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ENDGAMES

SPOT DIAGNOSIS

# A tired young man with a dysmorphic thumb

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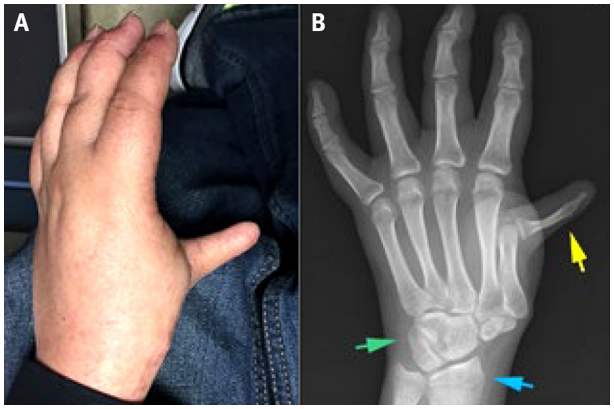
A 23 year old man with short stature, congenital malformation of the left thumb and both ears, and a single kidney presented with back pain, shortness of breath, fatigue, and easy bruising that had developed over several months. Physical examination revealed hepatosplenomegaly.

His brother had died in early childhood, more than 20 years ago. The patient's parents reported that his brother, "had similar but worse congenital malformations, including bad kidney problems."

Full blood count showed pancytopaenia, which prompted further laboratory investigations (table 1).

Radiography of the patient's left hand (fig 1) revealed a single fused phalanx, anomalous carpal bones, and a hypoplastic radial styloid.




(A) Dysmorphic left thumb. (B) Radiograph of left hand showing single fused phalanx (yellow arrow), anomalous carpal bones (green arrow), and a hypoplastic radial styloid (blue arrow)

Computed tomography imaging of the patient's neck showed partially fused cervical vertebrae and dysplastic ear healing after surgical reconstruction. What is the most likely diagnosis?

## Answer

Acute myeloid leukaemia secondary to Fanconi anaemia.

Pancytopaenia in patients with congenital abnormalities is suggestive of inherited bone marrow failure syndromes, such as Fanconi anaemia, dyskeratosis congenita, or Shwachman-Diamond syndrome.[1]

Thumb and radial anomalies (fig 1) are hallmarks of Fanconi anaemia.[1 3] Ear abnormalities affect one in five people with the condition.[3]

Congenital structural abnormalities of extremities, vertebrae, and kidneys are signs of VACTERL-H. VACTERL-H.is a collection of recognised congenital abnormalities that is found in approximately one third of patients with Fanconi anaemia.[4]

This patient's deformities are typical of Fanconi anaemia, but a lack of deformities does not exclude this syndrome: one in three individuals with Fanconi anaemia has no deformity.[5]

Fanconi anaemia increases a person's risk of developing myelodysplasia and acute myeloid leukaemia by over 300-fold in pre-teenage years and young adulthood.[2]

In this patient, the recent back pain, combined with the pancytopaenia, is likely caused by expanding abnormal haematopoiesis in the bone marrow rather than his vertebral abnormalities associated with Fanconi anaemia. This, along with a history of fatigue and bruising, is sufficient to raise suspicion of acute myeloid leukaemia/myelodysplastic syndromes and trigger further investigations, including bone marrow aspirate evaluation.

## Patient outcome

The patient's bone marrow evaluation showed myelodysplasia with 23% blasts and complex cytogenetic abnormalities. Chromosome breakage test coupled with gene sequencing confirmed Fanconi anaemia. His pain was caused by myelodysplasia evolving into acute myeloid leukaemia. He died from progressive disease before potentially life saving haematopoietic stem cell transplantation could be pursued.

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## Learning points

Early diagnosis of Fanconi anaemia reduces the risk of malignancies and complications (eg, life threatening bone marrow failure). This is because patients remain under multidisciplinary expert surveillance throughout their lives.

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Patient consent obtained.

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# Table

**Table 1| Initial laboratory investigations**

| Test | Result | Normal range |
|---|---|---|
| White blood cell count [k/mm$^3$] | 2.6 | 3.6-10.6 |
| Haemoglobin [g/dL] | 6.2 | 13.4-17 |
| Haematocrit [%] | 18.4 | 40-54 |
| Red blood cell mean corpuscular volume [fL] | 104 | 81-99 |
| Red blood cell distribution width [%] | 24.1 | 11.5-14.5 |
| Platelets [k/mm$^3$] | 143 | 150-450 |
| Absolute neutrophil count [k/mm$^3$] | 1.508 | 1.7-7 |
| Absolute lymphocyte count [k/mm$^3$] | 0.806 | 1-3.2 |
| Promyelocytes [k/mm3] | 0 | 26 |
| Macrocytes | Moderate | None |
| White blood cell morphology | Hypogranulated | Normal |