was disorientated in space and time. He was totally unable to take seven from 100 or to perform other simple acts of reasoning. He continually buttonholed passers-by and persisted in making long, incoherent, and confused complaints. He made continuous writhing movements of his right arm and hand and to a lesser extent of his right leg. As he spoke he made strange grimaces and continuously moved his lips and tongue in an uncoordinated fashion. He had no other neurological signs, and a psychiatric opinion at this time was that he was suffering from a toxic confusional state. Apart from the oxymetholone, he had been taking no medication. He had no fever and no other physical signs; in particular, he had no evidence of a bleeding tendency and his blood pressure was 120/70 mm Hg.

Full blood count showed a haemoglobin concentration of 13·7 g/dl, white blood count of $5{\cdot}8 \times 10^9$/l, and platelet count of 132×10^9/l. Results of liver function tests showed a mildly raised bilirubin concentration at 25 μmol/l (1·5 mg/100 ml) but no other abnormality. Serum B_{12} concentration was 281 ng/l, and serum folate concentration was 9·6 μg/l. Result of a Venereal Disease Research Laboratory test was negative. Findings on electroencephalography were normal. Findings on isotopic brain scan and a computed tomography scan of the skull were normal. The patient was sedated with thioridazine 225 mg day, and oxymetholone was withdrawn. His confusional state remained unchanged for 20 days but thereafter began to improve, and he was thought well enough to go home from hospital 25 days after stopping the oxymetholone. When seen in outpatients one month later, he was entirely normal and his aplastic anaemia had not relapsed.

Comment

Neither a toxic confusional state nor extrapyramidal movements have previously been reported in patients taking androgens. Nevertheless, the blood dyscrasia of this patient was in remission, making a vascular cause unlikely, and the absence of any other neurological lesion and the improvement on withdrawal of the oxymetholone make it likely that this drug was the cause of these symptoms. No mechanism can be suggested, but doctors should beware of this bizarre syndrome appearing in patients secretly taking androgens to improve athletic prowess.

We are grateful to Dr G Sedman for his psychiatric opinion on this patient.

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Effect of prostaglandins I_2 and E_1 on red cell deformability in patients with Raynaud's phenomenon and systemic sclerosis

The deformability of red blood cells measured by a filtration technique using whole blood has been found to be decreased in some patients with Raynaud's phenomenon and greatly improved by plasmapheresis.[1] Prostaglandins E_1[2] and I_2[3] (PGE_1 and PGI_2) administered intravenously have produced prolonged benefit in patients with symptomatic Raynaud's phenomenon associated with systemic sclerosis. To elucidate the possible mechanism of action of these drugs we measured red cell deformability in plasma-free conditions in 12 patients with systemic sclerosis and Raynaud's phenomenon.

Subjects, methods, and results

Red cell deformability was measured in 12 patients with Raynaud's phenomenon and systemic sclerosis and 12 normal controls matched for age and sex. It was also measured immediately before and after the infusion of PGI_2 (seven patients) and PGE_1 (five patients). PGI_2 and PGE_1 were administered as infusions through centrally placed intravenous catheters (total duration 72 hours). The dose of PGI_2 varied from 5 to 7·5 ng/kg/min, and the dose of PGE_1 was increased from 6 to 12 ng/kg/min by increments of 2 ng/kg/min. Red cell deformability was measured using the original technique of Schmid-Schonbein *et al*[4] with Reid's technical modification. Plasma-free conditions were used to ensure that the observed effects were on the red cells and not other constituents of whole blood.

Red blood cells were separated from heparinised venous blood by centrifugation and washed three times in phosphate-buffered saline (pH 7·4) containing 0·25% human albumin. The final red blood cell suspension (10% v/v) was passed through a Nucleopore polycarbonate sieve of pore diameter 3 μm, using a negative pressure of 10 cm water. After a steady flow through the filter had been achieved the filtration time per ml volume was registered from 1 ml to 10 ml volume and plotted on semilog paper. The slope of this line represented the filtrability (ml/min). Standard conditions were used. Triplicate determinations were performed on each sample of venous blood, the assay being performed in all cases within two hours of venepuncture at a temperature of 21 ± 1°C.

Red blood cell deformability was significantly different between the patients and controls, the mean ± SEM blood flow/min being $0{\cdot}257 \pm 0{\cdot}02$ ml/min in the patients (two women, 10 men) compared with $0{\cdot}512 \pm 0{\cdot}04$ ml/min in the controls ($p < 0{\cdot}001$).

Mean blood flow/min measured by filtration immediately before the infusion of PGI_2 (seven patients) and PGE_1 (five patients) for Raynaud's phenomenon confirmed the presence of reduced red blood cell deformability in these patients (table). After the 72-hour infusions of PGI_2 and PGE_1 the mean blood flow/min—that is, red blood cell deformability—was increased ($p < 0{\cdot}05$ and $p < 0{\cdot}01$ respectively).

Deformability of red blood cells from patients with systemic sclerosis before and after infusions of PGI_2 and PGE_1

	No of subjects		Mean ± SEM red blood cell filtrability (blood flow/min)*	Effect of infusion		p
	Men	Women		Patients improved	No change	
			Infusion of PGI_2			
Before	1	6	0·269 ± 0·03	6	1	<0·05
After			0·413 ± 0·06			
			Infusion of PGE_1			
Before	1	4	0·218 ± 0·01	5		<0·01
After			0·400 ± 0·04			

*Measured by 3 μm pore diameter filter.

Comment

PGE_1 affects different functions of platelets, polymorphonuclear leucocytes, and lymphocytes and increases both the deformability and the cyclic adenosine monophosphate content of red blood cells. Moreover, recent evidence suggests a role for cyclic nucleotides in regulating the shape and permeability of red blood cells.[5] The effect of PGI_2 on red blood cell behaviour has not been described previously.

The decreased red blood cell deformability in patients with Raynaud's phenomenon and systemic sclerosis may have pathophysiological importance, contributing to the microcirculatory insufficiency by increasing the occlusion of small blood vessels and blood viscosity at low shear rates. Possibly the decreased red blood cell deformability in patients with Raynaud's phenomenon and systemic sclerosis may be linked to a deficiency of cyclic adenosine monophosphate in the red cells of these patients, and the PGI_2 and PGE_1 may increase the red cell deformability by increasing the intracellular content of cyclic adenosine monophosphate.

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