RELAPSED ACUTE LYMPHOBLASTIC LEUKAEMIA DIAGNOSED USING FEMORAL HEAD HISTOLOGY

Dr Jennifer Ryan (Haematology Registrar), Dr Emily Chernucha (Haematology Registrar), Dr Andrew McMillan (Haematology Consultant)

BACKGROUND

With modern therapies, many patients diagnosed with acute lymphoblastic leukaemia (ALL) achieve remission. Unfortunately a proportion of these will relapse, with results from the international MRC UKALL XII/ECOG2993 trial[1] showing that 50% of under 55s and 60% of over 55s relapse following first remission. Relapsed ALL presenting with extramedullary disease has been rarely reported, with 10-16% of patients having extramedullary relapse with or without bone marrow involvement[1,2]

Avascular necrosis is a recognised complication of ALL treatment relating to factors such as bone perfusion, toxic effects of chemotherapy and repeated courses of high dose steroids. Roughly 4% patients treated on MRC UKALL XII/ECOG2993 trial developed avascular necrosis[3]. Avascular necrosis is most commonly treated with joint replacement surgery.

Recently at Nottingham University Hospitals, we have diagnosed three patients with relapsed ALL from femoral head histology following joint replacement for avascular necrosis of the femoral head.

Case Number	**1**	**2**	**3**
Age and Gender	21F	51M	22M
Initial Diagnosis	Philadelphia negative Precursor B-ALL	Philadelphia negative precursor B-ALL	Philadelphia negative T-ALL complicated by Hepatitis C
Initial Treatment	UKALL2011 (on trial)	UKALL14 trial, including allogenic stem cell transplant from a sibling. Remission was achieved, but relapsed disease was found on routine bone marrow biopsy after 9 months. The patient was re-treated with FLAG-IDA, Inotuzumab and Gemtuzumab	UKALL 11 protocol(off trial). Remission was achieved, however relapsed disease with spinal cord compression 8 months after maintenance therapy. Re-treated with Nelarabine, Cyclophosphamide and Etoposide, followed by autologous stem cell transplant.
Disease Status Post Treatment	Remission	Second Remission	Second Remission
Duration to Relapse	14 months	3 years	20 months
Procedure	Total hip replacement for avascular necrosis	Total hip replacement for avascular necrosis	Total hip replacement for avascular necrosis
Blood tests at time of relapse	FBC stable	FBC normal, donor chimerism 100%	Longstanding stable thrombocytopaenia
Histology; Femoral Head	interstitial infiltrate of lymphoblasts; immunophenotyping consistent with B-ALL.	replacement of the medullary cavity with necrotic tumour; immunophentyping consistent with B-ALL.	Femoral head histology showed sheets of small lymphoid blast cells; immunophenotyping consistent with T-ALL
Histology; Bone Marrow	Relapsed B-ALL	Negative for ALL. Multiple areas of active disease on PET-CT	Consistent with T-ALL
Subsequent Treatment	FLAG-IDA, followed by Blinatumumab due to ongoing minimal residual disease (MRD) positivity, before an allogenic stem cell transplant from a matched unrelated donor.	Localised radiotherapy to focal areas of disease. Regular bone marrow monitoring	Nelarabine, Cyclophosphamide and Etoposide with high dose Methotrexate.
Current Disease status	Remission	Active disease on PET-CT, no haematological relapse	Awaiting allogenic stem cell transplant.

LEARNING POINTS

From literature there are only a few case reports of relapsed ALL presenting in this manner and the definitive number of patients with evidence of disease in the femoral head is unknown. **We would recommend as a result of our experience always sending bone specimens for histology in patients with a history of ALL undergoing joint replacement surgery.**

Each patient in this case series had a stable full blood count at the time of diagnosis of relapse. This highlights a possible opportunity to recognise relapse earlier, although relapsed disease remains a therapeutic challenge.

REFERENCES

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[3] Patel B, et al. High Incidence of avascular necrosis in adolescents with acute lymphoblastic leukaemia: a UKALL XII analysis. Leukaemia 2008; 22: 308-312

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ALL and AML

Jennifer Ryan

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