bilateral pulmonary nodules. Histological examination of a biopsy sample of the thigh mass suggested synovial sarcoma.

Because of the metastatic pulmonary lesions 150 mg doxorubicin was given by intravenous injection. Three days later the haemoglobin concentration fell suddenly to 10·6 g/dl (reticulocytes 4·1%). Results of Coombs tests were negative. Supravital staining (cresyl blue) of a blood film showed numerous Heinz bodies. In addition, there was evidence of both haemoglobinaemia and haemoglobinuria. Over the next few days the haemoglobin concentration dropped to 9·2 g/dl (9·8% reticulocytes), but three weeks later it had returned to 14·0 g/dl (2·1% reticulocytes). At the patient's request no further chemotherapy was given, and he died three months after his initial presentation.

Comment

The sudden decrease in haemoglobin concentration after administration of doxorubicin strongly suggests that this drug was causally related to the acute haemolytic episode. Although a wide variety of treatments may induce haemolysis in patients with G6PD deficiency, I was unaware that antineoplastic agents might do so. None the less, metabolic insults to red blood cells have been described after exposure to cytotoxic drugs in vitro[2-5]; doxorubicin generates reactive oxygen compounds[3] and methaemoglobin[2] in normal human red blood cells in vitro. Furthermore, in red blood cells deficient in G6PD doxorubicin poses a potent oxidant stress, as shown by the production of hydrogen peroxide and depletion of reduced glutathione.[4] These findings support the suggestion that doxorubicin acts as an oxidant stress to both G6PD deficient and normal red blood cells. Thus patients with G6PD deficiency might be susceptible to haemolysis after receiving doxorubicin. Moreover, the possibility of oxidative haemolysis should be considered in any patient who shows an unexplained drop in haemoglobin concentration after treatment with this agent.

I thank Mrs G Congleton for her technical help in preparing the manuscript.

1 Heller P, Best BR, Nelson RB, Becktel J. Clinical implications of sickle-cell trait and glucose-6-phosphate dehydrogenase deficiency in hospitalized black male patients. *N Engl J Med* 1979;**300**:1001-5.

2 Barr RD, Davidson AR, Jung KL, Pai KRM. Erythrocytotoxicity induced by cancer chemotherapeutic agents. In vitro studies of osmotic fragility and methaemoglobin generation. *Scand J Haematol* 1980;**25**:363-8.

3 Henderson CA, Metz EN, Balcerzak SP, Sagone AL Jr. Adriamycin and daunomycin generate reactive oxygen compounds in erythrocytes. *Blood* 1978;**52**:878-85.

4 Sagone AL Jr, Burton GM. The effect of BCNU and adriamycin on normal and G6PD deficient erythrocytes. *Am J Hematol* 1979;**7**:97-106.

5 Sponzo RW, Arseneau JC, Canellos GP. Procarbazine induced oxidative haemolysis: relationship to in vivo red cell survival. *Br J Haematol* 1974;**27**:587-95.

(*Accepted 22 March 1983*)

Veterans Administration Center, Phoenix, Arizona 85012, USA
D C DOLL, MD, chief, oncology-hematology section

Abnormalities of lymphocyte subsets in polymyositis

Polymyositis (dermatomyositis if the characteristic rash is present) is an inflammatory myopathy of unknown aetiology. Considerable circumstantial evidence suggests that immune mechanisms play a part in its pathogenesis.[1] The functions of the different cellular components of the immune system have recently become easier to study because of the availability of monoclonal antibodies that recognise single antigenic determinants. These antibodies are used widely to identify lymphocyte subpopulations, and analyses of the different subgroups with a fluorescence activated cell sorter have shown changes in the ratio of helper to suppressor cells in several diseases.[2] A balance between these lymphocytes is presumably necessary for immune homeostasis, and it has been postulated that immunologically mediated disorders may be due to aberrations in T cell immune regulation. We therefore studied the lymphocyte subpopulations in patients with polymyositis.

Patients, methods, and results

We studied 18 patients with proved polymyositis; 11 had a concomitant rash. As there is no evidence that the presence of skin lesions is due to a different aetiology we did not distinguish between dermatomyositis and polymyositis in this study. The patients were divided into three groups as follows: five patients had acute disease of less than three months' duration and were not receiving treatment; eight had had chronic active polymyositis for from nine months to 10 years and were taking 5-10 mg prednisolone on alternate days; and five had made a complete recovery from the disorder six months to 11 years previously and were not receiving treatment. In addition we studied 15 control subjects with various neuromuscular disorders—for example, the Guillain-Barré syndrome, myasthenia gravis, alcoholic myopathy, seven of whom were taking prednisolone 5-10 mg on alternate days, and 20 normal healthy volunteers.

Mononuclear cells were isolated from heparinised peripheral blood using Ficoll-Hypaque (Pharmacia Fine Chemicals) gradient density centrifigation and then stained with Ortho-mune monoclonal antibodies (OK) T3, T4, T8, or Ia1 (Ortho Diagnostic Systems Ltd, Buckinghamshire) followed by fluorescein conjugated antimouse IgG (sheep F (ab)2 antimouse Ig, fluorescein conjugated, New England Nuclear, Boston, Mass, USA) as described.[3] Lymphocytes were analysed with a fluorescence activated cell sorter model IV (Becton Dickinson, Mountain View, California) using logarithmic amplification of the fluorescence signal[4] and with 90° scatter to eliminate all contaminating monocytes. The Ia1 percentage obtained was considered to represent only B cells and activated T cells.

Analysis of lymphocyte subpopulations in 18 patients with polymyositis (group results expressed as means (SEM))

Case No	% reactivity with monoclonal antibodies				T4:T8 ratio
	T3	T4	T8	Ia 1	
	Acute polymyositis (n = 5)				
1	53	49	10	27	5
2	78	70	10	16	7
3	41	39	4	53	10
4	61	57	13	25	4·4
5	56	43	27	19	1·6
	Chronic active myositis (n = 8)				
6	87	82	6	5	14
7	93	82	10	6	8
8	76	68	14	13	5
9-13	78 (2)	60 (3)	18 (3)	14 (3)	2·8 (0·1)
	Recovered from polymyositis (n = 5)				
14-18	71 (4)	52 (5)	24 (1)	19 (2)	2·1 (0·1)
	Neuromuscular disorders (n = 15)				
	70 (3)	45 (2)	24 (1)	19 (2)	2·0 (0·1)
	Healthy controls (n = 20)				
	75 (2)	49 (2)	25 (2)	12 (1)	2·1 (0·1)

The table shows the results. Patients with acute and chronic active disease had gross abnormalities in their lymphocyte subgroups: suppressor/cytotoxic cells were conspicuously reduced in both groups, total T lymphocytes and helper cells were decreased in patients in the acute phase, and helper cells were increased in patients with chronic active disease. The abnormalities persisted in patients with chronic active disease who were studied serially for three months.

Comment

These results show that lymphocyte subpopulations are disturbed in patients with acute and chronic active polymyositis, with a conspicuous decrease in the numbers of suppressor/cytotoxic cells. These findings are similar to those reported in other immunologically mediated disorders.[2] Some patients with multiple sclerosis show a similar loss of suppressor cells before a clinical relapse occurs, with reappearance of the cells when the disease remits.[2] In our cases the number of suppressor cells was reduced for at least three months in the patients tested serially. The findings documented here were not secondary to steroid treatment because the abnormalities were detected whether or not the patients were taking the drugs and no changes were present in control subjects taking a similar prednisolone dosage.

In a study of two children with dermatomyositis Bresnan *et al* reported a fall in circulating suppressor cells similar to the one shown here.[5] Muscle biopsy specimens taken at the same time contained a mixed mononuclear cell infiltrate in which inducer (helper) cells, not suppressor cells, were most prominent. Our preliminary studies, on the other hand, have shown one case in which T8 cells were prominent in the inflammatory infiltrate between muscle fibres.

These findings confirm that there is a gross disturbance of immunoregulation in polymyositis.

We acknowledge the excellent technical help of R A Gray and Mrs C Menzies. This work was supported by the Muscular Dystrophy Group of Great Britain. The fluorescence activated cell sorter model IV was provided by the Cancer Research Campaign.

[1] Behan WMH, Behan PO. A comparison between human polymyositis and the putative animal model, experimental allergic myositis. In: Rose FC, Behan PO, eds. *Animal models of neurological disease*. London: Pitman Medical, 1980:72-89.
[2] Weiner HL, Hauser SL. Neuroimmunology 1: Immunoregulation in neurological disease. *Ann Neurol* 1982;**11**:437-49.
[3] Reinherz EL, Kung PC, Goldstein G, Schlossman SF. A monoclonal antibody with selective reactivity with functionally mature human thymocytes and all peripheral human T cells. *J Immunol* 1979;**123**: 1312-7.
[4] Ledbetter JA, Rouse RV, Micklem HS, Herzenberg LA. T cell subsets defined by expression of Lyt-1,2,3 and Thy-1 antigens. *J Exp Med* 1980; **152**:280-95.
[5] Bresnan MJ, Hauser SL, Weiner HL, Reinherz E, Borel Y, Bhan A. Characterization of T-cell subsets in peripheral blood and muscle in childhood dermatomyositis [Abstract]. *Ann Neurol* 1981;**10**:283.

(*Accepted 7 April 1983*)

Glasgow University, Glasgow
WILHELMINA M H BEHAN, MB, FRCPATH, senior lecturer in pathology
P O BEHAN, MD, FRCP, reader in neurology

Edinburgh University, Edinburgh
H S MICKLEM, DPHIL, reader in zoology

Glasgow Royal Infirmary, Glasgow
W F DURWARD, MB, FRCPGLAS, consultant neurologist

Correspondence to: Dr P O Behan, Institute of Neurological Sciences, Southern General Hospital, Glasgow G51 4TF.

Cardiac arrhythmias during high spinal surgery

Sudden unexpected cardiac arrest during surgery on the upper thoracic spine has been reported, and there has been speculation about the role of sympathetic stimulation in precipitating ventricular fibrillation.[1] I report a case in which cardiac arrhythmias were observed related to surgical stimulation during total laminectomy at the level of the first and second thoracic vertebras for excision of an intradural neurofibroma.

Case report

The patient, a previously fit 62 year old woman, gave a two year history of increasing weakness of the left leg. There was radiological evidence of an intradural mass at the level of the second thoracic vertebra. As a result of a sudden deterioration in her neurological state immediate operation was decided on. She had received two previous general anaesthetics, the most recent being 15 months previously for a stapedectomy. There had been no problems during anaesthesia. Systematic inquiry elicited no symptoms related to the cardiovascular or respiratory system. She took no medication and had no known allergies. Pulse rate was 60 beats/min with a regular rhythm and blood pressure 130/80 mm Hg. Physical examination showed no abnormalities other than that in the central nervous system.

Anaesthesia was induced with sodium thiopentone 300 mg and suxamethonium chloride 75 mg. The trachea was then intubated with an 8·5 mm armoured latex endotracheal tube. Air entry to both lungs was checked by auscultation. Ventilation was maintained with a Cape Waine mark III anaesthetic ventilator using 30% oxygen and 70% nitrous oxide. Ventilation was adjusted to produce an end tidal carbon dioxide concentration of 3·0-3·5% with an inflation rate of 10 breaths/min. Expired tidal volume, measured with a Wright respirometer, was 650 ml. The inflation pressure was 20 cm water.

She was placed in the prone position with supports under the chest and pelvis. Anaesthesia was maintained with papaveretum given in divided doses to a total of 15 mg and halothane 0·5% delivered via a Fluotec mark III vapouriser. Muscle relaxation was maintained with pancuronium bromide 6 mg. Systolic blood pressure was measured with a sphygmomanometer cuff around the upper arm; throughout anaesthesia it remained within the range 100-120 mm Hg. An intravenous infusion was established, and a total of 900 ml crystalloid plus one unit of whole blood was infused during surgery and the immediate postoperative period.

At the start of surgery an electrocardiogram showed sinus rhythm with a rate of 80-90 beats/min. As the laminas were removed and dura exposed multifocal ventricular ectopics appeared with a frequency varying between one in six and one in 20 normal beats. The frequency of these ectopic beats was directly related to surgical stimulation, falling when surgery was stopped and immediately increasing when surgical stimulation was resumed. During this period the blood pressure remained stable with no evidence of any adverse haemodynamic effects. Neither additional analgesia in the form of further incremental doses of papaveretum nor withdrawal of the halothane appeared to affect the nature or frequency of the arrhythmias. The ectopic beats continued at a lower frequency for the next 24 hours. A 12 lead electrocardiogram obtained six days postoperatively showed normal sinus rhythm with no ectopic beats and no evidence of myocardial ischaemia. There were no cardiac enzyme changes.

Comment

It has been shown experimentally in primates that acute compression of the spinal cord in the mid-thoracic region can produce cardiac arrhythmias.[2] These effects are mediated via the sympathetic and parasympathetic nervous systems and may be abolished by adrenergic and cholinergic blockade. As cardiac arrest may occur during high thoracic laminectomy this may be the precipitating mechanism. The above case report emphasises the necessity of continuous electrocardiographic monitoring during the procedure, and the results of animal experiments suggest that prophylactic cholinergic or adrenergic blockade, or both, may be appropriate.

[1] Marshall MM. *Neuroanaesthesia*. London: Edward Arnold, 1979:58. (*Current Topics in Anaesthesia* No 3.)
[2] Evans DE, Kobrine AI, Rizzoli HV. Cardiac arrhythmias accompanying acute compression of the spinal cord. *J Neurosurg* 1980;**52**:52-9.

(*Accepted 15 April 1983*)

Department of Anaesthesia, Newcastle General Hospital, Newcastle upon Tyne NE4 6BE
P R RAYNER, MB, FFARCS, senior registrar

Correspondence to: Dr P R Rayner, Department of Anaesthesia, Royal Victoria Infirmary, Newcastle upon Tyne.

MEDICINES HOT IN THE FIRST DEGREE—Those are said to be hot in the first degree, which induce a moderate and natural heat to the body, and to the parts thereof; either cold by nature, or cooled by accident, by which natural heat is cherished when weak, or restored when wanting. The first effect then of medicines hot in the first degree is, by their sweat and temperate heat to reduce the body to its natural heat, as the fire doth the external parts in cold weather, unless the affliction of cold be so great that such mild medicines will not serve the turn. The second effect is, the mitigation of pain arising from such a distemper, and indeed this effect hath other medicines, some that are cold, and some that are hotter than the first degree, they being rationally applied to the distemper. These medicines the Greeks call *Anodyna*, and shall be spoken of in their proper places. In this place let it suffice that medicines hot in the first degree, make the offending humours thin, and expel them by sweat, or insensible transpiration, and these of all others are most congruous or agreeable to the body of man, for there is no such equal temperature of heat and cold in a sound man, but heat exceeds, for we live by heat and moisture, and not by cold. Medicines then which are hot in the first degree, are such as just correspond to the natural heat of our bodies; such as are hotter or colder, are more subject to do mischief, being administered by an unskilful hand, than these are, because of their contrariety to nature; whereas these are grateful to the body by their moderate heat. Thirdly, These take away weariness, and help fevers, being outwardly applied, because they open the pores of the skin, and by their gentle heat prepare the humours, and take away those fuliginous vapours that are caused by fevers. Yet may discommodities arise by heedless giving even of these, which I would have young students in physic be very careful in, lest they do more mischief than they are aware of, viz It is possible by too much use of them, to consume not only what is inimical in the body, but also the substance itself, and the strength of the spirits, whence comes faintings, and sometimes death: besides, by applying them to the parts of the body they are not appropriated to, or by not heeding well the complexion of the patient, or the natural temper of the part of the body afflicted, for the heart is hot, but the brain temperate. Lastly, Medicines hot in the first degree, cherish heat in the internal parts, help concoction, breed good blood, and keep it good in temper, being bred. (Nicholas Culpeper (1616-54) *The Complete Herbal*, 1850.)