public and professional awareness campaign.<sup>4</sup> This was associated with halving the time to diagnosis from 14.4 weeks to 6.7 weeks (median) in 5 years. The time from presentation to diagnosis was shortened from 3.3 weeks to 1 week.<sup>4</sup> Based upon this success, the model is being replicated for bone and abdominal tumours, where diagnostic delay is of concern and survival estimates are poorer compared with European counterparts.<sup>5,6</sup>

This article covers the clinical practice implications for bone tumours in children.

### THE CHALLENGES OF A BONE TUMOUR DIAGNOSIS

#### Non-specificity of symptoms

CYP with bone tumours present with non-specific symptoms that can be attributed to many other, more common illnesses and injuries.

A systematic review and meta-analysis were conducted to identify how bone tumours present in this cohort. This identified 29 bone tumour symptoms/signs.<sup>7,8</sup> The top symptoms, ranked by pooled proportions, were bone pain (76%), swelling (21%), fever (4%), history of trauma (3%), functional limitation (3%), palpable mass (3%), pain and swelling (2%), limp (2%), and pathological fracture (2%).

These symptoms are seen daily in CYP within primary care, and identifying those who need further investigation can be difficult.

#### Perceived rarity and lack of awareness

There is a misconception that childhood cancer is rare, despite it being the leading illness cause of child death in >1-year-olds. An individual's cumulative risk of cancer from birth to age 15 years is 1 in 450, with 1840 new cases diagnosed in CYP aged 0-15 years each year in the UK.<sup>2,9</sup>

As a result, public and professional awareness of childhood cancer is low. A face-to-face public survey ( $n=1000$ ) showed that the general public are unaware of childhood cancer risk, have a lack of confidence in recognising signs and symptoms, and have inaccurate knowledge of which symptoms could be caused by cancer in children.<sup>10</sup> Bone tumour symptom awareness was particularly low with considerably fewer than half of responders being aware of presenting symptoms of recurrent/persistent bone pain (23%), bone or joint swelling (27%), and slow recovery after injury (14%) as typical symptoms of malignancy.

This combination of perceived rarity and

# The diagnosis of bone tumours in children and young people:

## A summary for healthcare professionals



### CONSIDER A BONE TUMOUR IN ANY CHILD PRESENTING WITH:

- Bone Pain
- Swelling
- Palpable mass/ lump
- Limp/ restricted movement

#### Associated symptoms of:

- Bowel/bladder dysfunction
- Fever
- Weight loss



**ASK ABOUT COMMON PREDISPOSING FACTORS:**

Personal history of Li-Fraumeni syndrome or hereditary retinoblastoma

### ASSESS THESE CHILDREN WITH:

- History:**
- associated symptoms
  - any predisposing factors
  - family history
  - detailed injury history including timing of symptoms

#### Examination of:

- Joint/limb
- Joint above and below
- Weight
- Neurological examination
- P-GALS examination\*

\*<https://www.pimmonline.org/doctor/clinical-assessment/examination/>

### REFERRAL FROM PRIMARY CARE:

High risk of tumour: SAME DAY referral to secondary care

Lower risk\*: discuss with paediatrics via telephone to advise best route to be seen

#### IMAGING:

High risk of tumour: URGENT X-ray imaging

Lower risk\*: X-ray imaging within 4 weeks

\*Lower risk = bone tumour in differential diagnosis, low index of suspicion

### BONE PAIN

- Consider a bone tumour in any child with persistent\* bone pain
- Ask about the presence of the other symptoms of a bone tumour (swelling, palpable lump, restricted movement/limp, fever, weight loss, back pain and bowel/bladder/erectile dysfunction) in a CYP presenting with persistent bone pain.
- Bone pain from a bone tumour can occur at any time of the day or night
- Injuries can be a red herring. Take a detailed history of the events including the onset of the symptoms after the alleged injury. Pain secondary to an injury will get better day by day.

#### X-RAY IMAGING REQUIRED WITH:

- Persistent bone pain especially if worsening
- Localised bone pain that is waking a child or young person at night
- Unexplained bone pain (i.e. without any preceding injury)
- Bone pain that is out of proportion to the injury sustained or that does not improve 2 weeks from injury
- Bone pain with associated neurological symptoms
- Persistent back pain or pelvic pain (discuss with paediatric radiologist as X-ray may not be best imaging of choice).

#### COMMON PITFALLS:

- Attributing symptoms to an injury incorrectly
  - Assuming that a normal X-ray findings exclude a bone tumour
- \*Persistent = continuous or recurrent bone pain present for more than 2 weeks

### SWELLING

- Swelling from a bone tumour can be discrete or diffuse
- It can occur along the long bone or around a joint
- Swelling due to a bone tumour can present with overlying erythema
- Ask about the presence of the other symptoms of a bone tumour (bone pain, palpable lump, restricted movement/limp, fever, weight loss, back pain and bowel/bladder/erectile dysfunction)

#### X-RAY IMAGING REQUIRED WITH:

- Persistent swelling\* rapidly increasing in size.
- Persistent swelling\* not resolving despite treatment with regular anti-inflammatories or antibiotics.

#### COMMON PITFALLS:

- Attributing a red warm swelling to infection despite no improvement with antibiotics

\*Persistent swelling present for more than 2 weeks

### PALPABLE MASS/LUMP

- A bony mass/lump which is increasing in size can be a sign of a bone tumour
- Ask and examine for the other signs and symptoms suggestive of a bone tumour (bone pain, swelling, limp/restricted movement, fever, weight loss, back pain and bladder/bowel/erectile dysfunction) in CYP with a lump/mass.

#### X-RAY IMAGING REQUIRED WITH:

- A rapidly increasing lump
- A lump/mass with one or more other symptoms

#### COMMON PITFALLS:

- Attributing a bony lump/mass to infection despite no response to antibiotics

### LIMP/RESTRICTED MOVEMENT

- A bone tumour in the pelvis or lower limb can present as a limp
- A bone tumour in the upper limb can manifest as restricted movement
- Ask about the presence of the other symptoms of a bone tumour (bone pain, palpable lump, restricted movement/limp, fever, weight loss, back pain and bowel/bladder/erectile dysfunction.
- Have a high level of concern for a CYP who is normally highly active or sporty but is no longer able to play sport due to the presenting symptom.

#### X-RAY IMAGING REQUIRED WITH:

- A CYP who is non-weight bearing
- Persistent restricted movement despite adequate analgesia

#### COMMON PITFALLS:

- Failure to enquire about activities of daily living

\*Persistent = present for more than 2 weeks

### ASSOCIATED SYMPTOMS

- Bone tumours can present with systemic symptoms such as malaise or fever.
- Bone tumours causing spinal cord compression can affect bladder, bowel and erectile dysfunction. It is important to ask specifically for these symptoms, especially if the presentation is of back pain.



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Child Cancer Smart is a project of CCLG with University of Nottingham in partnership with Young Lives vs Cancer, Grace Kelly Childhood Cancer Trust and TYAC © CCLG 2023

Figure 1. Summary of bone tumour recommendations. Reproduced with permission from CCLG.

## REFERENCES

1. World Health Organization. *WHO Global Initiative for Childhood Cancer: an overview*. 2020.
2. Public Health England. *Children, teenagers and young adults UK cancer statistics report 2021*. 2021.
3. Weller D, Vedsted P, Rubin G, et al. The Aarhus statement: improving design and reporting of studies on early cancer diagnosis. *Br J Cancer* 2012; **106(7)**: 1262–1267.
4. Walker D, Wilne S, Grundy R, et al. A new clinical guideline from the Royal College of Paediatrics and Child Health with a national awareness campaign accelerates brain tumor diagnosis in UK children – ‘HeadSmart: Be Brain Tumour Aware’. *Neuro Oncol* 2015; **18(3)**: 445–454.
5. Herbert A, Lyratzopoulos G, Whelan J, et al. Diagnostic timeliness in adolescents and young adults with cancer: a cross-sectional analysis of the BRIGHTLIGHT cohort. *Lancet Child Adolesc Health* 2018; **2(3)**: 180–190.
6. de Aguirre-Neto JC, de Camargo B, van Tinteren H, et al. International comparisons of clinical demographics and outcomes in the International Society of Pediatric Oncology Wilms Tumor 2001 Trial and Study. *JCO Glob Oncol* 2022; **8**: e2100425.
7. Shanmugavadivel D, Liu JF, Walker D. A systematic review of the signs and symptoms of abdominal tumours in children and young people. *SIOP ABSTRACTS. Pediatr Blood Cancer* 2019; **66(S4)**: e27989.
8. Shanmugavadivel D, Liu JF, Stewart A, et al. P05 What are the signs and symptoms of bone tumours in childhood? Are the Great British public aware of them? *Arch Dis Child* 2020; **105(Suppl 1)**: A61–A62.
9. Walker DA. Helping GPs to diagnose children's cancer. *Br J Gen Pract* 2021; DOI: <https://doi.org/10.3399/bjgp21X715241>.
10. Liu JF, Shanmugavadivel D, Gamble A, et al. G176 Public awareness of childhood, teenagers and young adult cancer signs and symptoms in Great Britain. *Arch Dis Child* 2020; **105(Suppl 1)**: A62–A62.
11. Shanmugavadivel S, Liu J-F, Ranasinghe N, et al. 156 Even now as a Mum, I don't know what “just viral” means: parental perceptions of childhood cancer, the ChIP study. *Arch Dis Child* 2023; **108(Suppl 2)**: A285–A286.
12. Shanmugavadivel D, Liu J-F, Gamble A, et al. Assessing and investigating children with suspected bone and abdominal tumours: an e-Delphi consensus process. *BMJ Paediatr Open* 2023; **7(1)**: e001771.

## Competing interests

The authors have declared no competing interests.

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a lack of awareness contributes to lengthier diagnostic intervals. Qualitative research with parents who have experienced a childhood cancer diagnosis highlights that cancer was never on their radar prior to diagnosis and that healthcare professionals who saw them had not considered it as a diagnosis either.<sup>11</sup>

## DEVELOPING A CLINICAL GUIDELINE WITH EXPERT PRIMARY CARE OPINIONS

A Delphi consensus process was conducted to use professional expertise from all specialties who see CYP to incorporate the evidence from systematic reviews into a clinical guideline.<sup>12</sup> This consensus process involved 133 healthcare professionals, including 57 GPs. Consensus was reached on 64 statements through 2 rounds of Delphi, which will form the backbone of the new clinical guideline.

The statements were split into categories:

- Best practice in conducting the consultation: referral, imaging, predisposing factors;
- Bone tumours: general, bone pain, swelling, mass/lump, restricted movement/limp; and
- Abdominal tumours: general, abdominal pain, abdominal mass, haematuria, abdominal distension.

The key statements have been summarised in Figure 1.

## HOW CAN GPs USE THIS TO IDENTIFY ‘THE NEEDLE IN THE HAYSTACK’?

While these provide detailed guidance, here are some general principles that can aid prompt diagnosis:

### Think childhood cancer

‘Three strikes’ with the same complaint without a diagnosis should justify considering cancer as a potential differential.<sup>9</sup> A high index of suspicion should be maintained for bone tumours in children presenting with persistent or concerning symptoms. GPs should use the symptom checklist (Figure 1) in their consultations to identify symptoms and ask about duration. This will identify those who require further investigation. Persistent is defined as occurring on most days for 2 weeks. *Two or more persistent symptoms require imaging*. Imaging requests should be labelled as urgent and carried out within 24 hours; however, an imaging request should not delay referral.

## Phone a friend

*If you have a suspicion of cancer, call your local paediatrician for discussion.* Often, this will ensure that the CYP is seen in the most suitable place according to need, either the same day or in rapid-access or standard clinic settings. Discussing the case, rather than sending a written referral, provides the opportunity for a more nuanced discussion about probability, allowing more prompt and shared decision making.

## Address the elephant in the room

Parents and families who attend recurrently with the same symptoms often have a gut instinct that something is wrong, just as clinicians do. GPs should ask them directly, ‘*What are you worried this could be?*’ This allows honest and genuine discussion about their concerns, and whether they can either be reassured, reviewed, or referred for further investigations.

## Avoid the injury red herring

It is common for CYP presenting with bone symptoms to have some recall bias when asked if they have injured themselves, and so it is important to take a thorough injury history including mechanism, onset of symptoms, and any relieving factors. If symptoms are a result of an injury, it should have improved considerably within 2 weeks. *If no or slow improvement after 2 weeks, they need an X-ray.*

## CONCLUSION

Bone tumours can cause a diagnostic dilemma for primary and secondary care clinicians. Clear and concise tumour-specific guidance can empower GPs with the confidence and knowledge to assess and investigate those CYP who need it in a prompt manner. The full clinical guideline is due to be published later in 2023, with messaging amplified through a new childhood cancer awareness campaign, called Child Cancer Smart.

## Funding

The Delphi consensus was funded by the National Institute for Health and Care Research through a Doctoral Research Fellowship (DRF-2018-11-ST2-055). The systematic review and meta-analysis that informed this guideline development were funded by Cancer Research UK through the Population Research Committee Early Diagnosis Innovation Grant (C59357/A22874).

## Provenance

Freely submitted; not externally peer reviewed.