CASE REPORT

Neonatal acute lymphocytic leukaemia: an unusual presentation of a rare disease

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SUMMARY

Infantile acute lymphocytic leukaemia (ALL) seldom presents within the first month of life. Most are diagnosed before birth. Postnatal diagnoses are easily recognisable when characteristic features are present, namely hepatosplenomegaly, leukaemia cutis or infiltrative disease of the extramedullary and central nervous system. However, some children present with vague and non-specific symptoms masquerading as other diseases. We report an unusual presentation of infantile ALL in a 19-day-old infant, who struggled with feeding after a diagnosis of gastro-oesophageal reflux disease since birth. To the best of our knowledge, this is the youngest case report of neonatal ALL, presenting with vomiting, lethargy and dehydration. The neonate presented to our paediatric assessment unit acutely due to progression of her symptoms. General physical examination was unremarkable apart from signs of lethargy and dehydration. Blood investigation revealed an incidental finding of high white cells, including 90% blast cells. Early diagnosis in this case meant early treatment and a good prognosis.

BACKGROUND

Infantile acute lymphocytic leukaemia (ALL) is a rare disease process that rarely presents within the first month of life.¹ The reported incidence of infant ALL was about 4.7 cases per million live births in the UK between 1997 and 2007.² Other studies have reported infant ALL as 2.5–5% of total paediatric ALL.^{3–4} Most literature report a higher incidence of lymphocytic proliferation than myelocytic proliferation during this period. The youngest presenting case report to date, excluding cases presenting at birth, was a 3-week old neonate.⁵

Early diagnosis is important to ensure the best possible prognosis. The main clinical features of infantile ALL in published clinical studies to date include hepatosplenomegaly in 80% of patients,^{6–7} leukaemia cutis found in 60%^{6–8} extramedullary infiltration, and CNS infiltration which presents in more than a third of patients.⁹ Leukaemia cutis has been the presenting feature in about half of the cases.^{8–10} Table 1 shows the common clinical features of neonatal ALL and the likelihood of these signs occurring.

We present a 19-day-old infant, who is one of the youngest patients with ALL to date, with non-specific presenting symptoms of feeding intolerance and slow weight gain. She was previously treated for gastro-oesophageal reflux disease (GORD). A high index of suspicion and early diagnosis in

this case has ensured excellent prognosis and treatment outcome in this child.

CASE PRESENTATION

A female infant was referred by the general practitioner (GP) to a district general paediatric assessment unit (PAU) at 19-days of life. She was reviewed for poor feeding and increased vomiting over the past 3 days. Her antenatal history was unremarkable, apart from a longer than expected fundosymphyseal length from 28 weeks gestation and increased abdominal circumference from 35 weeks gestation. She was born at term via normal delivery to healthy and non-consanguineous parents.

Within the first few days of life, she had back arching during feeding and posset vomits post feeds. These symptoms were worse on lying down and improved when sitting upright. She was seen by the GP who had started her on gaviscon, which initially helped with her symptoms.

Her vomiting, however, had been worsening, especially over the preceding 3 days before her admission. On the day of admission, she was refusing her feeds and had a reduced urine output. Her parents felt that she was in pain but were unable to ascertain the cause of her distress.

A detailed paediatric clinical assessment at PAU was unyielding. She remained alert and active. Her observations were within normal limits. Her capillary blood gas was normal. She had regained her birth weight, and had continued to increase in weight. However, during her admission, it was evident that she was not tolerating feeds. She continued to vomit on reduced volume (120 mL/kg/day) and two hourly interval bottle feeding.

On further reassessment, the patient was admitted to the paediatric ward for a further workup to exclude pyloric stenosis and urinary tract infection. Routine bloods were sent for analysis and the infant was kept nil by mouth on intravenous fluids. The full blood count revealed a raised white cell count (WCC) of 97×10^9 cells (90% blast cells);

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Table 1 Most common clinical features of neonatal ALL

Clinical feature	Percentage of occurrences
Hepatosplenomegaly	80
Leukaemia cutis	60
Extramedullary and CNS infiltration	30

ALL, acute lymphocytic leukaemia; CNS, central nervous system.

this result was confirmed through a repeat sample. The diagnosis of neonatal ALL was later confirmed via bone marrow aspiration and phenotype.

INVESTIGATIONS

The pinnacle changing point of this case was the first-line investigations that were carried out on admission. Our patient was not biochemically dehydrated with sodium 137 mmol/L, urea 1.3 mmol/L and creatinine 30 μ mol/L. The full blood count was significantly abnormal with a WCC of 97×10^9 cells (90% blasts), a normal haemoglobin (144 g/L) and a normal platelet count (262×10^9 /L). These results were confirmed by a repeat sample and blood film. Further investigations at the tertiary paediatric oncology unit, including bone marrow analysis and phenotype, confirmed the diagnosis of ALL.

DIFFERENTIAL DIAGNOSIS

Vomiting and failure to thrive in the neonatal period is a common presentation to general paediatric departments and will initiate a number of differential diagnoses that need to be investigated.¹¹ The initial diagnoses are based on the following criteria:

1. Is the volume of feed too much for the neonate?
2. Is there a problem with the motility of the food through the gastrointestinal tract?
3. Are there concerns of infection or systemic disease?

The calculated volume of milk to ensure a bottle feeding neonate gains adequate weight is normally 150 mL/kg/day. A detailed history from parents and feeding observations are useful clues to diagnosis. Our patient was not able to tolerate 120 mL/kg/day of feed.

The motility of the gastroenterological systems can be assessed by the nature of the vomit, that is, milky vomits being a problem proximal to the bile duct, and bilious vomits being distal to the bile duct.¹² Our most common differential is GORD due to an immature oesophageal sphincter.¹³ This was assessed in our patient through monitoring of feeds and watching for related symptoms. An important differential considered in our patient was an early evolving pyloric stenosis. The blood gas result in our patient was not typical of pyloric stenosis. An abdominal ultrasound scan remains the recommended investigation for pyloric stenosis.

In parallel to investigating the aetiology of her vomiting, our main concern in this infant was an underlying systemic illness and clinical dehydration from decreased fluid intake. Routine serology was therefore taken for haematology and biochemistry assessment, which showed a raised WCC of 97×10^9 cells with 90% blast cells on the blood film.

TREATMENT

The patient was discussed and transferred to the tertiary paediatric oncology unit within 8 h of diagnosis for further management. Maintenance intravenous fluids were started to prevent tumour lysis syndrome, which could be precipitated by hyperleucocytosis and dehydration. Antibiotics were started as a precautionary measure. In the oncology department, she received interfant-99 protocol with a positive outcome. There was a marked reduction in the blast cells to normal values.

National guidance for paediatric ALL has been established through a number of clinical randomised trials with the outcome improved to 80–85% event-free survival. The same has not been established with neonatal ALL. The development of treatment protocols for neonatal ALL was first initiated in 1999 through a collaborative study group which aimed to standardise these

protocols in order to improve outcome. The interfant-99 protocol enrolled 17 study groups from 22 countries worldwide and included 482 patients stratified into standard therapy or a hybrid therapy. The interim analysis in May 2004 showed improved event-free survival and survival at 2 years. Further reports in 2007 showed 58% patients were in complete remission at follow-up (median 38 months) whilst 47% patients were event free at 4 years (SE 2.6, 95% CI 41.9 to 52.1).¹⁴

OUTCOME AND FOLLOW-UP

Her current management has been positive with reduction in the blast cells to normal values. Follow-up is through both the tertiary and local hospitals.

DISCUSSION

Significant vomiting in the neonatal period should always be regarded as a red flag and requires further exploration into the underlying aetiology.¹¹ These non-specific presentations can often be exceptionally difficult to evaluate, as the description of vomiting episodes tends to be inaccurate and subjective. In our case report, the progressive vomiting was associated with her regaining birth weight, which again makes the textbook sinister causes of vomiting unlikely. What did remain consistent and worrying throughout the case was the parental description of 'pain' and heightened anxiety in experienced parents.

We performed routine blood investigations to look for an underlying explanation to this presentation. The blood film incidentally revealed a classical pathological picture of infantile ALL with an extremely high WCC and high percentage of blasts. However, without the blood picture, there were no further clinical features of neonatal ALL.

Other cases referenced in the history of the literature are more typical of neonatal ALL, such as a 2-month neonate presenting with leukaemia cutis,¹⁵ and a congenital ALL presenting with antenatal polyhydramnios and hepatomegaly followed by petechiae noted after delivery.¹⁶ In general, congenital leukaemia is found on antenatal scanning through hepatosplenomegaly or secondary to genetic suspicion such as neonates with Down's syndrome.

This case elicits the sensitivity that paediatricians must have in order to detect the subtle signs, which distinguish common conditions from sinister diseases. There were almost no other clinical features suggestive of infantile ALL in our case report. Attending paediatricians had relied on their 'clinical gestalt' and pressed on with a systematic and stepwise approach in investigating for the underlying diagnosis. Although this intuition cannot be totally relied on for diagnosis, it can be important for

Learning points

- ▶ Although infantile acute lymphocytic leukaemia commonly presents with characteristic features of hepatosplenomegaly, leukaemia cutis or infiltrative disease of the extramedullar and central nervous system, and non-specific symptoms are not uncommon.
- ▶ Significant vomiting in the neonatal period should always be regarded as a red flag for further exploration into the underlying aetiology.
- ▶ Parental concerns should be used in conjunction with clinical suspicion or 'clinical gestalt', alerting clinicians to further investigations.

indirect decision-making in incomplete, unorthodox and difficult cases.^{16 17}

We hence conclude that despite its possibility, the most common differential diagnoses should be considered in most neonatal presentations with vomiting and failure to regain birth weight. A high index of suspicion and stepwise approach in management is key to reveal an important diagnosis such as this.

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