When should I suspect childhood leukaemia?

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The paper by Clarke et al. sheds light upon the initial presenting features of childhood leukaemia. It is a systematic review and meta-analysis of the clinical features present in children with leukaemia at presentation.

The clinical relevance of this is that there are several diseases that are notorious mimics. ‘Know syphilis in all its manifestations and relations, and all other things clinical will be added to you’ stated Osler in a previous century and something similar could be said of leukaemia by contemporary paediatricians. It is the ability of the various leukaemias to mimic prosaic viral infections in some patients, while in others is the stuff of the membership exam ‘grey case’ that fuels clinicians’ concerns about missing the diagnosis. There is no doubt that it is a serious disorder, but it is also relatively ‘common’ with about 500 children a year being diagnosed in the UK per year. It is likely that a generalist in a regional hospital will come across a few cases each year and be confronted with difficult cases at some point in their day-to-day practice.

In the paper, the authors whittle away at 95 presenting signs and symptoms to find five features present in more than 50% of children, namely: hepatomegaly (64%), splenomegaly (61%), pallor (54%), fever (53%) and bruising (52%). Additionally, there were eight features present in one-third to half of children: recurrent infections (49%), fatigue (46%), limb pain (43%) hepatosplenomegaly (42%), bruising and petechiae (42%) lymphadenopathy (41%), bleeding tendency (38%) and rash (35%). The authors conclude that children with unexplained illness require a thorough history and clinical examination that should include palpation of the abdomen, a search for lymphadenopathy and careful inspection of the skin. As a jobbing paediatric haematologist the features found in the paper are high in my mental checklist and my experience in practice mirrors the findings of the paper. This will be useful to the non-specialist clinician at the coalface and will help inform guideline and protocol writers.

Whereas the syphilis that Osler and his contemporaries battled is caused by a single species of infectious agent, the leukaemias of childhood are a number of different diseases adding to the spectrum of their clinical manifestation. Each often requires a specific diagnosis to guide therapy. That therapy is not necessarily always chemotherapy. It has been one of the major paradigm shifts that has happened over recent years how much the management of chronic myelogenous leukaemia has changed. The introduction of tyrosine kinase inhibitors has transformed the care for the majority of patients. It is likely that the next several decades will usher in other treatments into the management of other leukaemias that occur in children, as is already happening in the realm of adult haematology, where novel small molecule inhibitors and biological agents are abounding. The specific diagnostic entities are likely to alter, as the new technologies of next-generation sequencing and other techniques change our understanding of tumour biology and how to classify them. However, many of these aspects will be in the area of specialist care and may be of little help to the generalist who has an unwell child in front of them.

I am conscious of how lucky I am in that should include palpat
Death in childhood is fortunately a relatively rare occurrence in the developed world, but in the UK overall childhood mortality rate is higher than in some other European countries. Injury remains the most frequent cause of death after the first year of life, but cancer is the most common medical cause and leukaemia is the most common cancer. Fortunately, leukaemia relapse is now a rare disorder and the most likely outcome for most patients is cure with survival, but early detection and prompt treatment can only be good for patients. Grey cases will still appear from time to time to test all of us, the paper by Clarke et al adds detail to the presenting features of leukaemia in children.

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