H.A001 - LYMPHOCYTOSIS, CHRONIC LYMPHOCYTIC LEUKAEMIA (CLL) AND LOW GRADE LYMPHOMA WITH OVERSPILL

What is lymphocytosis?

- Lymphocytosis is a relatively common finding on routine FBCs; in younger patients it is usually transient and reactive; in older patients a persistent lymphocytosis may be due to an underlying lymphoid disorder such as CLL or lymphoma.
- In normal people blood lymphocytes are made of T cells (80%) and B cells (20%); most cases of CLL and NHL with overspill will have too many B cells in the peripheral blood.

What causes a lymphocytosis?

- Non-malignant causes include viral infections such as EBV, CMV, HIV and hepatitis; chronic infection with brucellosis; tuberculosis; syphilis and patients who have had a splenectomy.
- Chronic lymphoproliferative disorders will cause a persistent (>3 months) lymphocytosis which is usually >10 x 10^9/L.

What investigations are required for a persistent lymphocytosis?

Lymphocyte count	**Investigations**
<10 x 10^9/L with no other symptoms or signs	Repeat FBC and Blood film in 3-6 months • **If lymphocytes lower or the same level:** no further tests required • **If lymphocytes are > 10 x10^9/L:** request FBC and blood film and chronic lymphocytosis screen*
>10 x 10^9/L for >3 months and no other cause e.g. hyposplenism, found	FBC and blood film and chronic lymphocytosis screen*
Lymphocytosis **and** unexplained anaemia **or** thrombocytopenia **or** lymphadenopathy **or** splenomegaly	Discuss with/refer to Haematology

***immunophenotyping

What will the results of immunophenotyping tell me?

The immunophenotyping report will usually give you a diagnosis e.g. CLL, low grade lymphoma with overspill, other lymphoproliferative disorder or reactive lymphocytosis (where no clonal population is identified). Further information on CLL and low grade lymphoma with overspill is given on this sheet.

What are CLL and low grade lymphoma with overspill?

- These are low grade B cell lymphoproliferative disorders that behave and are treated in a similar way.
- They are incurable indolent diseases that are often asymptomatic.
- Many patients will remain stable for several years without treatment.
    - Treatment in these disorders is reserved for patients with symptomatic or progressive disease.

How do patients with CLL/ low grade lymphoma with overspill present?

- Incidental finding of lymphocytosis on a routine FBC.
- Lymphadenopathy usually with an associated lymphocytosis.
- Splenomegaly usually with an associated lymphocytosis.
- Anaemia +/- thrombocytopenia with lymphocytosis.
- Patients may or may not have constitutional symptoms such as weight loss and night sweats.

How do I monitor a patient with CLL/ low grade lymphoma with overspill?

Not all patients require specialist haematology review and may be adequately monitored in the primary care setting with 6-monthly review or sooner if clinically unwell:

- Clinically look for the development of splenomegaly and lymphadenopathy.
- FBC - looking at the trend in the white cell count (doubling in 6 months) and its effect on Hb and platelets which are more important than the absolute white cell number.
- Patients with a stable lymphocytosis < 10 x 10^9/L could have less frequent monitoring as their risk of significant lymphoproliferative disease is rare.

When should I seek further advice or refer patients with CLL/low grade lymphoma with overspill?

The haematology consultants will be happy to discuss any patient with lymphoproliferative disorders, but recommend referral of patients who present with or develop any of the following:

1. Disease-related symptoms e.g. sweating, weight loss or recurrent infections.
2. Bulky lymphadenopathy.
3. Hepatosplenomegaly.
4. Anaemia, Hb <100 g/L or thrombocytopenia, platelets < 100 x 10^9/l or wbc doubling in <6 months. **N.B**. the lymphocyte count may increase with an infection. Repeat FBC is recommended when infection has settled if isolated increase in lymphocytes.

What other precautions do I need to take in patients with CLL/low grade lymphoma with overspill?

Patients with low grade lymphoproliferative disorders are immunosuppressed and they should.

- CLL patients are in the 'clinically extremely vulnerable' group regardless of their stage of CLL.
- CLL patients are at increased risk of mortality from invasive pneumococcal infection. In line with the updated Department of Health recommendations, CLL patients should receive the pneumococcal conjugate vaccine (Prevenar® (PPV13)) followed by the pneumococcal polysaccharide vaccine (PPV23, Pneumovax II®) at least two months later. Pneumococcal polysaccharide vaccination should be repeated at five yearly intervals.
- Patients who have been previously vaccinated with pneumococcal vaccine only (PPV23 Pneumovax II®), should receive a "catch up" dose of the pneumococcal conjugate vaccine (PCV13, Prevnar®)
- CLL patients should receive the Hib vaccination and annual season flu and COVID-19 vaccines.
- CLL patients should **NOT receive live or attenuated (weakened) viruses.** These include yellow fever, oral polio, measles, mumps and rubella (MMR) and the live shingles vaccine (Zostavax). Please be aware of vaccination requirement if the patient is seeking to travel abroad and avoid live vaccination.
- Have shingles treated with antiviral drugs. CLL patients should receive the non-live (Shingrix) shingles vaccine if eligible (currently guidance >50 years old). If a patient has a history of

shingles, then they should still receive lifelong Aciclovir as secondary prophylaxis in addition to the Shingrix vaccine.
- The RSV vaccine is now included in the vaccination programme for those aged 75-79 and is safe for those with CLL to have it.
- Have bacterial infections treated promptly.
- There is also a risk of developing a second malignancy – smoking cessation should be encouraged.
- CLL patients are at increased risk of UV-related skin damage and skin cancers. CLL patients should be encouraged to wear sunscreen daily with at least a SPF30 and a 5-star UVA rating.

Information for patients

CLL information http://www.macmillan.org.uk/information-and-support/leukaemia/chronic-lymphocytic.
CLL support association website **www.cllsupport.org.uk**

References

BSCH Guidelines on the diagnosis and management of chronic lymphocytic leukaemia.
BCSH Guideline: Guidelines on the investigation and management of Chronic Lymphocytic Leukaemia published 2012.
Diagnostic criteria for monoclonal B-cell lymphocytosis. *BJ Haem 2005 130(3):325-32*
NSSG – L.68 v8.1 - CLLinformation for GPs on managing and supporting patients living well with high-count Monoclonal B-cell Lymphocytosis or CLL R

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