effective in saving magnesium when used in conjunction with other diuretics.

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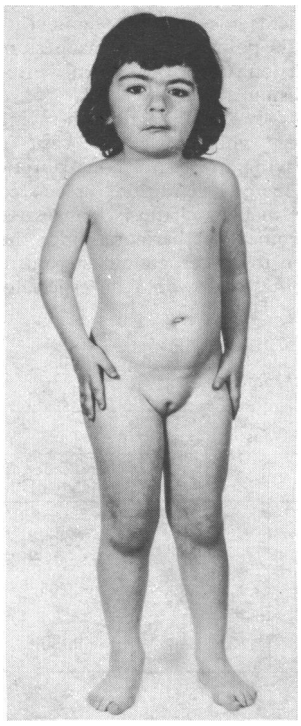
A typical case of Cornelia de Lange's syndrome

The de Lange's syndrome is generally accepted as being characterised by mental retardation associated with a characteristic group of physical malformations. Most cases described have been severely deformed, although many of the physical manifestations may be present in members of the normal population. The presence of severe subnormality has usually been a major factor in making this diagnosis.

Berg *et al*[1] have reported that the large majority have an IQ below 50. In only 15 patients has an IQ of 50 or above been noted, five of these being below 2 years old when assessed. Only two patients with de Lange's syndrome have been reported as having intelligence within normal limits.[2 3] The case reported here represents, therefore, the third published account of a patient with the syndrome having an IQ approaching, if not within, the normal range.

Case history

The girl is the first child of normal, unrelated parents. The father was aged 27 and the mother 29 at the time of her birth. There was no relevant family history. The delivery was full term and normal. The birth weight was 2970 g. She was bottle-fed. The first abnormality was failure to progress with speech. At 3 years 3 months her verbal comprehension level was 2 years 2 months, and expressive language was limited to 10 words. Six months' speech therapy resulted in a three-month equivalent increase in comprehension and her vocabulary expanded greatly. She attended a normal nursery school and is at present at a normal junior school where she has made good progress. At the age of 5 years 1 month she was referred to this hospital for confirmation of the diagnosis.



On examination her height was 0·97 metres, just below the third percentile for her age. Her weight was 16 kg, just above the third percentile, and her head circumference was 45 cm, just over three standard deviations below the mean. She was a dark-haired, attractive child, resembling her father in appearance, and was co-operative but shy. On closer examination she had the characteristic facial features of de Lange's syndrome, with synophrys, antimongoloid slanting eyes, a long philtrum, anteverted nostrils, thin lips turned down at the corners, and "film star" eyelashes. She was hirsute on her arms, legs, and sacrum and had a low hairline. She had short upper arms with increased carrying angle, and extension of the elbows was normal. She had proximally placed thumbs, clinodactyly, syndactyly of the second and third toes, and a single palmar crease on her left hand. Psychological testing with the Stanford-Binet (form L-M) test was as follows: MA=4 years 1 month; IQ=70 (1972 norm); and IQ=78 (1960 norms). The psychologist commented that this may have been an underestimate due to her shyness.

Discussion

In view of the confirmed diagnosis of de Lange's syndrome, the intelligence level of this girl was remarkably high compared with the great majority of cases described in published reports. She was an attractive child and it could well be that there are people with this syndrome in the general population who have not been diagnosed owing to their relatively normal appearance and lack of severe subnormality.

Today clinicians are more aware of this syndrome and are thus more likely to diagnose it when it presents with less dramatic stigmata. We hope the publication of this case will help to avert the distressing experience for other parents of being given an unduly pessimistic prognosis regarding their child's intellectual development, by showing that the diagnosis of de Lange's syndrome may not always be commensurate with a severe degree of subnormality.

I thank the girl's parents, Dr D N Lawson, Dr Valerie Cowie, and Mrs N Scott (principal psychologist) for their permission to publish this case and for all their help.

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Recurrent abruptio placentae treated with the fibrinolytic inhibitor tranexamic acid

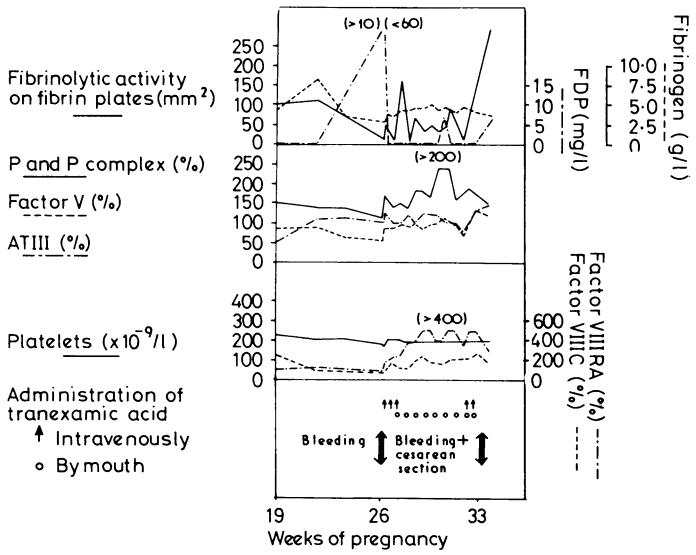
Abruptio placentae occurs in about 0·5% of all deliveries[1]; the risk is even higher in women who have had abruptio once or twice before—17% and 25% respectively.[2] In such cases the coagulation mechanism might be activated by mainly thromboplastic substances from the placenta or by amniotic fluid and the fibrinolytic system by mainly fibrinolytic activators from the endothelium of uterine vessels entering the maternal blood stream.

We describe here a patient whose previous pregnancies had been affected by abruptio placentae and who received a fibrinolytic inhibitor, tranexamic acid, during her third pregnancy.

Case report

This woman's first pregnancy in 1973 resulted in premature delivery with suspected abruptio placentae. The child did not survive. During the second pregnancy in 1974 abruptio placentae was diagnosed. At delivery the blood loss was massive, and the child was stillborn. Fibrinogen concentrations were barely measurable, and fibrinogen-fibrin degradation products (FDP) were found in the serum.

In 1976 the patient became pregnant again and was sent to our hospital in the 26th week of pregnancy. Analysis of the coagulation factors and components of the fibrinolytic system before admission had shown nothing abnormal, but bleeding occurred on the day of admission. Gynaecological and ultrasonic examination suggested abruptio placentae. Laboratory analysis (see figure) showed low concentrations of fibrinogen, factor V, and factor VIII and the presence of FDP. The platelet count and P and P complex (factors II, VII, and X)[3] were normal. The ethanol gelation test gave a negative result. The analysis indicated pathological proteolysis with activation mainly of the fibrinolytic system. The patient was therefore treated with the fibrinolytic inhibitor tranexamic acid (Cyklokapron), which is related to epsilon-aminocaproic acid, in a dose of 1 g intravenously every fourth hour. The bleeding stopped and her coagulation status became normal. After three days of intravenous administration tranexamic acid was given by



Coagulation factors and fibrinolytic components related to the episodes of bleeding and their treatment. FDP = Fibrinogen-fibrin degradation products. P and P complex = Factors II, VII, and X. AT III = Antithrombin III. Factor VIIIC Factor VIII procoagulant activity. Factor VIIIRA = Factor VIII related antigen.

mouth in a dose of 1 g four times a day throughout the rest of the pregnancy.

During the following weeks the patient felt well. Urinary excretion of oestriol and concentrations of human placental lactogen were normal. The growth of the fetus, monitored by ultrasonic examination of the biparietal diameter, was normal.

In the 33rd week minimal bleeding occurred. Oral administration of tranexamic acid was supplemented by intravenous injections of 1 g every four hours, and the bleeding stopped. Because of the risk of heavier bleeding caesarean section was performed at the beginning of the 34th week. The child was a boy and weighed 1430 g. He was awarded an Apgar score of eight points and has apparently been well since birth. Signs of earlier abruptio were found in the placenta as well as a small fresh coagulum.

Comment

Low fibrinogen and factor V concentrations, increased FDP concentrations, normal platelet count and P and P complex, and a negative ethanol gelation reaction indicated pathological proteolysis with activation of mainly the fibrinolytic system.

The cause of abruptio placenta is unknown. The initial bleeding and formation of haematoma will in turn dissect the placenta from the uterine wall and thereby increase the blood loss. As in our patient, plasminogen activators from the uterine wall might also enter the maternal blood stream and enhance the fibrinolytic activity. Intravenous administration of a potent fibrinolytic inhibitor, such as tranexamic acid, probably has two main effects: it stabilises local haemostatic coagula and inhibits the enhanced fibrinolytic activity of the blood. The oral administration probably prevented further bleeding accidents but was not always sufficient, as shown by the second slight bleeding, which was controlled by intravenous infusions of tranexamic acid.

Abruptio placenta is followed by a perinatal mortality of about 35-50%.[1] Treatment with tranexamic acid in cases of abruptio placenta should depress this mortality rate.

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Urinary concentration test with desmopressin

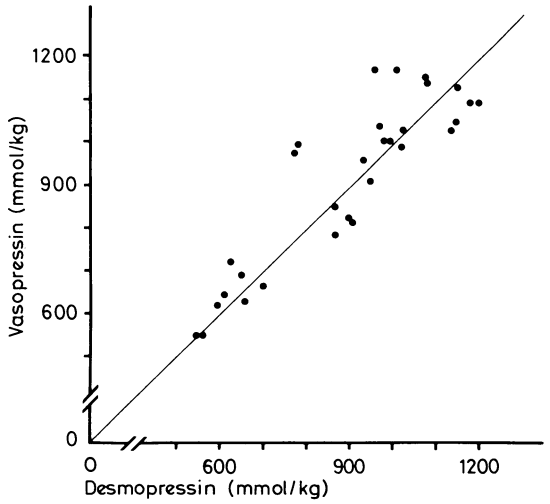
The physiological, and indeed the most potent, stimulus for urinary concentration is water deprivation. Because a test of kidney function based on this principle is unpleasant de Wardener in 1956 designed a test using vasopressin tannate in oil.[1 2]

In the mid-'60s a new modification of the antidiuretic hormone, desamino-d-arginine-vasopressine (desmopressin), was synthesised. The chemical modifications gave the compound a longer half life and deprived it of vasoactive effects, leaving its antidiuretic properties prominent. The drug is now widely used for treating diabetes insipidus.[3] Paediatricians also adopted the drug for urinary concentrating tests after it had been shown to be equipotent to, if not better than, a vasopressin injection.[4] We report here a comparison between desmopressin and vasopressin in adults.

Patients, methods, and results

Seventeen healthy volunteers and 15 patients were studied. Fourteen volunteers participated in two desmopressin tests and 15 underwent a vasopressin test; the 15 patients underwent both a desmopressin test and a vasopressin test.

Desmopressin test—Desmopressin (Minirin) was given intranasally. Each subject insufflated 40 μg desmopressin (0·2 ml in each nostril) using a small plastic tube. The desmopressin was given at 8 am after they had had nothing to drink overnight, and the osmolality was measured in samples taken after one, three, and five hours.



Correlation between maximum urinary osmolality in desmopressin and vasopressin tests. $y = 112 + 0{\cdot}9x$; $r = 0{\cdot}89$; $n = 30$.

Conversion: SI to traditional units—Osmolality: 1 mmol/kg = 1 mOsm/kg.

Vasopressin test—Vasopressin tannate in oil (5 IU) was administered intramuscularly at 8 am. There were no restrictions on drinking before the test, but fluid intake was restricted to 150 ml up to the end of the test. Osmolality was measured in urine produced from 8 pm to 10 pm the same day and between 10 pm and 7 am the next day.[5]

At least two days elapsed between the desmopressin tests and at least five days elapsed between a desmopressin test and a vasopressin test. Urinary osmolality was measured with an Advanced Instruments Osmometer. Statistical significance was tested with the aid of Student's t test in paired comparison tests. Lines were calculated by the method of least squares.

The mean difference between the highest osmolalities obtained in the two desmopressin tests was 25 ± 25 mmol (mOsm)/kg; this was not significant. After desmopressin administration the urine concentration increased rapidly and in many cases reached a peak at one hour. Nevertheless, the mean increase between one and three hours was statistically significant. Between three and five hours there was no further significant increase. The better of the results at one and three hours in the desmopressin test immediately preceding the vasopressin test was compared with the better result in the vasopressin test. The differences in urinary concentration on the two tests were not significant ($P > 0{\cdot}2$; see figure).