CASE REPORT

Precursor B cell lymphoblastic lymphoma presenting as periorbital swelling

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SUMMARY

An 11-year-old girl was admitted for further investigation as to the cause of her bilateral papilloedema and periorbital swelling. She had a 2-week history of headache and unilateral eyelid swelling, and a 2-day history of right-sided groin swelling. CT and MRI scans revealed soft tissue adjacent to the lateral orbital walls within the extraconal lateral aspects of both orbits, more on the right than the left. The scans also revealed extensive lymphadenopathy above and below the diaphragm. The patient underwent bone marrow studies and biopsy of the lymph node in her groin. The results revealed normal bone marrow with no evidence of malignancy. The lymph node histology confirmed malignant lymphoma in keeping with B cell lymphoblastic lymphoma. The patient was started on the UKALL 2011 chemotherapy trial.

BACKGROUND

Lymphoblastic lymphoma (LBL) is a rare subtype of non-Hodgkin's lymphoma, more common in children than in adults. This case describes the rare presentation of precursor B cell lymphoma presenting as an orbital soft tissue swelling.

CASE PRESENTATION

A 11-year-old girl initially attended her local optometrist due to a 2-week history of headaches. The optometrist had noted bilateral optic disc

swelling, with the left worse than the right, and flame haemorrhages, and had referred the girl to ophthalmology. Visual acuity was noted to be normal. The ophthalmologist agreed with this assessment but also noted swelling and bruising of the right lower lid (figure 1A, B) and a history of left groin swelling. Owing to these findings, the girl was admitted under the care of the general paediatric team at the regional tertiary hospital, for further investigation.

The headache was described as a band-like frontal headache, worse over the right temporal area, and had been present for 2 weeks. There was no history of trauma, migraine, balance problems or nausea and vomiting. The headache never woke her from sleep nor did it cause visual disturbance. It was most severe around midday, and exacerbated by bright lights. She found relief on lying flat and with simple analgesics.

The right eye swelling and bruising was noted to have slowly progressed over a 2-week period but was non-tender. The girl had lost some weight as her school skirt was looser than normal, although she was unable to quantify this. There was also a 2-day history of painful right groin swelling. There was no history of night sweats, fever, petechiae or other bruising.

Medical history consisted of a benign thyroglossal cyst, which had been removed 2 years earlier, and bilateral fractures to her radius following a fall

Figure 1 (A and B) Swelling and bruising of the right eye.

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Table 1 Initial presenting bloods

Test	Result	Reference range
Haemoglobin	127 g/L	115–155
White cell count	$4.3 \times 10^9/\text{L}$	5–13
Neutrophils	$2 \times 10^9/\text{L}$	2–8
Platelets	$158 \times 10^9/\text{L}$	170–450
Lactate dehydrogenase	1407 U/L	135–214
Sodium	139 mmol/L	135–145
Potassium	3.9 mmol/L	3.5–5.3
Chloride	102 mmol/L	95–108
Urea	3.6 mmol/L	2.5–7.8
Creatinine	55 $\mu\text{mol/L}$	40–110
Phosphate	1.6 mmol/L	0.8–1.5
Adjusted calcium	2.46 mmol/L	2.2–2.6
Total bilirubin	10 $\mu\text{mol/L}$	<21
Alkaline phosphatase	139 U/L	200–495
Aspartate aminotransferase	136 U/L	5–40
γ -Glutamyl transferase	12 U/L	6–42
Alanine aminotransferase	148 U/L	4–33
Albumin	45 g/L	35–50
No blasts were seen on the blood film		

3 months prior to this presentation. She was otherwise fit and healthy, and took no regular medications.

Examination demonstrated a 6×4 cm mass palpable in the right inguinal region and a right palpable supraclavicular node. Neither obvious hepatosplenomegaly nor other lymphadenopathy was palpable. Peripheral and cranial nerve examinations were unremarkable apart from the ophthalmology examination, as documented earlier.

The following day she was referred to the oncology team, for further investigation.

INVESTIGATIONS

Initial presenting bloods are shown in [table 1](#).

Ultrasound imaging demonstrated multiple lymph nodes present above and below the diaphragm as well as an enlarged spleen. The liver, gallbladder and kidneys were reported as normal.

Chest X-ray showed a soft tissue mass in the upper left mid mediastina region around the aortic arch, suggestive of lymphadenopathy. There was further soft tissue thickening noted in the left lower paraspinal region.

MRI of the head and spine showed no brain parenchymal abnormality. There was enhancing extraconal soft tissue within

Figure 2 (A and B) Coronal and axial MRI showing enhancing extraconal soft tissue within the lateral and superolateral right and left orbits bilaterally.

Figure 3 (A and B) Resolution of the right eye swelling and bruising.

the lateral and superolateral right and left orbits bilaterally adjacent to the bony wall, which abutted the lacrimal gland (figure 2A, B). No intraconal mass lesion was noted and the globes were normal. Additionally, there was an extradural soft tissue mass lesion noted dorsally at T11-12, which measured 2.6 cm in craniocaudal dimensions, and the suspicion of bony infiltration of the T12 vertebral body.

A CT of the neck, chest, abdomen and pelvis demonstrated prominent cervical, axillary, mediastinal, retroperitoneal and inguinal lymphadenopathy, consistent with the ultrasound. Neither lung parenchymal abnormality nor abnormal air space opacification was detected, and the remaining upper abdominal solid viscera appeared normal.

DIFFERENTIAL DIAGNOSIS

Leukaemia and lymphoma were considered the most likely differentials. In order to confirm the diagnosis, bone marrow aspiration and trephine were performed for morphology, cytogenetics and flow cytometry. Biopsy of the right inguinal node was also undertaken. Lumbar puncture to assess for central nervous system involvement was deferred initially in order to prevent possible systemic spread, and was performed once diagnosis and treatment had been decided.

The bone marrow trephine showed normal bone marrow morphology with no evidence of malignancy. Lymph node biopsy on histological examination showed malignant lymphoma with histomorphological appearances in keeping with B cell LBL, as flow cytometry was positive for CD79a, CD10, TdT and PAX-5. Cytogenetics of the lymph node were reported as normal. When cerebrospinal fluid was obtained postdiagnosis on starting of intrathecal chemotherapy, there was no evidence of central nervous system involvement.

TREATMENT

These results were consistent with a diagnosis of precursor B cell LBL. The patient was eligible and consented to treatment in the UKALL 2011 trial. The UKALL 2011 trial looks to improve the outcomes in children with leukaemia and lymphoma. All patients with precursor B cell LBL are treated as being high risk, according to the National Cancer Institute, and started on regimen B induction of the UKALL 2011 trial. Patients are started on a course of dexamethasone as well as a four-drug induction consisting of intrathecal methotrexate, intramuscular peg-asparaginase intravenous daunorubicin and vincristine. At the end of this 4-week induction phase, mercaptopurine is started orally. Further treatment is based on response to this initial induction phase.

Common short-term side effects of the chemotherapy include immunosuppression leading to infection, hair loss, constipation, rashes, mouth ulcers, lethargy, nausea and vomiting, and increased risk of bruising and bleeding from bone marrow suppression. Long-term side effects include possible infertility and cardiac problems associated with anthracyclines.

In the UKALL 2011 trial treatment, success in LBL is based on initial assessment of primary tumour mass at diagnosis and then repeat imaging at the end of induction, using the same scanning modalities to assess the percentage of tumour volume reduction. Patients who have a 35% or more reduction in tumour mass at the end of the induction are considered to be in remission and these patients continue on to regimen B postinduction therapy. Those with <35% mass reduction in tumour are considered to be poor responders and taken off protocol treatment. In comparison, treatment outcomes for patients with leukaemia treated within the UKALL trial have response to

induction treatment based on the amount of minimal residual disease within their bone marrow.

OUTCOME AND FOLLOW-UP

The patient has completed the induction phase of chemotherapy and clinically there appears to be resolution of the eyelid swelling and bruising (figure 3A, B) as well as the palpable right inguinal mass. Follow-up MRI showed a marked response to treatment. Lymphadenopathy and extraconal disease noted earlier have resolved. The globes, optic nerves and other orbital structures appear to be normal.

CT of the chest, abdomen and pelvis showed an adequate response to clinical treatment. No significantly enlarged lymph nodes remain in the mediastinum or in either the hilum or axillae. There is residual right pelvic adenopathy and small volume para-aortic/retrocaval nodes remain.

Given the above scan results, the patient was considered to have had a more than 35% volume reduction in her tumour

Patient's perspective

In September 2015, I started year 8 at my new school. After a few weeks I started having really bad headaches and I was feeling a bit more tired than usual. I didn't really want to do anything, not even my homework. Mum was giving me Calpol for the headaches but it didn't really help and she put the tiredness down to longer days at my new school. Then one day at school, after being out on the cricket pitches, my friends noticed that my right eye was all puffy and swollen. I didn't feel anything because it wasn't sore, but the teacher sent me to see the school nurse. She looked at it and told me to tell Mum to take me to the chemist for some eye drops as she thought there might have been an infection in it. Mum gave me some antihistamine, which seemed to help for a few days, but then my left eye started to go puffy as well, and both of them started to go black and looked as if they were badly bruised, but they still weren't sore. Because the headaches were not getting any better, Mum took me to the optician to have my eyesight tested. My eyesight was fine but the optician noticed that, behind my right eye, the optic nerves were swollen, so he referred me to the RVH eye clinic a few days later. The next night at home, the top of my right leg in my groin area started to hurt a little and I had a strange burning sensation in it. The next morning when I awoke, there was a huge lump at the top of my right leg; it wasn't sore at all. When we went to the eye clinic, the doctor put some horrible drops in my eyes, which I didn't like. Then they took some pictures of my eyes and saw what the optician had seen, and because of the lump on my leg, they referred me to the Children's Hospital. I stayed in the hospital for a week, and had loads of tests and scans performed, including blood tests, CT scans, ultrasound scans, MRI scans, lumbar puncture tests and a biopsy of the lump in my leg. I was a bit scared going to theatre the first time for the lumbar puncture, but it was ok. It wasn't painful and neither were any of the other tests. After all these tests, the doctors were able to find out what was wrong with me and explained everything to me. The doctors and nurses were all very good at explaining everything that was going to happen to me over the next few months. I was ok really, because I knew it was all to make me better. As long as it doesn't hurt me too much I am ok with it, although I don't really like needles, but I am getting better, I think!

mass and was therefore able to continue on with regimen B postinduction therapy. This consists of intrathecal methotrexate, intravenous cyclophosphamide and cytarabine, and oral mercaptopurine.

DISCUSSION

Lymphoma accounts for 11% of all childhood malignancies.¹ LBL is rare and represents only 2% of all non-Hodgkin's lymphomas.² It predominantly affects children and teenagers, and is subdivided into B cell and T cell lineages of which B is the least common, accounting for ~10% of cases.³ The median age of diagnosis in precursor B cell LBL is 8 years and there is no difference in gender distribution.⁴ T cell LBL commonly presents with a mediastinal mass in comparison with precursor B cell LBL, in which the skin, head, neck, bone and lymph nodes are mainly involved.^{5 6}

In children, ocular involvement in cases of lymphoma is extremely rare when compared with that in adults. This has been documented by Ferry *et al*,⁷ who reviewed 353 cases of lymphoma of the ocular adnexa and noted only five paediatric patients, of which one of these five had precursor B cell LBL. Ocular involvement in precursor B cell LBL in children has been reported in only a few cases.⁷⁻¹¹

LBL and acute lymphoblastic leukaemia (ALL) are morphologically indistinguishable. They both derive from precursor B cells and precursor T cells. Traditionally, they have been differentiated from each other based on the percentage of blasts in the bone marrow and peripheral blood. LBL is diagnosed when there is a mass lesion, and <25% bone marrow blasts and <10% blasts in the peripheral blood. Our patient had normal bone marrow and blood film. In 2008, the WHO classified LBL and lymphoblastic leukaemia as the same disease.¹²

Learning points

- This case highlights the need to be vigilant to unusual presentations of lymphoma in children. It shows the rarity of precursor B cell lymphoblastic lymphoma (LBL) and its morphological similarities to acute lymphoblastic leukaemia.
- It rarely presents with ocular involvement in children.
- Precursor B cell LBL is an uncommon cause of non-Hodgkin's lymphoma.
- LBL and lymphoblastic leukaemia are classified as the same disease as they are morphologically indistinguishable, and therefore have similar treatment regimens.

The treatment of LBL has been revolutionised over the past 20–30 years because of the use of successful treatment strategies derived from regimens designed for children with high-risk ALL. As a result, event-free survival has increased significantly. Most successful treatment strategies for advanced-stage paediatric LBL are derived from regimens designed for children with high-risk ALL as described above.¹³⁻¹⁶

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 National Registry of Childhood Tumours/Childhood Cancer Research Group. <http://www.ccrq.ox.ac.uk/datasets/registrations.shtml>
- 2 The Non Hodgkin's Lymphoma Classification Project. A clinical evaluation of the International Lymphoma Study Group classification of non Hodgkin's lymphoma. *Blood* 1997;89:3909–18.
- 3 Knowles DM. Lymphoblastic Lymphoma. In: Knowles DM, ed. *Neoplastic hematopathology*, 2nd edn. Philadelphia: Lippincott Williams and Wilkins, 2001:915–52.
- 4 Burkhardt B, Zimmermann M, Oschlies I. The impact of age and gender on biology, clinical features and treatment outcome of non-Hodgkin lymphoma in childhood and adolescence. *Br J Haematol* 2005;131:39–49.
- 5 Millot F, Robert A, Bertrand Y, *et al*. For the Children's Leukemia Cooperative Group of the European Organization of Research and Treatment of Cancer (EORTC). Cutaneous involvement in children with acute lymphoblastic leukemia or lymphoblastic lymphoma. *Pediatrics* 1997;100:60–4.
- 6 Grümayer ER, Ladenstein RL, Slavc I, *et al*. B-cell differentiation pattern of cutaneous lymphomas in infancy and childhood. *Cancer* 1988;61:303–8.
- 7 Ferry JA, Fung CY, Zukerberg L, *et al*. Lymphoma of the ocular adnexa: a study of 353 cases. *Am J Surg Pathol* 2007;31:170–84.
- 8 Chou YC, Shih IH, Yang CP, *et al*. Concurrent mycosis fungoides and precursor B cell lymphoblastic lymphoma in a 6-year-old child. *Pediatr Dermatol* 2005;22:23–5.
- 9 Kahwash SB, Qualman SJ. Cutaneous lymphoblastic lymphoma in children: report of six cases with precursor B-cell lineage. *Pediatr Dev Pathol* 2002;5:45–53.
- 10 Alford MA, Nerad JA, Conlan MR, *et al*. Precursor B-cell lymphoblastic lymphoma presenting as an orbital mass. *Orbit* 1999;18:17–24.
- 11 Faridpooya K, Mulder MMS, Merks JHM, *et al*. Precursor B lymphoblastic lymphoma of the orbit in a child: an unusual presentation of a non-Hodgkin lymphoma. *Orbit* 2006;25:153–7.
- 12 Swerdlow SH, Campo E, Harris NL, *et al*, eds. *WHO classification of tumours of haematopoietic and lymphoid tissues*, 4th edn. Lyon, France: International Agency for Research on Cancer, 2008.
- 13 Reiter A, Schrappe M, Ludwig WD, *et al*. Intensive ALL-type therapy without local radiotherapy provides a 90% event-free survival for children with T-cell lymphoblastic lymphoma: a BFM group report. *Blood* 2000;95:416–21.
- 14 Patte C, Kalifa C, Flamant F, *et al*. Results of the LMT81 protocol, a modified LSA2L2 protocol with high dose methotrexate, on 84 children with non-B-cell (lymphoblastic) lymphoma. *Med Pediatr Oncol* 1992;20:105–13.
- 15 Anderson JR, Jenkin RD, Wilson JF, *et al*. Long-term follow-up of patients treated with COMP or LSA2L2 therapy for childhood non-Hodgkin's lymphoma: a report of CCG-551 from the Children's Cancer Group. *J Clin Oncol* 1993;11:1024–32.
- 16 Goldberg JM, Silverman LB, Levy DE, *et al*. Childhood T-cell acute lymphoblastic leukemia: the Dana-Farber Cancer Institute acute lymphoblastic leukemia consortium experience. *J Clin Oncol* 2003;21:3616–22.

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