SHORT REPORTS

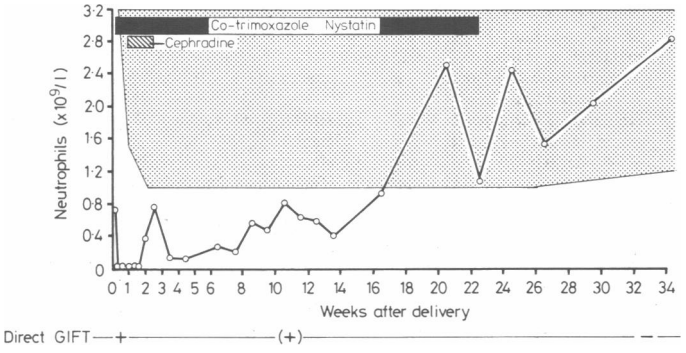
Neonatal neutropenia due to maternal autoantibodies against neutrophils

In autoimmune neutropenia most patients produce IgG antibodies against neutrophils.[1] During pregnancy IgG antibodies are transported by the human placenta from the maternal into the fetal circulation. Thus transient neonatal neutropenia could develop in children of women with active autoimmune neutropenia, a syndrome that may be associated with severe infections in the neonatal period. This possibility has never been described nor has the passage of the autoantibodies through the placental barrier been shown. We used the granulocyte immunofluorescence test[1] to diagnose the autoimmune character of neutropenia in a mother and the association of raised granulocyte-bound IgG concentration and transient neutropenia in the child. This test is based on the observation that aspecific fluorescence may be prevented by fixing the granulocytes with paraformaldehyde. Specific antiglobulin Fab reagents labelled with fluorescein isothiocyanate were used.

Case report

A 20 year old woman presented with a short history of skin infections and buccal ulcerations. She had no history of systemic illness, and physical examination showed no abnormalities. Neutropenia was diagnosed. The bone marrow aspirate showed a ratio of myeloid to erythroid of 8 to 1, normal cellularity, and normal myeloid precursors with a relative deficit of segmented neutrophils. There were no other haematological abnormalities. The granulocyte immunofluorescence test showed IgG autoantibodies against neutrophils. Granulocyte-specific antibodies in serum were shown by testing it in the indirect immunofluorescence test with granulocytes, platelets, and lymphocytes from the same donors. The autoantibodies were not specific for any blood group. Tests for antinuclear factor gave negative results. A presumptive diagnosis of autoimmune neutropenia was made. She failed to respond to an adequate course of steroid and azathioprine treatment.

At the age of 24 she became pregnant. Her antenatal progress was normal and an apparently healthy boy was born at term. Umbilical cord blood showed a very low neutrophil count and IgG antibodies to neutrophils were detectable on cord blood neutrophils with the direct granulocyte immunofluorescence test and in the cord blood serum with the indirect test. There were no other haematological abnormalities. On the second day prophylactic treatment with co-trimoxazole and nyastatin was started. On the third day the child developed a pustula and an umbilical infection due to *Staphylococcus aureus*, which was successfully treated with oral cephradine. The child was discharged after two weeks. After 16 weeks the neutrophil count came within normal limits and the direct granulocyte immunofluorescence test gave negative results, after which the prophylactic co-trimoxazole and nystatin treatment was stopped (figure). No other infections occurred in the neutropenic period and the child grew and developed normally.



Neutrophil counts and results of direct granulocyte immunofluorescence test on granulocytes of infant post partum. Shaded area denotes range of neutrophils in healthy infants. GIFT = Granulocyte immunofluorescence test.

Comment

Thirty years ago it was suggested that a humoral factor was the causative agent in idiopathic thrombocytopenic purpura after the observation that mothers with the disease give birth to children who develop transient thrombocytopenia.[2] The suspected platelet autoantibodies and their transfer through the placenta has recently been confirmed.[3] This first reported transient neonatal neutropenia supports the presumptive diagnosis of maternal autoimmune neutropenia. Moreover, we confirmed the presence of suspected IgG autoantibodies against neutrophils and their transfer through the placenta. The transient character of the neutropenia and the gradual disappearance of antibodies from the neutrophils in the child supports the theory that antibodies were passively acquired.

Antibiotic prophylaxis with co-trimoxazole and nystatin is recommended in patients with neutropenia.[4] The use of co-trimoxazole in infancy is disputed, however,[5] and there is no experience in large series of infants. We observed no side effects and apart from the short lasting skin infection during the first week, no infections occurred during the neutropenic phase. This could be ascribed to this prophylactic treatment.

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Nephrotic syndrome after treatment with psoralens and ultraviolet A

In an attempt to desensitise a case of polymorphic light eruption with psoralens-ultraviolet A (PUVA) treatment the patient developed nephrotic syndrome at the end of treatment. The temporal relation between the two events suggests that PUVA treatment was of pathogenetic importance in the development of the nephrotic syndrome.

Case report

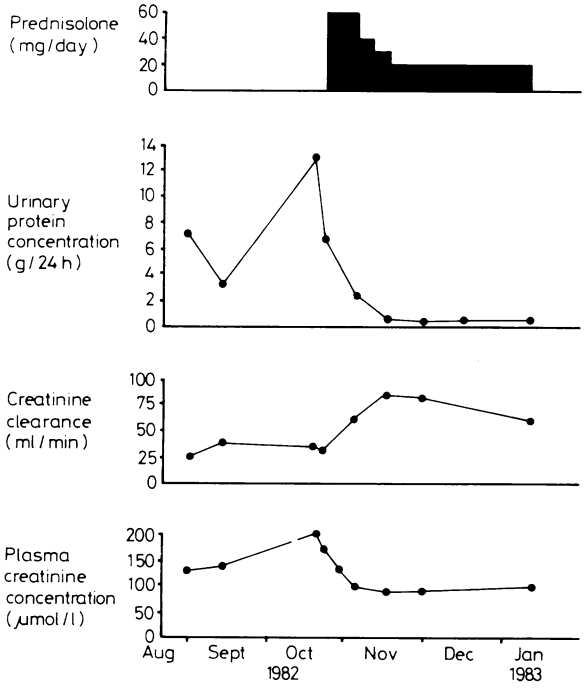
A 38 year old white woman had a history of polymorphic light eruption since the age of 10 years. In 1970 she was treated with trimethoxypsoralen (Trisoralen)[1] and was told to expose herself to increasing amounts of sunlight. This treatment was beneficial and there were no side effects. Further treatment with topical sunscreening agents, oral β carotene, and ultraviolet B produced no appreciable improvement. Between 1970 and 1982 her renal function was normal without proteinuria on several occasions.

In July 1982 she was given PUVA treatment twice weekly for five weeks. At the end of August 1982 she developed peripheral oedema and was found to have the nephrotic syndrome with a serum albumin concentration of 15 g/l (1·5 g/100 ml) and a urinary protein concentration of 7·1 g/24 hours. Her blood urea concentration was 9·3 mmol/l (56 mg/100 ml), plasma

creatinine concentration 140 μmol/l (1·4 mg/100 ml), creatinine clearance 41·4 ml/min, antistreptolysin O titre 60 U/ml (normal < 200 U/ml), serum C3 concentration 1·48 g/l (148 mg/100 ml) (normal range 1·05-1·35 g/l (105-135 mg/100 ml)) and serum C4 concentration 0·5 g/l (50 mg/100 ml) (normal range 0·2-0·5 g/l (20-50 mg/100 ml)). Antinuclear antibodies were present in the serum (titre 1/12). Anti-double-stranded deoxyribonucleic acid (DNA) antibodies were absent. Immune complexes were detected in the serum by the complement consumption technique.

A percutaneous renal biopsy showed a mesangial proliferative glomerulonephritis with no permanent renal damage. On immunofluorescence there was granular deposition of C3 alone on capillary walls and to a lesser extent in the mesangium, while electron microscopy showed small granular deposits subendothelially and widespread loss of pedicle structure.

Her oedema was controlled with treatment with bumetanide and spironolactone by mouth but her renal function deteriorated and proteinuria increased. She was treated with 1 g methylprednisolone sodium succinate intravenously daily for three consecutive days followed by oral prednisolone, which improved her general well being and renal function (figure). At present she is treated with 20 mg oral prednisolone daily and she is free of symptoms and oedema.



Serial measurements of plasma creatinine concentration, creatinine clearance, and 24 hour urinary protein before and after treatment with steroids.

Conversion: SI to traditional units—Plasma creatinine: 1 μmol/l ≈ 0·01 mg/100 ml.

Comment

PUVA treatment consists of the administration of a psoralen compound by mouth followed by irradiation of the skin with long wave ultraviolet light (ultraviolet A 320-400 nm). Impressive results have been obtained in psoriasis and possible success in mycosis fungoides and severe atopic dermatitis.[2] Treatment of polymorphic light eruption with trimethoxypsoralen and natural sunlight has been used for many years in the United States.[1] In countries where natural sunlight is unpredictable a specially designed apparatus is used to deliver ultraviolet light as in PUVA treatment.

Reported side effects during treatment have been few and not serious.[2] In one group of patients with severe psoriasis a high proportion developed antinuclear antibodies during treatment.[3] The titres were low, as in our patient, but were not associated with proteinuria. In another report systemic lupus erythematosus was associated with PUVA treatment of psoriasis.[4] The patient in this case had impaired renal function and proteinuria and a renal biopsy showed a mild focal increase in mesangium, but no immunofluorescence nor electron microscopy findings were reported. She was treated with steroids with a good response.

Psoralen interacts with pyrimidine bases in DNA to form a compound that is immunogenic after treatment with ultraviolet A.[5] An immune basis for the development of nephrotic syndrome in our patient is suggested by the presence of C3 in renal biopsy findings and of immune complexes in the serum and by the good response to steroids. We therefore recommend that the urine should be tested for proteinuria and serum antinuclear antibodies estimated during PUVA treatment.

We thank Drs Frain Bell and A W M Smith for referring the patient to us.

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Early non-radiological recognition of misplacement of central venous catheter

When an infraclavicular approach is used for central venous catheterisation the commonest site for catheter misplacement is the internal jugular vein.[1] This complication, reportedly occurring in as many as 25% of cases, is associated with phlebitis of the internal jugular vein if hyperosmolar solutions are infused.[2] Radiological confirmation of the position of the catheter in the superior vena cava is therefore mandatory albeit time consuming, particularly if the internal jugular vein is accidently cannulated, when the entire catheterisation procedure must be repeated.

For over two years we have used a catheter inserted by an infraclavicular approach into the subclavian vein. The catheter is supplied with a guidewire, which is passed down the lumen of the exploring needle after the subclavian vein has been located. This allows the needle to be removed and the catheter to be threaded over the guidewire, which is itself removed. This manoeuvre dispenses with the need to have the needle anchored to skin for as long as the catheter is in place: this was a clumsy and dangerous feature of earlier catheter design.

We noted on one occasion that on withdrawal the guidewire was curved in a cranial direction (it normally remains straight), and subsequent *x* ray examination showed the catheter to be cephaled directed. We carried out a study to evaluate guidewire distortion as a test for misplacement of the catheter into a neck vein.

Patients, methods, and [illegible]

We studied 25 men and women who required central venous catheterisation for measurement of central venous pressure or delivery of total parenteral nutrition. A 16 gauge Vygon Leader Cath (code 12017) was inserted by an infraclavicular route on the right side in every case. The end of the guidewire was grasped firmly between finger and thumb, withdrawn in a single movement to avoid twisting on its long axis, and carefully laid on a flat sterile surface. Any cephaled or caudal deviation of the guidewire tip was noted and the catheter position then checked radiologically.

In 22 cases the guidewire was deemed to be straight (16 cases) or deviated caudally (six cases). In all these patients *x* ray examination confirmed that the catheter was in the correct position in the superior vena cava. Misplacement of the catheter in the neck was demonstrated radiologically in the three cases in which cranial deviation of the guidewire had been noted.