Case reports


Diabetes insipidus and marked elevation of foetal haemoglobin in a case of acute leukaemia

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Summary

A case of acute myelomonocytic leukaemia is described in which diabetes insipidus was the presenting symptom.

Case report

A 46-year-old man first presented in Iran, in October 1972, with a history of polyuria, anorexia and fever for 2 weeks. He had lost 18 kg weight in the preceding year. On examination he was found to be anaemic (Hb 6·5 g), with hepatomegaly of 3–4 cm and a 'palpable' spleen. The urinary specific gravity was 1·002. Bone marrow at that time showed 'many abnormal cells'. A diagnosis was made of diabetes insipidus secondary to a malignant process and he was treated with 5 i.u. vasopressin tannate nocte with considerable improvement in the polyuria. This was subsequently changed to nasal pitressin t.d.s. in view of increasing pain at injection sites. He was transfused with three units of whole blood and transferred to Hammersmith Hospital for further investigation.

When first seen on 21 November 1972 he was found to have a Hb of 7·8 g, WCC 3000 (30% neutrophils, 20% blasts, 33% lymphocytes, monocytes 9% and eosinophils 8%) and platelets 192,000. Bone marrow showed acute myelomonocytic leukaemia. Alkali denaturation showed 47% resistant Hb; Hb A2 estimation was 1·2% and electrophoresis showed an Hb A/F pattern. The patient was therefore admitted for further investigation.

During the first week in hospital the nasal pitressin was stopped, and his mean urinary output was 6 l/day, average SG 1000 and average osmolality 1·05, and 260 for urine and plasma respectively. Detailed investigation of his hypothalamic-pituitary-adrenal function was carried out. A poor response to intravenous thyroid-releasing hormone was obtained, the TSH values at 0, 20 and 60 min following injection being 1·6, 2·5 and 2·8 μU/ml respectively. There was a normal basal level of luteinizing hormone and follicular stimulating hormone and following intravenous thyroid-releasing hormone was obtained, the TSH values at 0, 20 and 60 min following injection being 1·6, 2·5 and 2·8 μU/ml respectively. There was being 3·8, 22·0 and 28·0 respectively. However, serum FSH levels measured in μU/ml were 4·4, 5·9 and 7·6 respectively showing a poor and slow response of follicular-stimulating hormone. This is in keeping with the 'hypothalamic pattern of response' (Hall.

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tions had with mg chest
fuge preparation. in the patient
insipidus. Following a greater
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steroids and was tests
were steroids
24 hr tests were carried out and both confirmed
the presence of diabetes insipidus. The values on the 8 hr
tests were $U_3 = 90$, $P_3 = 300$; $U_3 = P_3 = 0.3$. $U_3$ represents the urine
passed in the sixth and seventh hours of the 8 hr
deprivation test and $P_3$ is the plasma sample in the mid-point of that period. In the normal person
the urine osmolality should be 600 mosmol/kg or more and the plasma osmolality should not be
greater than 300. The $U_3/P_3$ ratio should be greater than 2 in the normal and less than 1-9 in confirmed
diabetes insipidus. Following exogenous ADH
the patient was able to concentrate his urine normally
on an 8 hr water deprivation test. Radiography of the skull and pituitary fossa was normal as were the chest X-ray and intravenous pyelogram. Brain scan
was normal. Lumbar puncture showed an increase
in monocytes and normal CSF pressure; no
leukaemic cells could be identified on a cytocentrifuge preparation.

Treatment was started with chlorpropamide 250
mg b.d. and the patient subsequently had an average
urinary output of 2 l/day, SG 1-010 and osmolality
of 310.

In the normal individual, Hb F should account
for no more than 1% of the total haemoglobin after
the sixth month of life. In this patient the value of
presentation was 47%, and haemoglobin electrophoresis showed an Hb A and F. The Hb A_f was
reduced, 1-2%. A slight increase in Hb F has been
described previously in acute leukaemia (White,
1972), but to our knowledge the level found in this
case has not been previously described. Following
transfusion with a total of 7 units of blood, the Hb F
level fell to 8-8%. There are three possible explanations
for the marked increase in Hb F. (1) That the
patient had a form of thalassaemia; (2) that he was
heterozygous for the High Fetal gene; and (3) that it
was a consequence of his leukaemia. The first was
excluded by the finding that the relative rates of α
and β chain synthesis measured in his circulating
reticulocytes was 1:03 (normal range 0:95–1:1). The
second possibility was excluded by finding that the
Hb F was heterozygously distributed throughout the
red cells. We conclude therefore that the Hb F was
being synthesized by the same abnormal leukaemic
clon of stem cells. Chemical analysis of the chain is being undertaken.

Acute myelomonocytic leukaemia was diagnosed
on the bone marrow findings which also showed a
blast cell content of 70%. Since the patient was found
to have a high level of cytidine kinase in the bone
marrow cells (Tattersall, 1973) he theoretically
should have responded to cytosine arabinoside by
infusion. However, his blast cell count was 2900/μl
before a 24 infusion of cytosine arabinoside and had
fallen by only 70% (to 850/μl) 48 hr after the infusion
was finished. Because of this failure treatment was
started with the TRAP regimen ($T = $ thioguanine
100 mg/m²/day on days 1–5, p.o. R = rubidyomicin
40 mg/m² on day 1, i.v. A = cytosine arabinoside
100 mg/m²/day on days 1–5, i.v. and $P = $ predni-
solone 30 mg/m²/day on days 1–5, p.o.) (Spiers,
1972). In view of the probable leukaemic involvement
of his hypothalamus, external radiotherapy was
given to the hypothalamic area. Hyperuricaemia was
satisfactorily controlled with allopurinol. This
therapy produced a fall in the circulating blast cell
count, but with the concomitant neutropenia the
patient developed two episodes of pyrexia. The first
of these responded well to antibiotic therapy (Tat-
sersall et al., 1972), no cause for the pyrexia being
found. The second episode was associated with a
perianal abscess and E. coli septicaemia, and
responded well to surgical drainage and antibiotics.
Subsequently the patient developed pulmonary
oedema possibly on the basis of leukaemic infiltrat-
on of his myocardium. Therapy was unsuccessful
and the patient died on January 10, 1973. Permission
for necropsy was refused on religious grounds.

Discussion
Unfortunately, without necropsy the presumptive
toietiology of the diabetes insipidus in this case
could not be substantiated. However, in cases pre-
viously described in the literature (Castaigne and
Hubault, 1953; Eilersen, 1960; Fabiani and Lucent-
tini, 1955; Flynn and Bowes, 1947; Joseph and
Levin, 1956; Laakso, 1964; Malter, Gross and Tere-
ee, 1969; Miller and Campbell, 1971; Roszenzweig
and Kendall, 1966; Camarri and Fantoria, 1972) both
leukaemic deposits (Camarri and Fantoria, 1972) and
haemorrhage (Rosenzweig and Kendall, 1966) have
been found in the region of the hypothalamus.
Haemorrhagic lesions have usually been associated
with low platelet counts at presentation (Laakso,
1964; Roszenzweig and Kendall, 1966) which would
suggest that in this patient who was not thrombocytopenic, the hypothalamic lesion was a deposit. In previously reported cases, diabetes insipidus has been described as a presenting symptom (Joseph and Levin, 1956) and also has occurred during the course of the disease (Laakso, 1964). Most cases have been adults who have all had acute leukaemia and there are a few reports of children having diabetes insipidus as a complication of acute lymphoblastic (Malter et al., 1969) or acute myeloblastic leukaemia (Joseph and Levin, 1956).

No cases found in the literature had a markedly raised Hb F and it seems likely from our studies that this was a consequence of his leukaemia.

References
Fadani, F. & Lucentini, L. (1955) Case of acute hemocytoplastic leukaemia beginning and ending with the complicating disease of diabetes insipidus. Progressive Medicine, 11, 269.

Megaloblastic anaemia associated with the oral contraceptive pill

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Summary
A 27-year-old housewife suffered from severe headaches for a period of 2 years which developed after she started taking an oral contraceptive pill. During this time she gradually developed folic acid deficiency anaemia. This resulted from the inhibition by 'the pill' of the intestinal conjugase system required to deconjugate polyglutamic folate. The patient's headache did not recur after stopping the pill and her anaemia improved with folic acid supplement. The relation between folic acid metabolism and 'the pill' is discussed.

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