Treatment for control of life-threatening bleeding in a haemophiliac with inhibitors

The level of factor VIII inhibitor was measured using the method of Kasper et al. Three, 4, and 10 months after the second plasmapheresis, there was no detectable inhibitor in the patient's serum (Figure).

Discussion

Plasma exchange with fresh frozen plasma and factor VIII concentrates led to the lingual haemorrhage stopping in our patient, who had a high level of factor VIII inhibitor in his plasma. Serial analysis of the inhibitor level showed that it dropped from 10 to 3 Bethesda units after the first 2 days of plasmapheresis. Two days later however, it had returned to preplasmapheretic values, and it even rose to 12 units, corresponding probably to a rebound from the tissue pools. It was not surprising that bleeding started again a few days later, reaching a life-threatening rate in 10 days. After the second course of plasma exchange, bleeding stopped, and the level of the inhibitor fell to 2 units. Probably as a result of immunosuppressive treatment introduced at the time of the first plasmapheresis, the inhibitor level has remained low ever since. 10 months after plasmapheresis, the inhibitor level was nil, and the patient was symptom-free.

Plasmapheresis can lead to a rapid improvement of the clinical state in severe haemophilia with inhibitors. The secondary rise in the inhibitor level can most probably be avoided by more-prolonged intensive plasma exchange or by the simultaneous use of immunosuppressive treatment. Furthermore, as seems to be the case so far in our patient, the inhibitor may even disappear completely. Although the disappearance might have occurred spontaneously there is reason to believe that it was connected with the therapeutic procedure; however it is not possible at present to give a sound explanation. We recommend therefore a combination of plasmapheresis with simultaneous intensive immunosuppression.

References


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Nonaccidental poisoning: the elusive diagnosis

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SUMMARY Although nonaccidental poisoning in childhood is now more often recognised, it is still difficult to establish a diagnosis despite correct investigative procedures. In 1978 we were unable, initially, to establish the cause for intermittent episodes of loss of consciousness in a boy admitted to Sheffield Children's Hospital. Subsequently it was conclusively shown that his mother systematically poisoned him with Tuinal (amobarbital and quinalbarbitone) both before admission and while he was being treated in the hospital.

Most paediatricians are aware of the possibility of nonaccidental poisoning as part of the syndrome of child abuse, and a recent publication has heightened our own awareness of the possibility. Meadow described 2 cases which he attributed to a form of 'Munchausen's syndrome by proxy,' in which the children were deliberately and systematically poisoned by their parents. Verity et al. reported 2 similar patients who were being persistently poisoned by their mother. The main barrier to establishing a firm diagnosis is often the ingenuity of the parents in offering plausible explanations for the child's
symptoms and ensuring that the child is admitted to various hospitals, so that investigations are never carried to a firm conclusion at any one. This, indeed, was the case with our patient but further difficulties were encountered which delayed the diagnosis. The problems described illustrate not only the importance of a high index of suspicion and appropriate investigations, but also that the entire investigation screen should be repeated if the initial results are negative.

Case history

A 2-year-old boy was admitted to a peripheral hospital because his mother said he had had a painful foot for some days. Physical examination was negative, but during a period of observation a plaster cast was applied to the foot. The child suddenly became unconscious and was transferred to the Neurosurgical Unit in Sheffield. A history of possible head injury was elicited. A computerised tomography scan was normal and an electrocardiogram showed gross excess of fast activity associated with a moderate excess of slow activity, particularly on the right. The changes were said to be unusual and were correspondingly difficult to interpret, but they were similar to those seen as a result of barbiturate and other forms of intoxication. However, the boy recovered consciousness fairly rapidly and seemed perfectly normal. He was therefore returned to the first hospital, but as soon as he arrived there he again lost consciousness and was sent back to the Neurosurgical Unit. As there was no obvious neurosurgical explanation for his illness, he was transferred to the care of one of us (J L) at Sheffield Children's Hospital. There were no abnormal neurological findings and no focal signs, apart from the fluctuating level of consciousness. Poisoning, accidental or otherwise, seemed the likely explanation and his parents offered the suggestion that there were some fungi in the garden which he might have eaten. These were obtained and examined, but pronounced harmless by Professor A J Willis, Professor of Botany at the University of Sheffield. A toxicology screen was carried out, which showed only the presence of dexamethasone, which the patient had been given while on the neurosurgical ward. His parents denied that he had access to drugs of any kind. During his subsequent stay in hospital his mother was extremely critical of the nursing care given to the boy, pointing out that she herself was a nurse and knew what was required. She repeatedly asked that he should be transferred to another centre for further assessment. In the 14 days after his admission, he lost consciousness on at least 9 occasions (Table). During 2 of these episodes he had cardiorespiratory arrests requiring vigorous resuscitation with intubation and intermittent positive pressure ventilation, and once he required external cardiac massage. Extensive haematological and biochemical investigations were negative. In spite of the initial negative results, a repeat toxicology screen was carried out and this showed the presence of amylobarbitone 1·0 mg/100 ml and quinalbarbitone 0·4 mg/100 ml (constituents of Tuinal) in his blood. At the time this sample was taken, it was explained to his mother that further intensive laboratory investigations were being carried out in the hope of establishing a diagnosis.

The mother however, complained of a swollen, painful right leg and an episode of fainting. She was referred to the adult physicians (J P D R) and admitted to hospital. She gave a history of right deep venous thrombosis in December 1974, while she had been on oral contraceptives, and said she had been treated with anticoagulants. In July 1977, she had had a further episode of deep venous thrombosis in the same leg with pleuritic chest pain. She maintained that lung scan had been positive and that a diagnosis had been made of pulmonary embolus.

On this occasion she had difficulty in walking, with local tenderness in the calf, and Homans's sign was positive. There was no gross swelling and the muscle was soft. She was admitted for anticoagulation in view of her medical history. Within a few days she developed severe pleuritic chest pain, associated with a swinging pyrexia, but there were no localising signs and her chest was clear. She had headaches, photophobia and diplopia, neck stiffness, and a coarse nyctagmus. She had a rigor associated with a pyrexia of 44°C. At this time, anticoagulation difficulties were experienced and she required vitamin K for reversal of the anticoagulation.

Although she appeared quite unwell, the hyperpyrexia was inappropriate, and a rectal temperature was consistently recorded at 36·5°C. It was thought possible that there was anticoagulant noncompliance,

<table>
<thead>
<tr>
<th>Unconscious Date</th>
<th>Number of episodes</th>
<th>Additional features</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 August</td>
<td>2</td>
<td>Rash</td>
</tr>
<tr>
<td>13 August</td>
<td>1</td>
<td>Rash, Plantars †‡.</td>
</tr>
<tr>
<td>14 August</td>
<td>1</td>
<td>Reported by mother at onset.</td>
</tr>
<tr>
<td>15 August</td>
<td>1</td>
<td>Normal pupillary responses</td>
</tr>
<tr>
<td>17 August</td>
<td>1</td>
<td>Hypothermia</td>
</tr>
<tr>
<td>20 August</td>
<td>2</td>
<td>Intensive care unit</td>
</tr>
<tr>
<td>23 August</td>
<td>1</td>
<td>Respiratory arrest (IPPV)</td>
</tr>
</tbody>
</table>

IPPV — intermittent positive pressure ventilation.

Table Episodes of unconsciousness and accompanying clinical features
with the tablets saved and taken as a single dose later.

Further enquiries into the family history were made. Although no mention was made of this, it was discovered that the mother had been married previously and that 2 children by that marriage were in care. The general practitioner with whom the family were supposedly registered in the south of England, before moving to Derbyshire, had no record of the family. Previous addresses provided by the mother, in different cities, were found to be false and the general practitioner with whom she claimed to be registered with currently, had no knowledge of either the mother or the child. A London hospital had 'lost' all records of her admissions to them in 1974 and 1977, but an admission to hospital in 1976, during pregnancy, was confirmed. She had been an unbooked pregnancy, had been admitted in labour, and delivered at 38 weeks' gestation. She had claimed to have been a state registered nurse, but enquiries with the General Nursing Council showed that she had not so qualified. The hospital where she was said to have trained had no record of her.

As a result of these intensive investigations, further information came to light. In January 1974 the mother had had a complete abortion. Five months later, she complained of abdominal pain and was found to be 10 weeks' pregnant. A month later, she was said to have had an antepartum haemorrhage while in Stockholm and to have been admitted to hospital with a threatened abortion. She had a similar episode a month later on her return to the UK. She was eventually admitted with premature labour and had a stillbirth. Multiple admissions at 3 hospitals during this pregnancy were discovered only when she failed to attend at 40 weeks' gestation at one of the hospitals where she was booked for delivery. Despite this, no firm conclusions were made at this time.

In the light of all this evidence, a locker search was made and about 100 loose capsules of Tuinal were found, half of which were empty. Empty bottles labelled Tuinal in a different name were found, together with a foil pack of Triptafen (amitriptyline). An FP10 prescription pad and an enormous amount of paper relating to a depainting service, with which she was associated, were also found. Two thermometers, one reading 39.9°C and the other 41°C, were found in her bed and in her locker. At this stage it was clear that her illness was not organic, except for the signs possibly induced by barbiturate ingestion. However, examination of her serum for barbiturates was negative.

Reanalysis of the first blood sample from the boy, taken at the time of admission to hospital, showed that indeed there were amounts of quinalbarbitone and amylobarbitone present, which had not been detected in the first assay.

As a result of these investigations, the mother was interrogated and charged by the police. The matter has been dealt with in Court and the mother was sentenced to 3 years' imprisonment. The boy has remained perfectly well and has had no other episodes of unconsciousness. He has been placed in the care of his grandparents.

Discussion

In their excellent article, Rogers et al. described the various modes of presentation in cases of non-accidental poisoning. They also outlined a programme of management which is thorough and comprehensive. However, as our experience demonstrates, further problems may be encountered despite a high index of suspicion. The bizarre nature of the presenting symptoms without any logical organic cause resulted in toxicology screening being carried out on our patient when he was first seen by the paediatrician. Difficulty in the interpretation of this screening test arose for 2 reasons: (1) The administration of dexamethasone itself produced a peak on analysis which may have obscured the presence of barbiturate. (2) 'Blind' toxicology screening is less likely to be successful than a search for specific drugs, and at that time we had been unable to give any guidance to the laboratory on which drugs might be involved. The negative toxicology screen therefore had put us off our guard and subsequent samples were sent for analysis some time later in the illness. Indeed, the initial testing of these samples was also negative and only when it was found that the mother had a large supply of Tuinal in her handbag was further analysis stimulated and all previous samples then were found to give positive results.

Apart from this problem, the outstanding features of this case were the mother's plausibility and her apparent desperate concern for her child's welfare. The extraordinary sequence of events in her own history before the boy's admission to hospital did not come to light until she herself was admitted to hospital, apparently at a time when she felt it was likely that the boy's illness might be diagnosed. It is not clear why this woman tried to poison her son. She was seen by a psychiatrist who felt that she had a psychopathic personality and was a pathological liar. She demonstrates a history similar to that of the mothers described by Meadow.  

Analysis of this and other cases has enabled us to come to the following conclusions. We offer them in the hope that similar difficulties may be avoided. (1) If nonaccidental poisoning is suspected, samples of blood, gastric washings, and urine should be taken...
at times when the patient is symptomatic, so that
toxicology screening may be carried out. Tricyclic
antidepressants are more difficult to detect in blood
than in gastric washings or urine.
(2) The importance of a detailed family history with
a further check on conflicting items of information
is stressed here, and had the mother not developed
'symptoms' herself, it is possible that the outcome
might have been less satisfactory. Therefore, it is
important to pursue vigorously all elements of the
medical history of the family, with specific documen-
tation.
(3) A period of isolation of the patient from his
parents should confirm whether symptoms are
related to the presence of the parents. Although this
might be difficult to achieve in cases where the
diagnosis is suspected but not proved, it would
provide vital information and could be achieved by
excluding the parents from all physical contact with
the child. Additionally, only the nursing and medical
staff should be allowed to administer food, drink, or
drugs to the patient during the period of observation.
If necessary, a Place of Safety Order should be
obtained.
Among the many suggestions offered to us as a
result of our plea for assistance, was the availability
of a special room with closed circuit television so
that the patient could be watched throughout the
24-hour period, and any attempt by the parents to
give him drugs could then be seen. This would appear
to be the ideal way to monitor the child, but such
facilities are not readily available in our hospitals. It
is, however, quite clear that any attempt to give
drugs to a child would only be made when the
person thought she was not being observed.
This patient nearly died despite intensive efforts to
establish a diagnosis. The fact that the cause of his
illness was eventually ascertained was probably
fortuitous. We hope that we and others can learn
from this case and therefore prevent possible
tragedies.
We thank the readers of the Lancet for their speedy
and helpful response to our plea for assistance, and
we note that the majority of our medical replies
were on the right track. It is interesting to relate that
we also received a large number of replies from lay
people who provided a wide variety of less likely
explanations and treatments for this unusual illness.

We thank the staff of the Biochemistry Laboratories
at the Children's Hospital and the Hallamshire
Hospital, Sheffield, for their valiant efforts to assist
us in the management of this case, and Mrs J Gill
and Mrs G Wilson for secretarial assistance.

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Commentary
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Child abuse is, of course, nothing new although it
came to be widely recognised as all too common in
our society only after Kempe wrote about it in 1962,
and endowed it with the arresting title 'the battered
child syndrome'. Soon after the last war, that is some
35 years ago, I was concerned with a case in
Newcastle which bore many similarities to the case
described above, and was equally bizarre, but with
an even more catastrophic dénouement.
A well-spoken, middle-aged woman brought to
hospital her 2-year-old child in a coma. She stated
calmly that she knew what was wrong with her
child—tuberculous meningitis—since she had lost
her 2 previous children, both of whom had died from
this disease. She explained that the source of
infection was her husband, who had advanced
pulmonary tuberculosis, but who was a hopeless
ne'er-do-well who had refused all medical attention.
The child, she stated, had gradually become more
and more drowsy during the last week or so, just
as had her 2 older children, who had eventually died
in hospitals elsewhere in the country as a result of
proved tuberculous meningitis. All she wanted, she
went on, was for us to confirm that the child did
have tuberculous meningitis (at that time an
invariably fatal condition) after which she would nurse
the child at home until he died.
On examination the child was in deep coma, but
not wasted or febrile or otherwise ill. He presented
the 'Sleeping beauty' picture as often seen in children
with tuberculous meningitis in those days, when that
disease was not uncommon.
A lumbar puncture was done and to everyone's
surprise the CSF proved normal. A Mantoux test