SHORT REPORTS

Maternal autoimmune thrombocytopenia and the newborn

That a humoral factor was the causative agent in idiopathic thrombocytopenic purpura was suggested nearly 30 years ago after the observation that mothers with the disease often give birth to children who develop transient thrombocytopenia.¹ Maternal platelet autoantibodies were presumed to pass into the fetal circulation. With present techniques^{2,3} platelet autoantibodies are detectable in most patients with idiopathic thrombocytopenic purpura. We have therefore tried to confirm the passage of autoantibodies through the placental barrier and determine their immunochemical characteristics. We used specific antiglobulin reagents labelled with fluorescein isothiocyanate.

Patients and methods

We studied four pregnant women who fulfilled the criteria for idiopathic thrombocytopenic purpura.³ Three were primigravidae whose thrombocytopenia was first diagnosed during pregnancy. Two had platelet counts below $40 \times 10^9/l$ ($40\,000/mm^3$) on the day of diagnosis and were treated with prednisone two and three weeks, respectively, before delivery. The fourth woman was in her second pregnancy. During her first pregnancy she had also suffered thrombocytopenia ($70 \times 10^9/l$) which did not need treatment. The infant did not have purpura, although the platelet count in the neonatal period was not determined. All four women were delivered vaginally without excessive blood loss. The infants showed no evidence of haemorrhagic tendency or severe thrombocytopenia in the neonatal period. The table lists the results of the serological investigations.

Ether eluates prepared from platelets from maternal and cord blood in one case were tested against a panel of normal donor platelets typed for the platelet-specific alloantigens Zw, Ko, and Bak* and with the platelets of a patient with Glanzmann's thrombasthenia. Both eluates reacted equally well with all normal donor platelets, but not with thrombasthenic platelets, a reaction observed in about two-thirds of patients with autoimmune idiopathic thrombocytopenic purpura (unpublished observations).

Comment

In all four cases we confirmed the suspected transfer of IgG autoantibodies through the placenta. We also showed in two cases that additional IgM antibodies did not pass the placental barrier. The gradual disappearance of antibodies from the infants' platelets supports the passively acquired nature of these antibodies. This is further supported by the finding that the IgG subclass and blood group specificity pattern of the autoantibodies in two cases were identical in the mother and newborn.

None of the newborns developed severe thrombocytopenia, and no relation was found between the degree of platelet sensitisation in mother and child and the platelet count in the neonatal periods. Mothers, in remission of idiopathic thrombocytopenic purpura after splenectomy,¹ or with autoantibodies and moderate thrombocytopenia ($80-180 \times 10^9$ platelets/l), however, may give birth to a severely thrombocytopenic infants. Alloantibodies against platelets may also be formed by the woman during pregnancy, usually resulting in a more severe transient neonatal thrombocytopenia but with completely different therapeutic consequences.⁴ The introduction of reliable tests for detecting antibodies against platelets makes it possible to determine the presence of these antibodies and to differentiate between their autoimmune and alloimmune character.^{4,5} This enables optimal

measures and precautions to be taken in the present or future pregnancy, delivery, and neonatal period.

We thank the clinicians who participated in this study.

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Acquired megacolon associated with acute lead poisoning

The cause of acquired megacolon in adults is often obscure. Although lead poisoning is mentioned in some standard texts¹ as a cause, we have not been able to find any documented report linking the two conditions. We describe a patient with acute plumbism who presented with reversible megacolon.

Case report

A 39-year-old man had been employed as a painter and decorator for three years. Two weeks before admission he developed episodes of muscular weakness and colicky abdominal pain, together with a sensation of abdominal bloating and distension. One week after the onset of these symptoms he developed pains in his ankles, knees, hips, and wrists. He lost his appetite and also noted a diminution in his sense of taste, though during this period he observed an unusual craving to drink large amounts of milk. Towards the end of the second week of his illness he developed complete constipation, worsening of the abdominal pain and increase in his girth, insomnia, increased nervous irritability, and paraesthesia, principally in the arms and legs. During the three weeks before the onset of symptoms he had been cleaning the paint off the outside of an old building, down to the original surface, using a motorised wire brush. The original surface paint was applied in the 1920s. He had not worn any protective mask while doing this

Results of serological investigations in four mothers with autoimmune thrombocytopenia and their infants

Case No	Maternal blood			Infants' blood			3rd-day platelet count ($\times 10^9/l$)	Direct platelet immuno-fluorescence test	4th-week platelet count ($\times 10^9/l$)	Direct platelet immuno-fluorescence test
	Platelet count ($\times 10^9/l$)	Direct platelet immuno-fluorescence test	Ig class	Cord blood platelet count ($\times 10^9/l$)	Direct platelet immuno-fluorescence test	Ig class				
1	70	+	G	135	(+)	G	220	(+)	238	—
2	104*	++	G + M	145	++	G	196	(+)	256	—
3	140*	++	G ₁ + M	199	(+)	G ₁	240	—	> 200	Not tested
4	70	++	G ₁	202	++	G ₁	101	+ + / +	238	(+)

*After treatment with steroids.

and wondered whether the inhalation of the dust particles might have caused his illness. Regrettably, no samples of the old paint were available for laboratory analysis.

Physical examination on admission showed no abnormality. In particular, the patient had no pallor, no perianal or gum lead line (he was edentulous), his blood pressure was normal, there were no cardiovascular or objective neurological signs. A straight abdominal radiograph showed gas-filled, dilated loops of bowel with several fluid levels. A barium enema examination showed grossly distended and redundant colon, which accommodated 6 litres of barium with only partial filling (see figure). The haemoglobin concentration was 7.9 g/dl with small (mean cell volume 69.8 fl) hypochromic red cells showing pronounced basophilic stippling. Blood lead concentration (whole blood) on admission was 6.8 $\mu\text{mol/l}$ (140 $\mu\text{g}/100\text{ ml}$), and the erythrocyte protoporphyrin concentration was 1.94 ng/l (normal values: lead <1.5 $\mu\text{mol/l}$ (30 $\mu\text{g}/100\text{ ml}$); erythrocyte protoporphyrin <0.49 ng/l). The blood lead concentration was measured by anodic-stripping voltametry; the erythrocyte protoporphyrin concentration was measured fluorimetrically.² An electrocardiogram showed T-wave inversion in the lateral leads with high amplitude QRS complexes, suggesting left ventricular hypertrophy and strain. Manometric studies showed normal function of the myenteric plexus of the lower colon.³

X-ray film of barium enema, showing grossly distended and redundant colon.

Treatment was a modification of the method outlined by Chisholm,⁴ using a five-day course of a combination of dimercaprol 3 mg/kg four hourly intramuscularly and sodium calciumedetate 12.5 mg/kg four hourly intramuscularly. After five days of chelation treatment was continued with penicillamine 500 mg orally twice daily for six weeks, when the blood lead concentration had fallen to 3.1 $\mu\text{mol/l}$ (65 $\mu\text{g}/100\text{ ml}$), and the urinary lead excretion was 0.77 $\mu\text{mol/l}/24\text{ h}$ (160 $\mu\text{g}/24\text{ h}$). The patient has remained symptom-free, and a barium enema examination performed two months after treatment had been completed showed no abnormality.

Comment

The mechanism of lead colic is still unknown, though the condition was familiar to Hippocrates (370 BC), and lead poisoning in people handling paints was mentioned by Pliny (AD 27-79). In 1678 Vernatti (cited by Hunter⁵) graphically described lead colic: "The accidents to the workmen are, immediate pain in the stomach, with exceeding contortions in the guts, and costiveness that yields not to cathartics, hardly often to repeated clysters . . ."

The common symptoms and signs of individuals who become intoxicated with lead include colic; muscular weakness, which may lead to palsy—for example, wrist-drop; a lead line on the gums and about the anal margin, caused by bacterial action on the blood lead at these sites, precipitating out insoluble lead sulphide; pains in the muscles and joints; and anaemia. Severely affected individuals may develop encephalopathy and optic atrophy. Chisholm gives a complete review.⁴

Our patient had colic, muscular weakness, paraesthesia, joint pains, and anaemia. The profound degree of anaemia together with basophilic stippling and raised erythrocyte protoporphyrin values suggest that

he may well have experienced more chronic exposure than was apparent from the immediate history. The remarkable feature of this case, however, is the surprising degree of colonic dilatation when the patient first presented and the remarkable return to normal, both functionally and radiographically, once chelation treatment was completed. Acute dilatation of the colon may not be uncommon in patients with lead colic and may even play a part in the pathogenesis of the extreme constipation and pain.

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Myopathy induced by rifampicin

Myopathy is a well-recognised complication of treatment with certain drugs, particularly corticosteroids and anti-malarial agents,¹ but has not been reported with any of the conventional antituberculous drugs. We report a case of severe proximal myopathy caused by rifampicin.

Case report

A 44-year-old woman presented in 1974 with typical active pulmonary tuberculosis proved by sputum culture. She was treated for 16 months with isoniazid and rifampicin, supplemented for the first three months by daily injections of streptomycin.

In October 1980 symptoms recurred and chest radiography showed fresh cavitation. Direct smear of sputum was negative for acid-fast bacilli, but Löwenstein-Jensen cultures subsequently yielded colonies of mycobacteria. Treatment was started with streptomycin, rifampicin, isoniazid, and ethambutol. After four weeks she was readmitted, complaining of increasing proximal muscle weakness in the arms and legs and inability to stand unaided. There was no paraesthesia, anaesthesia, or muscle pain. Facial and ocular muscles were not affected, and she did not have dysphagia or abnormal fatigability to suggest myasthenia gravis.

Physical examination showed no abnormality apart from appreciable proximal muscle weakness, which was greater in the legs than the arms and was accompanied by symmetrical proximal muscle wasting. No rash, muscle tenderness, or fasciculation was present. Normal values were obtained for full blood count; urea and electrolyte, serum calcium, and plasmaprotein concentrations; creatine kinase activity; and thyroid function tests. Erythrocyte sedimentation rate was 48 mm in first hour. A Tensilon test showed no response in any muscle group.

All drugs were stopped and within 24 hours muscle power had increased dramatically. An electromyogram performed six days after the drugs were stopped showed no abnormality. Eight days after the drugs were stopped muscle power had returned to normal. Isoniazid was reintroduced at full dosage without any problems. Rifampicin was then added at full dosage and within 24 hours severe muscle weakness recurred. An electromyogram again showed no abnormality, but a muscle biopsy specimen showed predominant type II muscle fibre atrophy associated with sarcolemmal nuclei proliferation and increase in connective and fatty tissues, consistent with a drug effect. Rifampicin was withdrawn and within five days power returned to normal. Ethambutol was subsequently reintroduced without any further problem. Rifampicin antibodies were absent six weeks after the drug was stopped.

The mycobacterium cultured from the original sputum and a specimen one month after treatment was identified as *Mycobacterium xenopi*, highly resistant to all antituberculous drugs except rifampicin and streptomycin. Lobectomy was performed to eradicate the disease.