

Fanconi Anaemia

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Crumlin

Child A

- Age 3years
- 4 month Hx lethargy
- 1 month Hx easy bruising
- FH cousin died of leukaemia

Examination

FBC

Hb 8.6g/dl

WCC $2.1 \times 10^9/l$

Neutrophils 0.6

MCV 104

Platelets $10 \times 10^9/l$

?

Differential Diagnosis

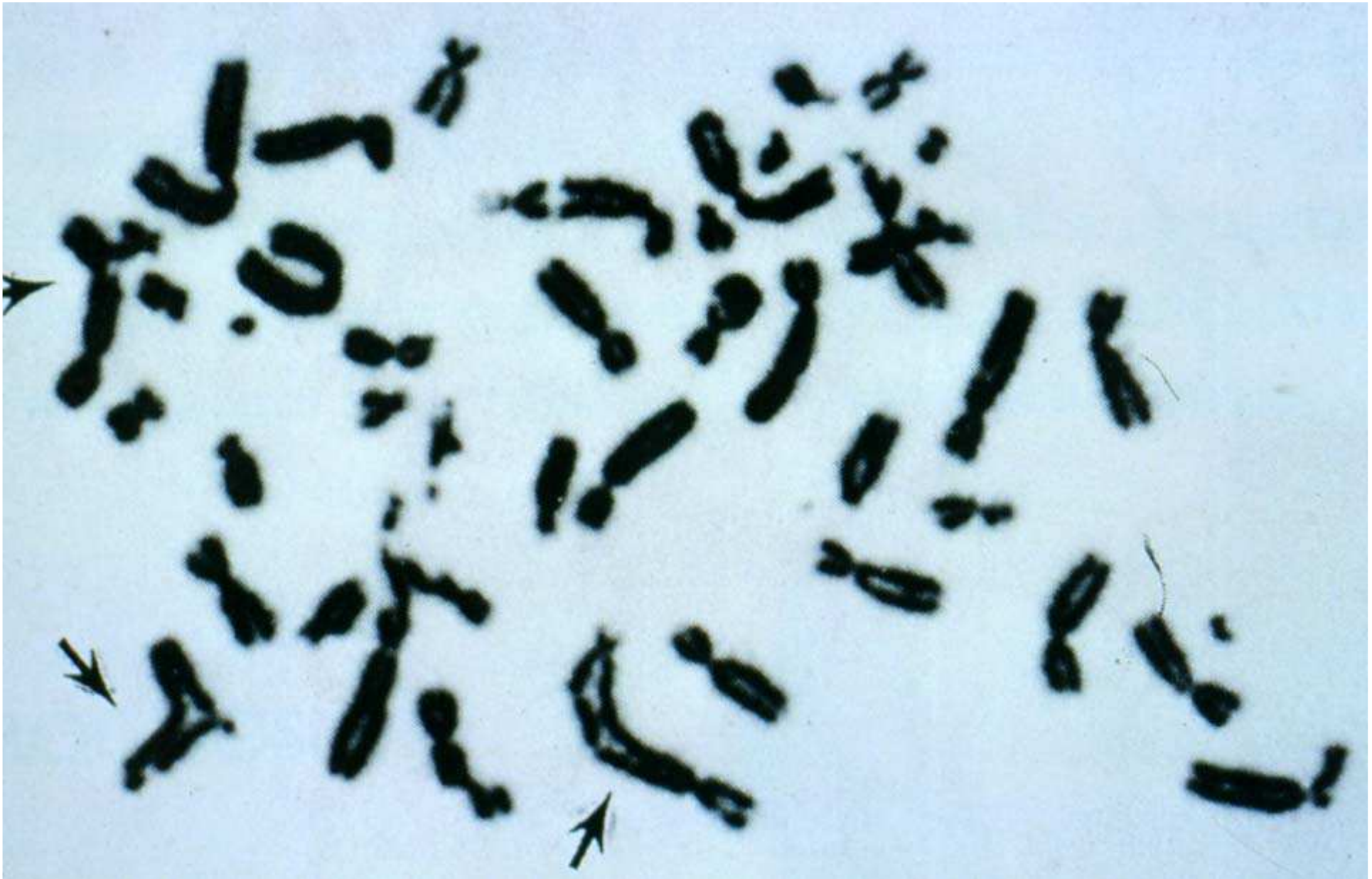
- Viral insult
- Drugs/chemicals
- Haemotinic deficiency (B12/Folate)
- Leukaemia
- Myelodysplasia
- Neoplasm
- Bone marrow failure syndrome
 - Fanconi Anaemia
 - Dyskeratosis Congenita
 - Swachmann Diamond syndrome
- Aplastic Anaemia
- PNH

Further Examination

- Microcephaly
- Microphthalmia
- Short stature
- Café au Lait spots
- Abnormal thumbs
- Hypospadias
- Single kidney

Investigation

- Bone marrow examination
- Cytogenetics
- Chromosome Stress testing
 - Mytomycin C
 - DEB



Metaphase spread – chromosomal breakage and tri-radial formation

Fanconi Anaemia

Pathophysiology

- DNA repair defect
- Abnormal cell cycle control
- Increased oxygen sensitivity – increasing chromosome breakage
- Increased apoptosis

Outcome

- Decline in haematopoietic stem cells
 - Bone Marrow Failure

- Development of mutant clones
 - Myelodysplasia
 - AML

Clinical features

- Skeletal Abnormalities
- Skin Pigmentation
- Growth retardation
- Endocrinopathy (44% GH↓/36% T4↓)
- Developmental delay
- Renal Abnormalities
- Genital abnormalities
- GI abnormalities
- Cardiac defects (PDA/VSD/PS/AS/Coarctation)

Haematological Features

- FBC normal at birth
- Macrocytosis
- Thrombocytopenia & neutropenia
- Pancytopenia 5-10yrs (median 7yrs)
- ↑ risk of malignancy with age (M>F)
- Median age of Leukaemia 11.3yrs
- Median age of solid tumours 28.9yrs (X50 GP)
 - Head & neck/oesophagus/liver/vulva/cervix

Types of Fanconi Anaemia

- 6 FA genes (FANCA, C, D2, E, F, G)
- FANCD1 & FANCB are BRCA2

- FANCA – 66%
- FANCC & FANCG – 25%
- FANCE & FANCF – 8%

None of the genes have homology to each other

The FA Genes

- FANCA – largest gene; 40% large mutations
 - Early anaemia and leukaemia
 - Less endocrinopathy
- FANCC – Severe phenotype
 - Multiple congenital abnormalities
 - Early onset bone marrow failure
- FANCG – most severe cytopenia and leukaemia

Treatment options

- Supportive care
- Androgens
 - ↑WCC/Platelets ±
 - May take 6-12 months/ majority relapse when stopped
- Bone Marrow Transplantation
 - ↑ 2^o tumours
 - Toxicity/GVHD/Infection
- Gene Therapy

Fanconi Anaemia in Irish Population

- Common in Traveller population
- FANCA – Large deletion

- 1982-2001 19 children (11 F:8M)
- 3 Families - 2 children
- 1 family - 3 children

Reasons for diagnosis

- Family History – 16 cases
- Physical appearance – 3 cases
- Short stature – 3 cases
- Failure to Thrive – 3 cases
- Bruising – 4 cases

Outcomes

- 7 children died of disease
- 7 received BMT
- Donors
 - 2 sibling
 - 5 matched family donors
- Complications
 - 1 Haemorrhagic cystitis
 - 1 VOD
 - 1 GVHD

Conclusions

- FA rare but important cause of BM Failure
- V common in Irish Traveller population
- Unique gene abnormality
- Severe phenotype
- Consider Dx in children with FTT
- Transplant when counts ↓
- Monitor for 2^o AML/Tumours

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