Management of the patient with suspected leukaemia

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See also: Oncology guidelines on Microguide > Paediatric & Neonatalogy > Paediatrics > Oncology guidelines

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Introduction

- Acute leukaemia is the most common malignancy in young children. Presenting symptoms are often non-specific. There are 2 main types affecting children: acute lymphoblastic leukaemia (ALL) and acute myeloid leukaemia (AML).
- Management from the time of presentation to the time of confirmation of diagnosis follows the same principles for both types.
- When the diagnosis of acute leukaemia is suspected, patients will be transferred to the ‘primary treatment centre’ (PTC) at the earliest possible opportunity for diagnostic work-up and initiation of potentially curative treatment.
- Prior to transfer, it is essential that the patient’s condition is stabilised and appropriate supportive care is initiated.

Patients with leukaemia have the potential to deteriorate rapidly, so require prompt assessment.

Discuss patient with on-call consultant paediatrician as soon as diagnosis is suspected. Notify paediatric oncology shared care (POSCU) consultant.

Assessment

When to suspect acute leukaemia:

<table>
<thead>
<tr>
<th>History</th>
<th>Examination</th>
<th>Investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue/lethargy/pallor</td>
<td>Low Hb</td>
<td></td>
</tr>
<tr>
<td>Petechial rash/bruising</td>
<td>Low platelet count</td>
<td></td>
</tr>
<tr>
<td>Epistaxis and other bleeding symptoms</td>
<td>Abnormal coagulation screen</td>
<td></td>
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<tr>
<td>Weight loss</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fever, night sweats</td>
<td>Clinical focus of infection</td>
<td>Raised inflammatory markers</td>
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<tr>
<td>Recurrent infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>Non-tender enlarged nodes</td>
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</tr>
</tbody>
</table>
When to suspect acute leukaemia cont.

<table>
<thead>
<tr>
<th>History</th>
<th>Examination</th>
<th>Investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent or persistent infection</td>
<td>Neutropaenia or high WCC, usually lymphocytosis</td>
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<tr>
<td>Abdominal pain or distension</td>
<td>Hepatosplenomegaly Abdominal mass</td>
<td>Abnormal LFT</td>
</tr>
<tr>
<td>Limp/bone pain</td>
<td>Abnormal gait</td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>Abnormal respiratory examination</td>
<td>CXR</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>Exacerbation of symptoms/drop in SaO2 when lying supine</td>
<td></td>
</tr>
<tr>
<td>Stridor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wheeze</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chest pain, palpitations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Facial swelling</td>
<td>Signs of SVC obstruction</td>
<td></td>
</tr>
<tr>
<td>Testicular swelling</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headaches</td>
<td>Papilloedema</td>
<td></td>
</tr>
<tr>
<td>Facial weakness</td>
<td>Cranial nerve palsy</td>
<td></td>
</tr>
<tr>
<td>Squint</td>
<td>Other focal neurological signs</td>
<td></td>
</tr>
<tr>
<td>Visual disturbances</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin infiltration</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>High urea, creat, PO4, urate</td>
<td></td>
</tr>
</tbody>
</table>

Differential diagnosis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Distinguishing features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral infection</td>
<td>Isolated transient neutropaenia Clear history of viral infection</td>
</tr>
<tr>
<td>EBV infection</td>
<td>History of sore throat Haemolytic anaemia Pancytopenia unusual; resolves spontaneously Monospot +ve EBV IgM+ve and/or EBV PCR elevated</td>
</tr>
<tr>
<td>Parvovirus infection</td>
<td>‘slapped cheek’ syndrome Isolated red cell aplasia +/- neutropaenia</td>
</tr>
<tr>
<td>Pre-existing neutropaenia with infection</td>
<td>Isolated neutropaenia May get stomatitis</td>
</tr>
<tr>
<td>ITP</td>
<td>Isolated thrombocytopenia Well child</td>
</tr>
<tr>
<td>Aplastic anaemia</td>
<td>Pancytopenia with no blasts on blood film</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>lymphadenopathy, mediastinal mass, hepatosplenomegaly, high ESR, LDH&gt;1000, FBC may be normal</td>
</tr>
</tbody>
</table>
Important points in the history

- History of presenting complaint: See above
  - Past medical history (including previous chicken pox or HSV)
- Drug history, allergies and immunisations
- Family history
  - Are there any family members with cancer/leukaemia; ‘problems with their blood’ or bone marrow transplant?
- Social history
  - Patients/parents will often worry about how they are going to cope in practical terms, so helpful to ascertain social history

Examination and emergency management

**ABCDE approach**

The patient is at high risk of sepsis and other oncological emergencies, so should be triaged accordingly and reviewed by a senior doctor.

Observations: temperature, heart rate, respiratory rate, SaO2, blood pressure
Weight, height
Surface area (obtain from weight/surface area chart at back of paediatric BNF)

**Identify high risk features:**

- Mediastinal mass
- SVC obstruction
- Tumour lysis syndrome
- Coagulopathy
- Sepsis
- High WCC >50
- Neurological symptoms/signs
- Requirement for HDU or PICU care for another reason

If any high risk features are present, it is essential that these are highlighted to the paediatric consultant on-call (+ paediatric anaesthetic consultant on-call) at RACH and to the Marsden team.

Such patients are likely to require care by the Marsden team at St George’s Hospital
Contact STRS early as they may need retrieval (even if not requiring intubation or inotropic support).

If signs of raised ICP, discuss with Marsden Oncology Consultant and liaise with neurosurgical team at St George’s Hospital
Initial investigations

Ideally complete initial blood tests before any blood product transfusion
Insert cannula at outset and insert 2nd cannula for further monitoring blood tests.
Please do not send samples to PTC by courier or post, unless this has been agreed by the POSCU consultant.

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Sample type</th>
<th>Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBC and blood film</td>
<td>EDTA 1ml</td>
<td>Request blood film report by consultant haematologist on call</td>
</tr>
<tr>
<td>Group and save</td>
<td>EDTA pink cap 2ml</td>
<td>2 samples may be needed-discuss with lab</td>
</tr>
<tr>
<td>Immunophenotyping</td>
<td>EDTA red cap 4ml, Store at room temp.</td>
<td>Discuss with BSUH consultant haematologist on call</td>
</tr>
<tr>
<td>Coagulation screen</td>
<td>Citrate tube; filled to line</td>
<td>APTT, INR, fibrinogen, (D-dimers)</td>
</tr>
<tr>
<td>Venous blood gas/glucose/lactate</td>
<td>Capillary tube</td>
<td>Analyse using blood gas machine</td>
</tr>
<tr>
<td>U&amp;E</td>
<td>Clotted blood, gold cap</td>
<td>Sample more likely to haemolyse in tumour lysis syndrome.</td>
</tr>
<tr>
<td>Ca, Mg, PO4 urate</td>
<td>full adult or paediatric tube</td>
<td>If this occurs:</td>
</tr>
<tr>
<td>LFT</td>
<td></td>
<td>-Take sample to lab immediately after it has been taken.</td>
</tr>
<tr>
<td>CRP</td>
<td></td>
<td>-Do not put in the pod system</td>
</tr>
<tr>
<td>LDH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Viral serology</td>
<td>Clotted blood, gold cap</td>
<td>Request CMV, EBV, HSV, VZV, toxoplasma, hepatitis, measles</td>
</tr>
<tr>
<td>TPMT genotype and phenotype</td>
<td>EDTA; 4ml, Store at 4C</td>
<td>Ask lab ‘send away’ team to send to Purine Research Laboratory at St Thomas' Hospital. Tel 020 7188 1266</td>
</tr>
<tr>
<td>Blood cultures, urine cultures, bacterial and viral throat swabs, (COVID testing)</td>
<td></td>
<td>Infection screen</td>
</tr>
<tr>
<td>12-lead ECG</td>
<td></td>
<td>Do not do lumbar puncture</td>
</tr>
<tr>
<td>Chest X-ray</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT or MRI head</td>
<td></td>
<td>If focal neurology or signs of raised ICP</td>
</tr>
</tbody>
</table>

Management pathway

See next page
Initial management

Respiratory distress or features of mediastinal mass or signs of SVC obstruction?

Yes

- Do not allow patient to lie flat.
- Administer O₂
- Urgent anaesthetic review
- Discuss with STRS

No

Active bleeding?

Yes

- Local bleeding control measures
- IV access (ideally not in right upper limb)
- IV tranexamic acid 10 mg/kg (see BNFc for further dosing and administration)
- Administer blood products as per guidelines

No

Signs of shock?

Yes

- Manage as per APLS guidelines
- Urgent anaesthetic review
- Discuss with STRS
- Administer blood products as per guidelines

No

Fever or signs of infection?

Yes

Start broad spectrum IV antibiotics as per acute oncology admission antimicrobial flowchart (Microguide > Paediatrics & Neonatology > Paediatrics > A-Z > O > Oncology)

NB. If neutrophil count normal treat as if neutropenic

No

- Start IV 0.9% sodium chloride / 5% glucose at 2 litres/m²/24hours. Do not add potassium to fluids.
- Start allopurinol 100 mg/m² TDS. Max. dose = 400 mg/day
- If high risk of tumour lysis, consider IV rasburicase 200 mcg/kg once day (relatively contra-indicated in G6PD deficiency)
- Paracetamol for fever or pain. No NSAIDS or PR medication.
- Consider blood product transfusion - ensure all necessary blood samples taken beforehand
- Complete preliminary investigations and follow ongoing monitoring guidelines
- Refer patient to PTC + ensure that responsible CED/general paediatric consultant has reviewed patient + discuss with POSCU consultant
- Consultant or senior registrar to discuss likely diagnosis and management plan with family
Ongoing management

Monitoring

✓ Observations
  At least 4-hourly
  Temperature, heart rate, blood pressure, respiratory rate, SaO2, pain scores
✓ Fluid balance
  Aim urine output >3ml/kg/hr (caution if renal/cardiac failure)
  Daily weight
✓ Pain management
  Use usual pain management pathway, but avoid NSAIDs and PR medication
✓ Blood tests
  U&E, PO4, Ca, urate
    6-hourly; more frequent if unstable
    If patient has tumour lysis syndrome, cells are fragile so samples should be taken immediately to pathology reception by hand
  FBC  12-hourly, unless unstable or bleeding symptoms
  LFT  Daily
  Coagulation screen
    Daily unless unstable or bleeding symptoms

Blood product support

• Most patients will not require CMV negative or irradiated blood products.

• Indications for CMV negative products:
  Neonates,
  All patients with relapsed leukaemia/lymphoma

• Indications for irradiated products:
  Infants <6mths of age who have received in-utero transfusion,
  All patients with relapsed leukaemia/lymphoma,
  Patients with severe T-lymphocyte immunodeficiency syndromes
  All bone marrow/peripheral blood stem cell donors from 7 days before & during harvest
### Investigation | Transfusion threshold | Instructions
--- | --- | ---
haemoglobin | <70g/L | Transfuse to achieve Hb of 100
Instructions: (100-actual Hb)/10 x 3.5 x patient weight
Prescribe as ml and give over 3 hours
Caution if high WCC or if neurological signs or if Hb<60; transfuse slowly aiming for increase in Hb of 20 rather than aiming for Hb 100
platelets | <20 | Transfuse 1 pool (or 15ml/kg if infant) over 30mins
FFP | Elevated APTT ratio | Usually only necessary if active bleeding
cryoprecipitate | Low fibrinogen | Volume needed:
If patient has APML/AML M3, correct in the absence of active bleeding as patients can develop DIC

### Tumour lysis syndrome

**Characterised by** abrupt and massive release of cellular components due to rapid lysis of malignant cells

**Triggered by** steroids, fever, chemotherapy, dehydration; but can occur prior to starting treatment

Highest risk at presentation and up to 72hrs post induction chemo

**High risk factors:**
- T-Cell ALL
- Oliguria, dehydration, renal infiltration or renal failure
- WBC >100 x10⁹/L
- Bulky disease (i.e. lymphadenopathy, hepatosplenomegaly)

**Symptoms:** nausea, vomiting, diarrhoea, anorexia, paraesthesia, muscle cramps, tetany, fluid overload, cardiac arrhythmias, seizures, haematuria, renal impairment,

**Biochemical abnormalities:**
- Early: high / rising phosphate, high urate (but urate usually normalised after rasburicase, even in presence of tumour lysis syndrome)
- Later: Low calcium, high urea and creatinine, high potassium

**Treatment:**
Prevention: IV fluids hyperhydration + allopurinol (Rasburicase if high risk of tumour lysis)
If biochemical changes suggesting tumour lysis syndrome, increase IV fluid infusion by 0.5L/m²/day and recheck electrolytes 2-4 hours later.
May also need treatment for hyperkalaemia (K+ >5.5mmol/l)
Other oncology emergencies

Refer to pan-London Paediatric Oncology Shared care guidelines
BSUH Microguide > Paediatrics & Neonatology > Paediatrics > A-Z > O > Oncology guidelines > Supportive Care Protocols

Referral and consultation

Discuss with on-call paediatric/CED consultant
Admit to ward/HDU
Inform POSCU consultant on call
Contact:
  → Paediatric Oncology Registrar on call at RMH (if patient ≥1yr) 020 8642 6011
  → Paediatric haematology registrar at GOSH (if patient <1 year) 020 7405 9200

E-mail referral letter including:
  → Patient demographics & GP details
  → History, examination & information shared with family
  → investigation results
  → Send imaging via IEP (contact PACS Team on 3573 in hours or on call radiographer out of hours)

What should you tell the patient/parents?

Try to give some ‘warning shots’
The child may have leukaemia, a form of childhood cancer
The prognosis is good in most cases
The child will need to be transferred a primary treatment centre (usually Marsden)
In the meantime, the child will need to remain in hospital for supportive care and monitoring
At the primary treatment centre:
  − Bone marrow aspirate under GA to confirm diagnosis
  − When diagnosis has been confirmed, chemotherapy treatment will be initiated at the PTC
  − The child will usually remain an in-patient at the PTC for at least 1 week, before being discharged home or transferred back to RACH
Treatment and supportive care will be delivered at RACH, when possible
USEFUL CONTACT DETAILS

Royal Marsden Hospital
- Switchboard 0208 642 6011
- Paediatric oncology registrar on call: cordless phone 1450 (via switchboard)
- Shared care co-ordinator 020 8915 6248

Great Ormond Street Hospital
- Switchboard 020 7405 9200-paediatric haematology (non-clotting) registrar on call for leukaemia

South Thames Retrieval Service
- 0207 188 5000

Kings College Hospital (acute neurosurgical referrals)
https://nww.ihtl.nhs.uk/neurosurgery/
- 020 3299 9000

University College London Hospital
- 020 3456 7890