1. Introduction

Acute lymphoblastic leukemia (ALL) is the most frequent childhood malignancy. Extramedullary involvement of the kidneys is seen in around 7% when assessed by intravenous pyelography and defined as nephromegaly. When present it seems associated to high white blood cell count [1]. Kidney enlargement has no prognostic value and radiologic examination is not preformed routinely. Interestingly, kidney enlargement is usually not associated with renal function [2]. Acute renal failure (ARF) has a large variety of etiologies but when associated to ALL it is typically due to treatment-induced tumor lysis syndrome. Within the first days after start of chemotherapy biochemical signs of tumor lysis (increase in uric acid, potassium, phosphate, creatinine and blood urea nitrogen, and a decline in calcium) are often present but clinical tumor lysis syndrome is uncommon [3]. Pretreatment spontaneous tumor lysis syndrome is rare in ALL.

We present a boy who was admitted with visual disturbances and developed ARF, hyperuricemia, and bilateral renal enlargement. Both kidneys and bone marrow showed massive lymphoblast infiltration despite normal peripheral blood count except slight anemia. The case underlines the importance of both kidney biopsy and bone marrow aspiration and biopsy in cases of unexplained ARF in children.

2. Case report

A 10-year-old previously healthy Caucasian boy presented with blurred vision, headache, nausea, and vomiting. The symptoms occurred intermittently without circadian variability. The patient had bilateral papilledema. He was pale but otherwise unaffected without enlarged lymph nodes or abdominal organs by palpation. Urinary production was normal. The blood pressure was elevated: 128/91 mmHg. Creatinine 101 μmol/l, urea 6.7 mmol/l, hemoglobin 9.5 g/l, platelets 150 × 10^9/l, white blood cell count 4.5 × 10^9 cells/l, absolute neutrophil count 1.65 × 10^9 cells/l, and lactate dehydrogenase 645 IU/l. Uric acid was 0.97 mmol/l and rasburicase was administered twice, resulting in a rapid decrease (Fig. 1). Urine analysis showed marginal proteinuria of 0.2 g/day. An MRI scan of the cerebrum performed on day 3 showed no signs of malignancies or increased intracranial pressure.

The renal failure progressed reaching a peak creatinine level of 534 μmol/l. An ultrasound of the kidneys and urinary tract showed no signs of obstruction but bilateral diffuse enlargement of the kidneys (16 cm in cranialocaudal length on both sides). A renal biopsy and a bone marrow aspiration and biopsy were performed on the fourth day from admission. The kidney biopsy showed massive infiltration of immature lymphoblasts (Fig. 2). The bone marrow biopsy showed 90% blasts of T-cell lineage (CD3+, CD4+, CD10+, CD117+, CD7+, CD5+, and CD8−). Lumbar puncture showed CNS involvement with 12 × 10^6 cells/l; most of the cells were lymphoblasts.

Treatment was initiated according to the NOPHO-ALL 2008 high-risk protocol. Due to high risk of tumor lysis, treatment was started with low-dose prednisolone alone (Fig. 1). Kidney function improved rapidly following initiation of therapy and dialysis did not become necessary.
The patient responded well to the leukemia treatment and remains in first complete remission three years after diagnosis. No further renal complications have occurred during the course of therapy and kidney size has returned to normal.

3. Literature search

We searched PubMed for case reports up to July 2013 using the search terms “acute renal failure” and “acute lymphoblastic
leukemia”. We limited our search to the Scandinavian languages, German and English. References from papers identified were searched for additional case reports. We used Web of Science to find newer papers that had cited main articles and case stories of this article. We excluded cases of mature B-cell leukemia, patients >19 years at diagnosis, and cases where the presenting symptoms only was related to an abdominal mass.

4. Discussion

This case is unique in many ways. First, as the patient presented early with signs of CNS disease (headache, visual disturbance, and papilledema) we were able to document the progression of ARF that developed within a few days. Second, the ultrasound examination showed nephromegaly and was followed by a kidney biopsy. Third, the patient has been followed at our hospital since the presentation documenting no further renal complications, no relapses and normal renal function as well as normal kidney size.

In a few case reports it is evident that ARF was due to leukemic infiltration. Escobar et al. reported a 6-year-old girl who presented with uremia, slightly elevated lactate dehydrogenase, uric acid level of 11.5 mg/dl (0.68 mmol/l) [4]. The peripheral blood count was normal. The most likely diagnosis was thought to be dehydration and thereby the true diagnosis of T-ALL was delayed. MRI showed massive renal enlargement. Sato et al. reported a 5-year-old boy who presented with facial edema and oliguria [5]. He needed hemodialysis despite normal uric acid level of 5.4 mg/dl (0.32 mmol/l). Bone marrow aspiration later revealed the diagnosis of ALL. Like our patient, both cases had massively enlarged kidneys with severe lymphoblast infiltration. As seen in Fig. 1, administration of prednisolone was in our patients followed by a prompt decrease in creatinine, which must be due to rapid decrease in leukemic infiltration. This is also reflected in the second increase in uric acid level. In a study by Hann et al., the six patients (7%) with a renal size over two standard deviations all had white blood cell counts over 20 x 10^9 cells/l [1]. Interestingly, our patient, as well as the two other cases, had very large kidneys and uremia but normal white blood cell count. The prognostic effect of kidney enlargement at diagnosis of ALL is controversial. However, in children treated with intensive protocols renal failure at diagnosis seems unrelated to prognosis [6].

Uric acid level was high at presentation but not at a level where nephropathy is usually expected. Yet, uric acid increased with creatinine until administration of rasburicase. Whether this increase was enough to cause or contribute to the ARF is uncertain. Comparably, Larsen and Loghman-Adham reported on two girls of eight and six years of age who were both diagnosed with ALL [7]. They presented with high uric acid values, 57.4 mg/dl (3.41 mmol/l) and 59.2 mg/dl (3.52 mmol/l), but normal kidney size. Jones et al. reported three children who presented with hyperuricemia and was diagnosed with T-ALL [8]. Table 1 summarizes previous case reports on acute renal failure as presentation of ALL. In most cases the patients needed dialysis, but no late renal complications were reported in any of the cases. The majority of cases were T-cell ALL with a white blood cell count within normal range.

There are two likely explanations for ARF in our patient. First, interstitial infiltrations of leukemic blasts that caused vascular stasis but did not cause permanent damage to the nephrons. Second, tumor lysis syndrome and acute uric acid nephropathy may also have led to ARF. Moreover, an additive effect of these two causes cannot be ruled out. In conclusion, leukemia should be considered in cases of unexplained progressive ARF with or without hyperuricemia. Bone marrow examination should be performed even when no other objective signs of leukemia are present.

References

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Table 1

| Author | Age | Gender | Presentation | Uric acid (mmol/l) | WBC (10^9/mm³) | Dialysis +/– | Diagnosis |
|---|---|---|---|---|---|---|---|
| Present case | 10 | Male | Headache, nausea, blurred vision | 0.97 | 4.5 | – | T-cell ALL |
| Larsen and Loghman-Adham[7] | 6 | Female | Hematuria and oliguria | 3.41 | 5.8 | + | T-cell ALL |
| Larsen and Loghman-Adham[7] | 6 | Female | Oliguria, nausea | 3.52 | 19.2 | + | T-cell ALL |
| Sato et al.[5] | 5 | Male | Oliguria, edema | 0.32 | 3.2 | + | Pre-B ALL |
| Bunchman et al.[9] | 10 | Female | Malaise, pallor, vomiting | 1.31 | 6.7 | + | Pre-B ALL |
| Jones et al.[8] | 12 | Female | Oliguria, nausea, progressive lethargy | 3.51 | “Normal” | + | T-cell ALL |
| Jones et al.[8] | 12 | Male | Headache, nausea, weight loss | 2.22 | “Normal” | + | T-cell ALL |
| Jones et al.[8] | 13 | Female | Easy bruising, intermittent epistaxis, nausea | 2.95 | 9.3 | + | T-cell ALL |
| Escobar et al.[4] | 6 | Female | Dehydration, anorexia, oliguria | 0.68 | 9.3 | – | T-cell ALL |
| Kobayashi et al.[10] | 5 | Female | Malaise, pallor | 1.78 | 5.1 | + | T-cell ALL |