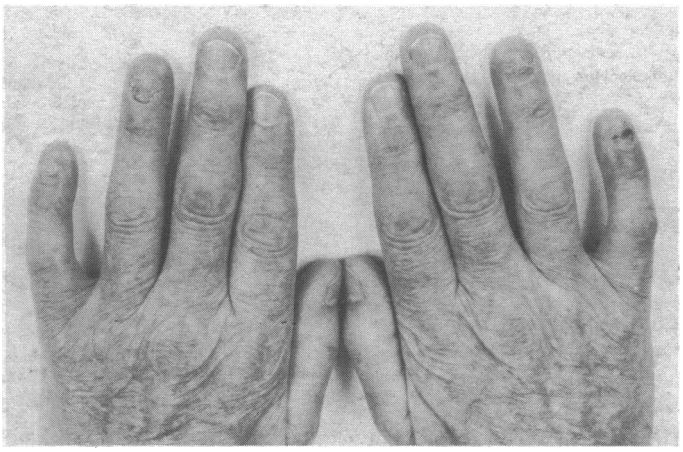
Nail dystrophy due to diabetic neuropathy

Nail changes may occur in diabetics in association with trophic changes or ischaemia. We describe a diabetic patient in whom fingernail dystrophy occurred as a result of a bilateral ulnar neuropathy.

Case report

A 72-year-old man presented in 1979 with a two-year history of changes affecting the nails of the ring and little fingers of both hands. During this time he had experienced numbness and tingling of these fingers and some difficulty in moving them. He had also had numbness and tingling of both feet for 17 years and difficulty in moving the right foot for one year. A known diabetic since 1962 with retinopathy and glaucoma, when seen he was taking glibenclamide 15 mg daily, metformin 500 mg twice daily, and acetazolamide 500 mg daily.

Examination showed shortening, fragility, and yellow discolouration of the nails of the ring and little fingers of both hands (figure). Neurological examination showed wasting of the interossei, decreased ability to adduct and abduct the fingers, right foot drop, decreased pinprick and light touch sensation over the ring and little fingers of both hands, decreased pinprick and light touch sensation up to the mid-shin level on both sides, absent vibration sensation over the ankles, and absent ankle jerks. Mycological examination of clippings from the affected fingernails gave negative results. It was concluded that he had a mononeuritis multiplex affecting the ulnar and right popliteal nerves and that the fingernail dystrophy was related to the ulnar neuropathy.



Fingernails, showing the distribution of nail dystrophy.

Comment

Nail changes may occur as a result of neurological lesions. Mitchell[1] found that cerebral palsy with or without sensory loss caused decreased nail growth or nail dystrophy, or both, on the affected side. He subsequently reported on a patient in whom dystrophy of the nail of the little finger developed after an ulnar nerve "wound".[2] A similar patient whose little fingernail became dystrophic after the cutaneous branch of the ulnar nerve to that finger was severed was described by Sharpey-Schafer.[3] Some authors state that sensory loss alone does not cause decreased nail growth or nail dystrophy and that a motor weakness[4] or some form of immobilisation[5] is necessary. Our case does not contribute further to this problem as there were sensory and motor changes involving the affected digits. We have been unable to find any previous reports of nail dystrophy caused by a mononeuritis multiplex.

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Paraquat ingestion with methaemoglobinaemia treated with methylene blue

We describe a case of methaemoglobinaemia and haemolysis associated with ingestion of paraquat.

Case report

A 32-year-old horticultural worker presented to the casualty department having drunk a bottle of whisky, four pints of beer, and about three mouthfuls of Gramanol (10% paraquat) in an episode of depression. Initially he refused all treatment, and even after 10 hours he agreed to take only 20 ml Fuller's earth and magnesium sulphate solution by mouth. He had a sore throat, abdominal pain, nausea, and vomiting.

On examination about 10 hours after he had taken the paraquat he was drowsy and confused and had central cyanosis with a slate-grey complexion but was not dyspnoeic. He had periodic respiration. Spider naevi were present. Blood pressure was 130/90 mm Hg with good peripheral perfusion, and the chest was clear. Chest radiography was normal, and his arterial blood looked blue-black despite an arterial oxygen pressure of 32 kPA (240 mm Hg) while receiving 8 l oxygen/min by mask. Spectroscopy showed the presence of methaemoglobin. Although his serum creatinine concentrations and urine output were normal initially, haemodialysis through an arteriovenous shunt was started in case he had taken an unknown oxidising agent in addition to paraquat. Methylene blue 1 mg/kg was infused to reduce the methaemoglobin. The effect was dramatic: his colour reverted to normal, and he was more alert and co-operative. Oxygen was discontinued.

Six hours later we learnt that the paraquat concentration on admission had been 55 μg/l (12 hours after ingestion). This was below toxic concentrations. We also learnt that methaemoglobin had constituted 18·7% of total haemoglobin (that is, 3 g/dl) before methylene blue was given and 1·6% of total haemoglobin afterwards. A few Heinz bodies were seen. During the next week he developed mild renal impairment and a cough with purulent sputum. Both resolved quickly. He then developed haemolysis, the haemoglobin concentration falling to 11·5 g/dl, with a reticulocytosis of 5%. This too recovered. Glucose-6-phosphate dehydrogenase activity was normal. There was no permanent lung damage.

Comment

Analysis of Gramanol showed paraquat 10% and monolinuron, a dispersing agent that is not known to cause methaemoglobinaemia. There was no chlorate or nitrate. Paraquat is an electron acceptor, increasing oxidation of nicotinamide-adenine-dinucleotide phosphate. The reduced paraquat is then reoxidised to paraquat by oxygen with production of superoxide ions.[1] These ions damage tissues and produce hydrogen peroxide, which can cause peroxidation of lipid cell membranes.

Theoretically it is possible that superoxide ions and hydrogen peroxide could oxidise haemoglobin to methaemoglobin, leading to oxidant-induced haemolysis. We have not found any published evidence for this or any evidence that alcohol potentiates the toxicity of paraquat. The apparent improvement in his drowsiness and confusion after methylene blue cannot be explained by a greater oxygen capacity in the blood, as the methaemoglobinaemia was not severe enough to reduce this capacity appreciably. The lung damage caused by paraquat takes several days to develop[2-4] though may occur more quickly if a large amount is ingested.[5] Cyanosis within hours of ingestion of paraquat should therefore lead to the suspicion of methaemoglobinaemia. If this is confirmed, treatment with methylene blue may well be worth while.

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Response of thrombotic thrombocytopenic purpura to chlorpromazine

Thrombotic thrombocytopenic purpura is a rare disorder characterised by haemolytic anaemia, thrombocytopenia, neuropsychiatric disturbances, and hyaline arteriolar occlusions.[1] It was previously associated with high mortality,[2] but repeated plasma exchange has improved the prognosis.[3] We describe a patient in whom chlorpromazine appeared to produce complete and sustained remission of the disease.

Case report

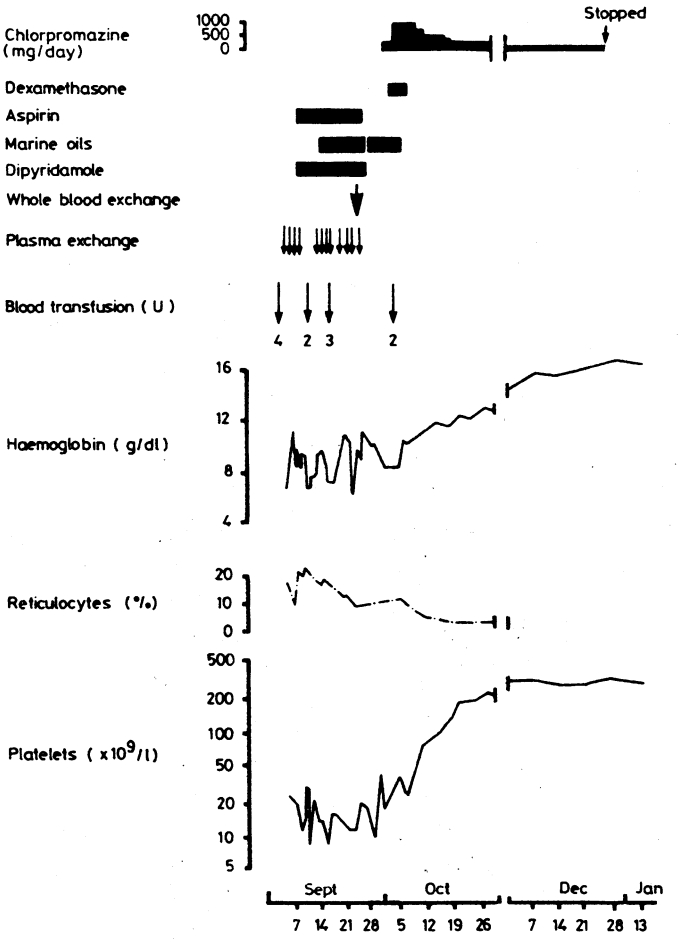
A 50-year-old industrial engineer had a two-month history of increasing lethargy, malaise, and anorexia and a two-week history of fever and painless haematuria. On admission to hospital he was confused and showed clinical anaemia, icterus, and a petechial rash. Haemoglobin concentration was 6·4 g/dl, platelet count 40×10^9/l, and reticulocyte count 5% (figure). A blood film showed polychromasia, anisopoikilocytosis, microspherocytosis, and red-cell fragmentation. Coagulation studies were mildly abnormal, with prothrombin time 17·5 s (control 15 s), activated partial thromboplastin time 48 s (control 35 s), and thrombin time 28 s (control 25 s) and the titre of fibrin and fibrinogen degradation products 1/16 (normal $<1/8$). A direct Coombs test and Ham's test yielded negative results. Free haemoglobin was present in the urine. Bone-marrow cytology showed hyperplasia of all circulating cell precursors. Blood cultures showed no growth. Thrombotic thrombocytopenic purpura was diagnosed.

He rapidly became comatose with severe cerebral irritation. Intensive treatment by repeated plasma exchange produced considerable but temporary benefit with normal conscious level and slight but transient improvement in circulating platelet concentrations. Intermittent red-cell transfusions were required for anaemia. Two grand mal seizures were treated by intravenous diazepam, and prophylactic phenytoin was given. No clinical or haematological improvement followed treatment with dexamethasone, marine oils (Maxepa; British Cod Liver Oils, Hull), low-dose aspirin, or dipyridamole.

Six weeks after admission he again became confused and showed amnesia, paranoia, sexual disinhibition, and visual and persecutory auditory hallucinations. An acute organic confusional state was diagnosed and high-dose (1 g daily) chlorpromazine prescribed, with rapid and permanent improvement in his mental state. Serial blood counts showed a sustained improvement in haemoglobin concentration and platelet counts and a reciprocal diminution of reticulocytosis. After two weeks' treatment with chlorpromazine the platelet count became normal ($>150 \times 10^9$/l) and after a further four weeks the haemoglobin concentration was greater than 14 g/dl. The chlorpromazine was gradually withdrawn and relapse did not occur.

Comment

The start of a course of chlorpromazine corresponded in our patient with the onset of eventual total remission of thrombotic thrombocytopenic purpura. We believe that this represents a true response of this unpredictable disease to the drug but recognise that it might have been fortuitous and due to a spontaneous remission. We had no opportunity for re-evaluating the effect of chlorpromazine as our patient remained in complete remission.



Time relation of changes in haematological variables to administration of oral chlorpromazine and other treatment.

The pharmacological properties of chlorpromazine lend weight to our argument that this was a true drug-related response of the disease. Chlorpromazine is a cell-membrane stabiliser that is antihaemolytic in vitro at concentrations that are found therapeutically,[4] and it also diminishes the haemolysis produced by shear stress at pressures similar to those found in arterioles.[5] The hyaline arteriolar lesions of thrombotic thrombocytopenic purpura[1] might represent the cause or effect of haemolysis at sites of high shear stress. Chlorpromazine may prevent haemolysis with its consequent liberation of adenosine diphosphate, which is a powerful platelet-aggregating agent.[5] This might be the underlying mechanism of the thrombocytopenia. We suggest that chlorpromazine should be evaluated as soon as possible in further cases of thrombotic thrombocytopenic purpura.

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