is healthy and has had neither recurrent infections nor shown any signs of lipodystrophy, and her mild arthralgia has had no influence on her work as a clerk. The origin of the C3 activation in her case cannot be certain, but there are two possibilities. Firstly, a genetic deficiency, though her 14-year-old son has normal C3 and C4 (certainly this does not exclude a genetic origin, but it makes it less likely). Secondly, originally the complement activation might have been provoked by an infection, such as her tonsillitis and post-infectious arthritis.

At present this patient seems "healthy," apart from mild arthralgia in her fingers. Is the latter related to her hypocomplementaemia? Does her immune deficiency have any clinical importance? Finally, will her immunological deficiency eventually manifest itself as a nephritis?

Professor Anna-Britta Laurell, Lunds Lasarett, Sweden, analysed the complement factors and also gave good helpful advice.

[1] Spitzer, R E, *et al*, *Science*, 1969, **164**, 436.
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Carcinoma in-situ of cervix in sisters

"There are no 'cancer families' in which the cervix has been the organ affected."[1] Yet if, as claimed,[2] early age at first coitus, having a first baby while a teenager, multiplicity of partners and pregnancies, and low socioeconomic class are relevant to the development of cervical cancer, it should not be surprising that example and environment might combine to lead to similar lesions occurring in sisters. In the family here described, the mother had four sons and four daughters and died at 50 from myocardial infarction. The pattern among the four daughters, all in socioeconomic class V, is as follows.

Case reports

Daughter No 1 was born in March 1936. First coitus was at age 18. She was pregnant when she married at 19 but aborted. She was still 19 when she had a baby. When 22 she divorced her husband and "had three chaps" before remarrying at 27, again when pregnant. That baby was premature and is backward. When 29 she had trichomonas vaginitis but her cervical smear was negative. She did not take the pill. She was 33 when at examination for secondary infertility her smear was reported positive. Cone biopsy confirmed carcinoma-in-situ of the cervix. Five and a half years later she is well, the cervix looks healthy, and the smear is negative.

Daughter No 2 was born in February 1941. First coitus was at 18 and first baby (premature) at 19. She married when 22 and had three babies and three miscarriages. The last pregnancy, a successful one, was at 28. She was 31 when at request for sterilisation she was found to have a positive smear. She had been taking the pill for the previous 18 months. The cone biopsy taken at tubal ligation showed carcinoma-in-situ. Three and a half years later she is well, the cervix looks normal, and the smear is negative.

Daughter No 3 was born in May 1942. First coitus was at 15 and she married at 16. She had one baby at 18 before she was divorced. She remarried and had three babies. She was on the pill from age 24 to 30. She was 32 when at request for sterilisation she had a positive cervical smear. Biopsy showed varying degrees of dysplasia and one area of carcinoma-in-situ. As she also had prolapse, she was treated by vaginal hysterectomy with repair. One year later she is well with a negative vault smear.

Daughter No 4 was born in October 1947. First coitus was at 17. She had her first baby when 19 and the second, by the same consort, when 24. Since then she has had two other partners, one for a few months and the other for nearly 3 years, and is still single. When 26 she had vulval warts, vaginal thrush, and trichomonas vaginitis at different times, but her cervical smear was negative. She took the pill for 18 months up to this time. She was 28 when two smears were reported as positive. Cone biopsy in August 1975 showed areas of dysplasia but no carcinoma-in-situ.

Comment

Note that none of the sisters was aged more than 33 years at the time of the first positive smear. The moral seems to be that if a woman of low socioeconomic level has an intra-epithelial lesion of the cervix, she should be asked if she has any sisters.

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Aplastic anaemia and hair dye

Patients with aplastic anaemia for which no obvious cause is found continue to be seen. Recent reports on the carcinogenicity and mutagenicity of hair colourants[1 2] have re-emphasised the potential dangers of these products, which are in widespread use. We should like to report a case of fatal aplastic anaemia in a patient using a new hair dye. Although anecdotal and in no way establishing a cause and effect relationship, this case emphasises once more the need for careful questioning and continuing enquiry of such patients.

Case report

A 52-year-old housewife was admitted to hospital for investigation of spontaneous bruising and purpura of one month's duration. Four months previously she had received a short course of oxytetracycline and then penicillin from her general practitioner for a mild upper respiratory tract infection. One month before the onset of her haemorrhagic tendency she had started using a new hair dye containing paratolylenediamine. So far as she or her husband could remember there had been no other exposure to new cosmetic, household, or other toxic agents. She looked well but was anaemic and had numerous petechiae and eccymoses on the skin and mucous membranes. There was no lymphadenopathy or hepatosplenomegaly and she was not jaundiced. Investigations showed a haemoglobin of 9·9 g/dl, with slight macrocytosis; the WBC was $8{\cdot}5 \times 10^9$/l (8500/mm^3) and platelet count 8×10^9/l (8000/mm^3). Coombs test was negative. The LE phenomenon was not detected and tests for ANF were negative. Leucocyte and platelet antibodies were not found, and there was no evidence of haemolysis. Bone marrow examination showed complete absence of megakaryocytes and erythroid hypoplasia.

She was treated initially with prednisolone in high doses and infusions of platelet-rich plasma. There was no appreciable response to steroids and oxymethalone, 300 mg per day, was added, again without benefit. Over the next five months she received fresh blood and platelet transfusions as necessary but remained thrombocytopenic, anaemic, and, during the later stages, leucopenic. Repeat bone marrow examinations during this time showed severe hypoplasia of all three haemopoietic components and she died six months after presentation from an intracranial haemorrhage. Necropsy confirmed bone marrow aplasia.

Discussion

It is unlikely that either tetracycline or penicillin caused this patient's aplastic anaemia. The hair dye used contained paratolylenediamine (2-methyl 1.4 phenylenediamine) in a concentration of 0·03%. Phenylenediamine has been used for many years in the dyeing industry and its effects on the bone marrow are well known.[3] Two groups have recently reported studies on the mutagenic and carcinogenic properties of the various paraphenylenediamine dyes.[1 2] The mutagenic properties are retained even after mixing with hydrogen peroxide, the oxidant used in the lotion developer, and appreciable

quantities may be absorbed through the skin during one episode of hair dyeing. Although individual sensitivity is extremely rare, these substances used in hair dyeing must continue to be the subject of close scrutiny.

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[3] Bomford, R R, and Rhoades, C P, *Quarterly Journal of Medicine*, 1941, **10**, 175.

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Successful treatment of myeloma kidney by diuresis and plasmaphoresis

We report a patient with myeloma kidney and severe renal failure treated by forced diuresis and plasmaphoresis. Excellent recovery of renal function has been maintained for nine months, a survival far longer than expected in such a case.

Case history

A 29-year-old Englishman developed a lump on his head in September 1974. Three months later he presented with nocturia and tiredness. He looked ill, with a fluctuant swelling 3 cm by 3 cm over the right parietal bone; tenderness over the left ribs and lower thoracic spine; and some anterior angulation at D8. Haemoglobin was 6·0 g/dl, white blood count $4·1 \times 10^9$/l (4100/mm^3), erythrocyte sedimentation rate 69 mm in 1 hour. Immunoelectrophoresis showed a monoclonal excess of IgG (44 g/l) with low IgA and IgM. Bence Jones protein was present in the urine (1·2 g/24 h). Skeletal survey showed widespread lytic deposits. The diagnosis of multiple myeloma was confirmed by narrow aspirate, showing 20% primitive plasma cells. His blood urea was 44·8 mmol/l (270 mg/100 ml); creatinine 1220 μmol/l (13·8 mg/100 ml); plasma calcium 2·2 mmol/l (8·9 mg/100 ml); urine specific gravity 1031, urate 0·50 mmol/l (8·4 mg/100 ml). Urine osmolality was 310 mmol/kg (310 mosmol/kg), 24-hour urine calcium and urate were not elevated. There was no amino-aciduria.

He was treated initially with melphalan 5 mg daily for one week. Renal biopsy showed myeloma kidney with tubular casts, tubular dilatation, and atrophy with surrounding inflammation. The glomeruli were normal, and there was no amyloid or vascular change.

Over the next two weeks the renal function deteriorated (blood urea rising to 78 mmol/l (470 mg/100 ml)) despite saline repletion, and he developed pleural and pericardial effusions, drowsiness, and confusion. He was treated with peritoneal dialysis from 31 December 1974 to 7 January 1975; simultaneously a diuresis was induced with 5 litres daily of intravenous saline, and frusemide, 500 mg daily. Urine pH was above 6.

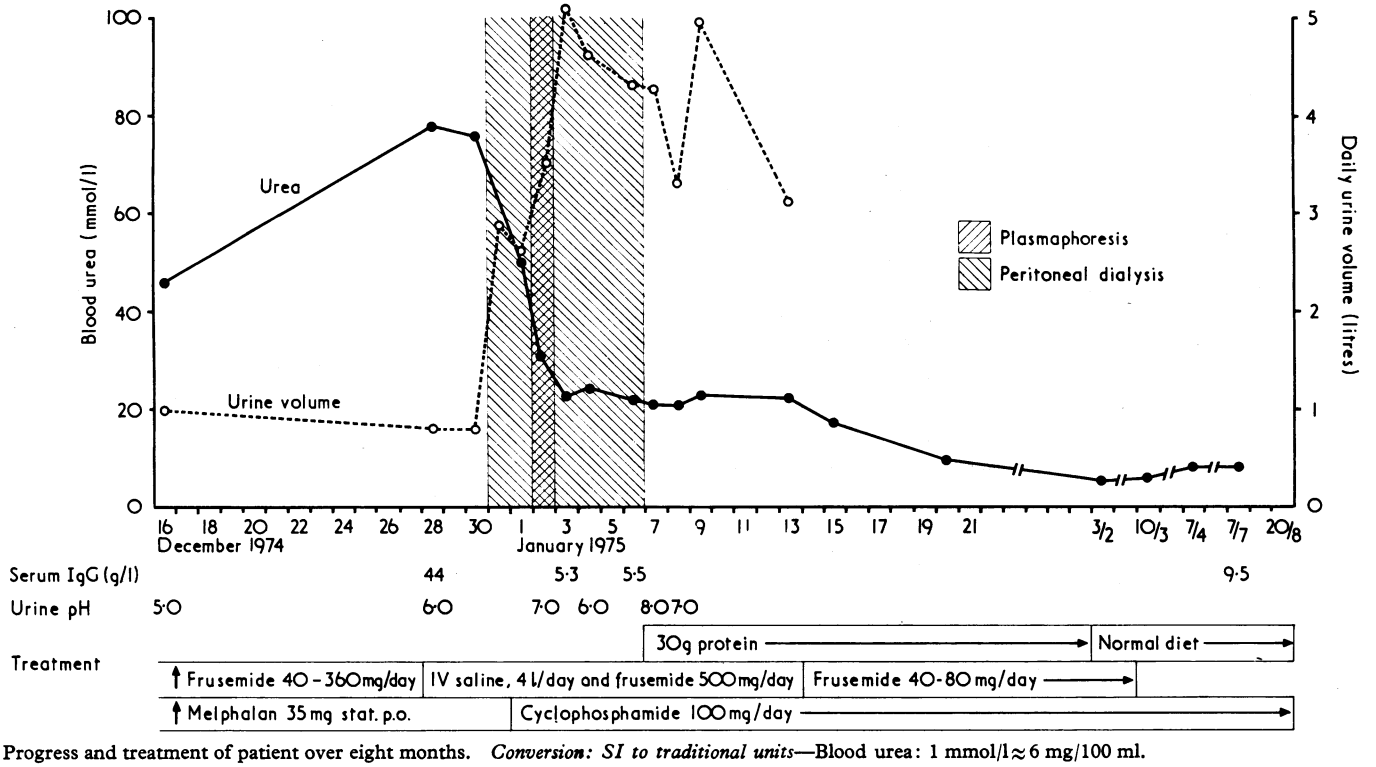
On 2 January 1975 plasmaphoresis was performed, exchanging 1180 ml plasma for plasma protein fractions, at which his IgG fell from 44 g/l to 5·5 g/l, and Bence Jones proteinuria ceased. He improved greatly, the blood urea and creatinine continuing to fall after dialysis was stopped. Nine months later he is well and working normally; the haemoglobin 12 g/dl, blood urea 10·0 mmol/l (60 mg/100 ml), creatinine 160 μmol/l (1·8 mg/100 ml), creatinine clearance 66 ml/min, IgG 9·3 g/l, 24-hour urine protein 300 mg. He is maintained on intermittent courses of melphalan.

Discussion

When acute renal failure occurs in myelomatosis the prognosis is poor: in one series 13 of 14 patients died within two months[1]. There is a strong correlation between the occurence of Bence Jones proteinuria and renal failure in myeloma.[1 2] The precise role of these proteins in the pathogenesis of renal failure is uncertain, but direct toxicity of light chains to the renal tubule,[3] and tubular obstruction by casts[4] have both been postulated.

It seems reasonable to treat myeloma kidney by attempting to remove Bence Jones proteins from the kidney, and to prevent reaccumulation by removing them from the serum. Bence Jones protein precipitates most readily if the urine is concentrated, the pH is below 6, and solutes and albumin are present.[5] An alkaline diuresis should thus help to prevent cast formation, and possibly remove existing casts. Such treatment has been shown to protect mice with Bence Jones proteinuria from renal damage, reducing cast formation, and has prevented progression of renal failure in a patient with myelomatosis.[4]

Our patient deteriorated on conventional treatment. Treatment with a sustained alkaline diuresis and plasmaphoresis to remove



Progress and treatment of patient over eight months. *Conversion: SI to traditional units*—Blood urea: 1 mmol/l ≈ 6 mg/100 ml.