

CASE SIX

Short case number: 3_28_6

Category: Immune and Haemopoietic systems

Discipline: Paediatrics

Setting: General Practice_rural

Topic: Acute Lymphoblastic Leukaemia.

Case



Alexander 'Sandy' Thomas, is 5 years old, he and his family are well known to you and the practice. Sandy presents today with his father John, who just wants you to have a look at the bruises on his legs. *"I'm sure he's fine, you know what he's like always running around tripping over his own feet..but we are just a bit concerned because he seems to be very tired, probably because he has just started school...it takes it out of him a bit"*
You note that Sandy is a lot quieter than usual and appears pale.

Questions

1. You are concerned that Sandy may have leukaemia, what are the key features of your history and examination and why?
2. What differential diagnoses would you consider?
3. What initial investigations would you undertake and why?
4. What are the findings on FBC that suggest acute lymphoblastic leukaemia and how does this differ from acute myeloid leukaemia.
5. Sandy's FBC confirms your fears and he has acute lymphoblastic leukaemia, how would you explain this to his parents?
6. Sandy needs to travel to the Children's Hospital to receive tertiary level care, his parents ask about where they can stay and can they share a room with him at the hospital, what would you explain to them? How could you find out about the available services for families from rural areas? Is it possible for Sandy to receive any of his treatment locally?
7. Outline the principles of management of acute leukaemia in terms of induction, consolidation, CNS directed therapy, reinduction and maintenance?
8. What are the prognostic risk factors for acute lymphoblastic leukaemia?

Suggested reading:

- South M, Isaacs D editors. Practical Paediatrics. 7th edition. Edinburgh: Churchill Livingstone;2012.
<https://www.schn.health.nsw.gov.au/find-a-service/health-medical-services/cancer-oncology/sch>

ANSWERS

1. You are concerned that Sandy may have leukaemia, what are the key features of your history and examination and why?

Sandy is very tired, quieter than usual, and has bruises on his legs and appears pale. A common presentation of leukaemia is a 3-4 week prodrome which may include pallor, increased bruising or bleeding, lethargy, anorexia, recurrent infections or fevers, anorexia, bone pain or reluctance to walk.

Physical examination in children presenting with ALL (Acute lymphoblastic leukaemia)

80% have pallor,
50% petechiae,
35% lymphadenopathy and
50-60% hepatomegaly or splenomegaly.

2. What differential diagnoses would you consider?

The differential diagnosis would include infections (Lymphadenopathy and hepatosplenomegaly) would be consistent with infection such as infectious mononucleosis /cytomegalovirus), juvenile rheumatoid arthritis (if the presentation includes involvement of bones and joints) idiopathic thrombocytic purpura/aplastic anaemia.

3. What initial investigations would you undertake and why?

Peripheral blood film – usually demonstrate the presence of leukaemic blasts with or without anaemia and thrombocytopenia (and then a bone marrow aspirate would be needed to confirm the diagnosis).

4. What are the findings on FBC that suggest acute lymphoblastic leukaemia and how does this differ from acute myeloid leukaemia?

Peripheral blood film ALL usually demonstrates the presence of leukaemic blasts with or without anaemia and thrombocytopenia AML (20% of acute leukaemia/can have similar signs – pallor/bleeding/fever/anorexia/malaise/bone pain).

Abnormal proliferation of lymphoblasts (ALL) or myeloblasts (AML) in the bone marrow- these occupy marrow space, leading to reduced numbers of haematopoietic cells, resulting ultimately in pancytopenia.

5. Sandy's FBC confirms your fears and he has acute lymphoblastic leukaemia, how would you explain this to his parents?

Parents often ask: *How did this happen to my child?*

Did this happen because of something I have done or passed on to my child?

→only a small percentage of paediatric cancers have a clearly hereditary component and despite extensive epidemiological studies few environmental agents have been consistently linked to childhood malignancy. It is thought that cancer initiation results from a series of genetic mutations that result in the inability of a cell to respond normally to signals (intracellular and/or extracellular) that control cell proliferation, differentiation or death. In acute lymphoblastic leukaemia a mutant stem cell, capable of indefinite renewal, gives rise to abnormal proliferation of lymphoblasts in the bone marrow.

6. Sandy needs to travel to the Children's Hospital to receive tertiary level care, his parents ask about where they can stay and can they share a room with him at the hospital, what would you explain to them? How could you find out about the available services for families from rural areas? Is it possible for Sandy to receive any of his treatment locally?

The Sydney Children's Hospital has 'Ronald McDonald House' which provides accommodation for country families whose children are being treated at Sydney Children's Hospital as inpatients, or outpatients. Cost of accommodation is approximately \$30 per night and is claimable through the Isolated Patients Travel Accommodation Assistance Scheme. Many rural areas have local cancer support groups such as Can Assist (the Cancer Council has information on local cancer support groups). Paediatric chemotherapy is usually given in a unit where staff are trained in its use and see the numbers of cases necessary to maintain those skills, although some can be given on an outpatient or day-stay basis. Rural areas need to be able to manage the complications of treatment, such as infections due to a drop in white cell count following chemotherapy.

7. Outline the principles of management of acute leukaemia in terms of induction, consolidation, CNS directed therapy, reinduction and maintenance?

The first month of therapy is **induction** (induction aimed at killing leukaemic cells and inducing remission) with 3 – 4 drug combination chemotherapy (vincristine, asparaginase, prednisone, daunorubicin). Remission will be achieved in more than 95% of patients. Further combination therapy is required to prevent relapse (**consolidation**). Optimal duration of therapy is not known most centres elect to treat for 2 – 3 years. **CNS targeted therapy** using high-dose intravenous and intrathecal methotrexate has allowed for cranial irradiation to be generally avoided except in patients with overt CNS disease at diagnosis (spared potential deleterious effects on cognition and growth). Continuation or **maintenance** therapy, often at lower doses, to kill cancer cells that may re-grow and cause a relapse.

What are the prognostic risk factors for acute lymphoblastic leukaemia?

Combination chemotherapy protocols for ALL result in cure of 80%:

- *Poor prognosis* induction failure
<12 months age
poor prednisone response
high MRD (minimal residual disease) level.
- *Good prognosis* age 2- 10 year
WCC <50x 10⁹
no CNS or testicular disease
rapid response to induction therapy
not T-cell phenotype.