PROBLEMS IN DIAGNOSIS AND TREATMENT OF ADENINE AND HYPOXANTHINE-
GUANINE PHOSPHORIBOSYLTANSFERASE DEFICIENCY

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Adenine (APRT) and hypoxanthine-guanine (HGPRT) phosphoribosyltransferase deficiency were originally identified in children. The spectrum of manifestations in both is broad with similarities, but also important differences. Both are associated with urinary calculi and can cause severe renal damage. Severe neurological problems are also found in complete HGPRT deficiency but have not been noted in APRT deficiency. We have investigated 2 children presenting in renal failure that emphasise the problems of diagnosis and treatment of these 2 deficiencies and the particular difficulties encountered in the presence of impaired renal function.

PATIENTS

Case 1 (S.B.) A 4-year-old girl was the second child of unrelated healthy parents who lived on vegetarian diets. From 2 years of age she had episodic mild abdominal pain and aged 3 years an isolated occurrence of haematuria. Following a 6 day illness consisting of abdominal pain, vomiting, diarrhoea and increasing drowsiness she became anuric and comatose. On admission she was dehydrated, clinically anaemic, normotensive, deeply comatose but without any focal neurological signs. Serum creatinine was 815 umol/l and urate 0.58 mmol/l. Cerebrospinal fluid was normal and a toxicology screen negative. A C.T. brain scan showed diffuse cerebral oedema. A plain abdominal X-ray revealed no radio opaque calculi and there was no excretion of contrast medium by either kidney. There was no vesico-ureteric reflux on a micturating cystogram. Renal ultrasound demonstrated enlarged kidneys, dilated collecting systems with bright echo clusters casting strong acoustic shadows suggestive of bilateral renal calculi confirmed by retrograde pyelography.
Initial treatment consisted of assisted ventilation, peritoneal dialysis, rehydration and blood transfusion. Consciousness was regained and renal function improved. A renal biopsy (at pyelolithotomy) examined under polarised light demonstrated numerous birefringent crystals suggestive of uric acid. The crystals were in the lumina and epithelial cell cytoplasm of the cortical tubules and also in the interstitium.

The stones and urine were analysed for purine content by methods described previously. The stones were reported to be uric acid by thermogravimetric analysis but spectral analysis showed 2.8 dihydroxyadenine. The urine contained 2.8 dihydroxyadenine, 8-hydroxyadenine and adenine in addition to the normal purines. APRT activity in S.B., the mother and sister was measured in lysed erythrocytes. This was initially raised in S.B. because of the recent blood transfusion but 3 months later was nearly undetectable. The mother had heterozygote levels (25% of normal) but the sister was normal. (Table 1)

Treatment was started with allopurinol (5 mg/kg/24h) and a low purine diet. Urinary purines and allopurinol metabolites were measured to monitor treatment. Aluminium hydroxide was administered to control hyperphosphataemia and co-trimoxazole as a prophylactic urinary antiseptic. Renal function remains impaired (plasma creatinine 160 umol/l) and she has had several episodes of unexplained coma with cerebral oedema since her initial presentation. These have responded to dexamethasone, correction of fluid and electrolyte imbalance and allopurinol. Lack of compliance with allopurinol medication was not confirmed but at least 1 attack of neurological disturbance was linked to excess intake of high purine foods. An adenosine-like substance and other unidentified compounds were found in the urine.

Table 1. APRT Activity In Lysed Erythrocytes (mmol/mg Hb/h)

<table>
<thead>
<tr>
<th></th>
<th>S.B. (7-10 days after blood transfusion)</th>
<th>S.B. (3 months later)</th>
<th>Mother</th>
<th>Sister</th>
<th>Control range</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>11.0</td>
<td>&lt;0.01</td>
<td>5.4</td>
<td>20.0</td>
<td>16-32</td>
</tr>
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</table>

Case 2 (L.W.) A 5-week-old boy was the first child of healthy unrelated parents. From 3 weeks of age he thrived poorly, had feeding difficulties and was extremely irritable. On admission he was markedly irritable and the thumb and first 2 fingers of the right hand were red, swollen and painful. Neurologically he was slightly hypotonic. Plasma creatinine was 350 umol/l and urate disproportionately high at 1.13 mmol/l. Plain abdominal X-ray showed no radio