Acute leukaemia - suspected

Background information

Acute leukaemia - clinical presentation

History and examination

Investigations

Consider differential diagnoses

Suspected acute leukaemia

Refer to haematology/oncology multidisciplinary team (MDT)

MDT team review

Further investigations

Suspicion of acute promyelocytic leukaemia

Provide patient information

Consider referral to specialist centre

Refer to specialist centre

Suspected acute lymphoblastic leukaemia (ALL)

Suspected acute myeloid leukaemia (AML)

Go to ALL in children - management

Go to AML in children - management

Go to ALL in adults - management

Go to AML in adults - management
1 Background information

Quick info:

Scope:
- assessment and management of acute leukaemias (acute myeloid leukaemia [AML] and acute lymphoblastic leukaemia [ALL]) in children in primary, secondary, and specialist care
- assessment and management of AML in adults in primary, secondary, and specialist care

Out of scope:
- chronic leukaemias and lymphomas
- ALL in adults

Definition:
- AML – type of acute leukaemia in which the white blood cells produced in excess are immature granulocytes or monocytes (types of white blood cells formed from myeloid stem cells):
  - to be called acute, the bone marrow usually must include greater than 20% leukemic blasts
  - acute promyelocytic leukemia (APL) is a subtype of AML and involves different treatment
- ALL – type of acute leukaemia in which the white blood cells produced in excess are immature lymphocytes (white blood cells formed from lymphoid stem cells)

Incidence:
- incidence of acute leukaemia is estimated to be approximately 2400 in adults in England and Wales [1]
- most people with ALL are under age 65 years [1]
- incidence of AML is highest amongst elderly patients [1]
- in the UK, 450 new cases of ALL and 70 new cases of AML are diagnosed annually in children [2]
- peak incidence is age 5 years and under in children with ALL, and age 10 years and over in children with AML [2]

Risk factors associated with AML:
- inherited syndromes:
  - chromosomal imbalances, eg Down’s syndrome
  - chromosomal instability syndromes
  - syndromes of growth and cell survival signalling pathway defects
- acquired syndromes, eg severe aplastic anemia
- myelodysplasia
- myeloproliferative agents
- exposure to:
  - ionizing radiation
  - therapeutic radiation, especially in people exposed to alkylating agents
- chemicals such as:
  - benzene
  - ethylene oxide
  - petroleum products
  - embalmig fluids
  - herbicides and pesticides
- risk of AML/myelodysplastic syndrome (MDS) has been found to increase in patients receiving chemotherapy with granulocyte colony-stimulating factor (G-CSF) support [5]

Risk factors associated with ALL include:
- exposure to:
  - ionizing radiation
  - agricultural chemicals
  - benzene
- chromosomal disorders such as Down’s syndrome
- HTLV-1

Prognosis:
- prognosis is variable and dependent on a number of factors, including [8]:
  - age
  - sex
  - ethnicity
  - laboratory parameters, eg white blood cell (WBC) count, immunophenotype, and karyotype
  - initial response to treatment
- 5 year survival:
  - for children with ALL is 85-90% [2]
  - for children with AML is 60-65% [2]
Acute leukaemia - suspected

• for adults with ALL is 26% [1];
  • however, patients under age 60 years who are treated on clinical trials have a 5 year survival rate of 30-40% [3]
• for adults with AML is 8% [1]
  • however, patients under age 60 years who are treated on clinical trials have a 5 year survival rate of 40-50% [3]
• age-related differences in survival time are particularly marked in AML [1]

NB: This information appears on each page of this care map.

References:

2 Information resources for patients and carers

Quick info:

The following resources have been produced by organisations certified by The Information Standard:
  • 'Acute lymphoblastic leukaemia' (URL) from Bupa at http://bupa.co.uk/
  • 'Acute myeloid leukaemia (AML)' (URL) from Bupa at http://bupa.co.uk/
  • 'Leukaemia - a general overview' (URL) from Bupa at http://bupa.co.uk/
  • 'Acute lymphoblastic leukaemia' (URL) from Cancer Help UK at http://www.cancerhelp.org.uk
  • 'Acute myeloid leukaemia (AML)' (URL) from Cancer Help UK at http://www.cancerhelp.org.uk
  • 'Leukaemia statistics - key facts' (PDF) from Cancer Research UK at http://www.cancerresearchuk.org
  • 'Leukaemias: acute' (URL) from Datapharm at http://www.medguides.medicines.org.uk
  • 'Acute lymphoblastic leukaemia' (URL) from Macmillan Cancer Support at http://www.macmillan.org.uk
  • 'Acute myeloid leukaemia (AML)' (URL) from Macmillan Cancer Support at http://www.macmillan.org.uk
  • 'Acute lymphoblastic leukaemia' (PDF) from Patient UK at http://www.patient.co.uk
  • 'Acute myeloid leukaemia (AML)' (PDF) from Patient UK at http://www.patient.co.uk
  • 'Leukaemia - a general overview' (PDF) from Patient UK at http://www.patient.co.uk

Information for carers and people with disabilities is available at:
  • 'Caring for someone' (URL) from Directgov at http://www.direct.gov.uk
  • 'Disabled people' (URL) from Directgov at http://www.direct.gov.uk

Patient stories describing their care journeys are available at 'Healthtalkonline' (URL) from DIPEX at http://www.healthtalkonline.org

Explanations of clinical laboratory tests used in diagnosis and treatment are available at 'Understanding Your Tests' (URL) from Lab Tests Online-UK at http://www.labtestsonline.org.uk

The Map of Medicine is committed to providing high quality health and social care information for patients and carers. For details on how these resources are identified, please see Map of Medicine Patient and Carer Information.

NB: This information appears on each page of this care map.

3 Updates to this care map

Quick info:
Interim update: 29-Jul-2011

Information added in line with the following reference:

Date of publication: 29-Apr-2011

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Acute leukaemia - suspected

Information added in line with the following references:
Date of publication: 31-Jan-2011

The scope of this care map has been extended to include acute myeloid leukemia in adults.
This care map has been updated with the following guidelines:

Further information was provided by the following references: [3,5,6,15-17]
For more information, please see the care map's Provenance.
NB: This information appears on each page of this care map.

4 Acute leukaemia - clinical presentation

Quick info:
Patients presenting as emergencies [1]:
• likely to have acute infections
• the disease is usually diagnosed by a blood test at the time of admission

Acute leukaemia may present with the following signs or symptoms [1]:
• anaemia
• breathlessness
• unexpected bruising/petechiae
• recurrent infections
• persistent bone pain
• generalised symptoms, eg:
  • fatigue
  • bleeding

Reference:

5 History and examination

Quick info:
Enquire about the following:
• fatigue
• unexplained irritability
• unexplained fever
• night sweats
• unexplained bleeding/petechiae
• persistent or unexplained bone pain
• persistent or recurrent upper respiratory tract infections
• persistent or unexplained limp

Clinical examination may reveal:
• pallor
• lymphadenopathy
• hepatosplenomegaly
• petechiae or ecchymosis
• focal neurological signs
• abdominal or testicular masses
• skin infiltrations
• unexplained bruising
Acute leukaemia - suspected

- gum hypertrophy or bleeding
- skin lesions suggestive of skin deposits

Central nervous system (CNS) involvement is rare at presentation; signs and symptoms of CNS involvement include:
- seizures
- visual disturbances
- headaches
- mental changes
- unilateral sensorineural deafness
- signs of increased intracranial pressure (ICP) (headache, vomiting)
- cranial nerve palsy

This information was drawn from the following references:

6 Investigations

Quick info:
Consider all the following:
- full blood count (FBC) [10]:
  - in acute leukaemia this will typically show a raised white cell count with low haemoglobin and platelets [3]
- platelets [10]:
  - platelets count is usually low [3]
- chemistry profile [10]:
  - this should include [3]:
    - uric acid
    - calcium and phosphate
    - liver function tests (LFTs)
    - renal screen
    - LDH and immunoglobulins
  - acute Epstein-Barr virus (EBV) infection may also be diagnosed by EBV polymerase chain reaction (PCR) [3]
- coagulation profile [10]
- blood film [1]:
  - usually shows the presence of excess blasts [3]
  - however, in some cases clearly identifiable blasts may not be present, or the white blood cell (WBC) count may even be lower than normal – the only abnormal sign in these cases may be a few atypical cells in the blood film or the presence of leucoerythroblastic features [11]
- erythrocyte sedimentation rate (ESR) [1]
- monospot or Epstein-Barr virus (EBV) IgM [2]
- lactate dehydrogenase (LDH) [2]
- chest X-ray to rule out mediastinal lymphadenopathy [3]

For children with a persistent headache, undertake a neurological examination; if the primary healthcare profession is unable to perform an adequate examination, an urgent referral to a paediatrician should be made [2].

NB: Normal blood count should not be interpreted as definitive evidence that a haematological malignancy is not present [1].

References:

7 RED FLAG!

Quick info:
Urgent referral:
Acute leukaemia - suspected

- patients presenting with any of the following should be referred urgently to the multidisciplinary team (MDT) [1]:
  - blood count/film reported as suggestive of acute leukaemia
  - bone pain associated with anaemia and a raised erythrocyte sedimentation rate (ESR) or plasma viscosity
  - constellation of three or more of the following symptoms:
    - fatigue
    - breathlessness
    - bruising
    - recurrent infections
    - bone pain
    - lymphadenopathy (greater than 1cm) persisting for 6 weeks
    - hepatosplenomegaly
- referral within the MDT should be to a consultant haematologist, or a paediatrician with responsibility for children with acute leukaemia [3]

Immediate referral – those with acute leukaemia discovered by a blood test would normally be admitted to hospital within 24 hours [1]

References:

8 Consider differential diagnoses

Quick info:
Differential diagnoses include:
- chronic leukaemias
- leukemoid reaction to infection
- Epstein-Barr virus (EBV)
- cytomegalovirus
- thrombocytopenic purpura
- solid tumour, particularly neuroblastoma
- parvovirus B19
- severe aplastic anaemia
- myelodysplasia
- lymphoma
- toxoplasmosis
- auto-immune diseases

This information was drawn from the following references:

11 Suspected acute leukaemia

Quick info:
Initial diagnosis is likely to be made by examination of blood films by a local haematologist [1]:
- a member of a leukaemia multidisciplinary team (MDT) should take immediate responsibility for managing any patient who appears to have leukaemia [1]
- this should be a consultant haematologist, or a paediatrician with responsibility for children with acute leukaemia [3]

Typical haematological features of both acute lymphoblastic leukaemia (ALL) and acute myeloid leukaemia (AML) are:
- low haemoglobin [6]
- thrombocytopenia [6]
- neutropenia [2]
Acute leukaemia - suspected

- leukocyte count may be low, normal, or high (although more than 100x10^9/L is unusual) [6]
- blast cells on blood film [6]

NB: Whilst AML and ALL blasts are different morphologically, it is not possible to be certain of the type of leukaemia by morphological examination alone. Any child whose blood count or blood film indicates leukaemia should be referred immediately to a paediatric haemato-oncologist, or alternatively to a paediatrician if the former is not possible [2].

References:

13 MDT team review

Quick info:
An oncologist or haematologist should take immediate responsibility for managing any patient who appears to have leukaemia – in children this should be a paediatric oncologist or haematologist [3]:
- subsequent management will be by the multidisciplinary team (MDT) [1]
- blood specimen should be sent to specialist pathology laboratory for further assessment [1]
- bone marrow samples are likely to be required for precise assessment of the disease [1]
- patients with acute leukaemia are likely to require treatment before a precise diagnosis is available [1]
  - however, management should be discussed at the earliest possible meeting of the leukaemia MDT
- review management when a complete pathological assessment, including molecular analysis, has been carried out

MDT structure:
- MDT should contain enough core members for the following to be present at every meeting [1]:
  - haemato-oncologists (at least two; principally haematologists, some medical oncologists)
  - haemato-pathologist
  - nurses – clinical nurse specialist (CNS) should normally be the initial point of contact for patients who feel they need help in coping with their disease, its treatment, or consequences
  - palliative care specialist (at least one)
  - support staff
- extended team members:
  - clinical member of the transplant team to whom patients could be referred [1]
  - microbiologist [1]
  - pharmacist [1]
  - vascular access specialist [1]
  - state registered dietitian (SRD) [1]
  - clinical oncologist (provision of cranial radiotherapy for patients with acute lymphoblastic leukaemia [ALL] is an important role for a clinical oncologist) [1]
  - laboratory technical staff if appropriate – specifically for immunophenotyping and cytogenetic/molecular laboratories [3]:
    - cytogenetic analysis is important for risk profile and treatment decision
    - cytogenetic results should be available ideally within 1 week
  - haemato-pathologist – to review bone marrow trephines [3]
- other specialists who may be required for specific cases [1]:
  - dermatologist
  - gastroenterologist
  - ENT surgeon
  - interventional radiologist
- support for patients and carers:
  - allied health professionals, including rehabilitation specialists [1]
  - liaison psychiatrist and/or clinical psychologist [1]
  - social worker [1]:
    - specifically for practical issues and advice on disability benefits [3]
  - bereavement counsellor [1]
- for paediatric cases, team should also include [3,18]:
  - key worker
  - nurses from inpatient and day care units
  - play specialist; activity coordinator/youth worker
  - teacher
Acute leukaemia - suspected

• specialist outreach nurse

References:

14 Further investigations

Quick info:

Further investigations for acute leukaemia:
• blood specimen should be sent to specialist pathology laboratory for further assessment [1]
• bone marrow:
  • bone marrow samples are likely to be required for precise assessment of the disease [1]
  • bone marrow with cytogenetics is mandatory for AML [10]

Diagnosis of AML also includes:
• immunophenotyping and cytochemistry [10]
• fluorescent in situ hybridization (FISH) [3]
• evaluations for c-KIT, FLT3-ITD, NPM, and CEBPA mutations [10]
• CT/MRI if neurologic symptoms present [10]
• lumbar puncture – routine in children, consider for adults if symptomatic [3]
• cardiac scan if any of the following are present [10]:
  • prior cardiac history
  • prior anthracycline use
  • clinical symptoms that raise concern about cardiac function
• central venous access device of choice [10]
• HLA typing [10]
• cytogenetics [8]
• flow cytometry [3]

NB: In patients with poor risk factors and no sibling donor, consider early evaluation for alternative donor search [10].

Diagnosis of ALL also includes:
• immunophenotyping [7]
• cytogenetics – assessing for [7]:
  • chromosome number
  • chromosomal translocations
  • intrachromosomal amplification of chromosome 21
  • other molecular genetic abnormalities
  • gene polymorphisms in drug metabolic pathways
• fluorescent in situ hybridization (FISH) [3]
• assessing morphology [7]
• studies for minimal residual disease (MRD) [3]
• molecular studies [3]:
  • BCR ABL
  • MLL
  • TEL AML1

References:

15 Suspicion of acute promyelocytic leukaemia
Quick info:
In patients with clinical and pathologic features of acute promyelocytic leukemia (APL), start all trans-retinoic acid (ATRA) on first suspicion of APL to prevent lethal complication of bleeding [10]:
• APL usually presents with laboratory and clinical features of disseminated intravascular coagulation at the time of diagnosis [3]
• if cytogenetic and molecular testing does not confirm APL, discontinue ATRA [10]
• testing can also be performed by the use of a PML antibody in an immunophenotyping laboratory [3]

Differentiation syndrome [3]:
• can occur in patients with APL who are treated appropriately with ATRA
• presents with symptoms such as fevers and dyspnoea secondary to pulmonary oedema
• more prevalent in patients with a higher presenting white count (greater than 10x10⁹/L) and in patients who do not receive concomitant chemotherapy eg with an anthracycline
• can be prevented or treated with steroids such as dexamethasone
• consider prophylactic dexamethasone especially if presenting white blood cell count is high

References:

16 Provide patient information

Quick info:
Ensure patients receive clear, honest, and consistent information from the outset [1]:
• clinical nurse specialist is crucial in this, but all those involved in caring for the patient should be open and willing to share information
• sensitive communication at the consultation at which patients learn they have cancer is essential:
  • encourage patient to bring a close friend or relative to such consultations
  • consultation should be in a private room with a senior clinician and adequate time for questions
  • clinical nurse specialist should be present during this consultation and should remain with the patient afterwards to offer individualised support and further information
  • offer patients the opportunity to discuss treatment options, and respect their views
• tell patients as early as possible if any of the following are suspected:
  • requirement for successive courses of treatment
  • recovery that entails an extended period of time
• offer patients as much information in an accessible form about their disease and management as they wish to have:
  • offer a record in writing or on audiotape, together with appropriate information leaflets
  • encourage patients to return to MDT members for additional information and clarification as required
  • give patients an outline of their overall treatment plan as soon as possible, together with potential time-scales
  • be clear about the risk that treatment might do more harm than good, and ensure the patient understands when treatment can only be expected to produce temporary remission
• when English is not the patient’s first language, ensure an interpreter is available

Information given to patients should include [1]:
• sufficient information about basic anatomy and pathology for patients and their carers to understand the disease
• the range of individual variation in the impact and rate of progression of the disease
• aims, risks, and likely effects of proposed diagnostic procedures
• balanced information with clear explanations about potential treatment options
• information about other potential effects of the illness and its treatment on both patients and carers, such as anxiety and depression
• reasons for not offering interventions patients might anticipate

NB: A record of the information given to patient, patient preferences for involvement in decisions, and a comprehensive summary of the management plan should be given to the patient’s GP within 24 hours so that primary care staff can provide additional support for patients and carers [1].

Reference:
Acute leukaemia - suspected

Specialist diagnostic services will be required for immunophenotyping, molecular biology, and cytogenetics [1].

Referral to specialist clinical services:

• patients with acute myeloid leukaemia (AML) should be managed at experienced leukaemia centres [10]
• children and adolescents with cancer should be referred to a principal treatment centre for children and young people [3,18]

References:


19 Suspected acute lymphoblastic leukaemia (ALL)

Quick info:
The white blood cells produced in excess are immature lymphocytes [1].

Reference:


20 Suspected acute myeloid leukaemia (AML)

Quick info:
The white blood cells produced in excess are immature granulocytes or monocytes [1].

Reference:

Acute leukaemia - suspected

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The Chief Knowledge Officer of the NHS:

Evidence summary for Acute leukaemia - suspected

This care map has been developed according to the Map of Medicine editorial methodology (http://mapofmedicine.com/whatisatemap/editorialmethodology). The content of this care map is based on high-quality guidelines [1,4,7,8,10,13], and critically appraised meta-analyses and systematic reviews [5,9,11,12,14-17]. Practice-based knowledge has been added by contributors with front-line clinical experience [2,3,6], including any literature endorsed by the contributor group [18].

Search date: Aug-2010

References

This is a list of all the references that have passed critical appraisal for use in the care map Acute leukaemia

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3 Contributors representing the National Cancer Action Team. 2011.
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Acute leukaemia - suspected

ID Reference
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