Macroglobulinaemia: Case Features

Author	Sex and Age	Duration (Years)	Lymphocytosis		Macroglobulin	
			Blood	Bone Marrow	Mobility	Sedimentation Constant
Waldenström (1944)	M 62	8	Yes	Yes		19.2
	M 65	2	"	"	Between β and γ	19.7, 25, 29.3
Bichel <i>et al.</i> (1950)	M 76	14	"	"	β	20
Tischendorf and Hartmann (1950)	M 66	2	"	"	β	Mol. wt. 1,800,000
McFarlane <i>et al.</i> (1952)	M 52	14	"	"	Between β and γ	18, 28
Schaub (1952)	F 32	3	"	"	Between β and γ	19-20
Pernis <i>et al.</i> (1954)	M 68	2	"	"	γ	17.5, 24
	M 64	1½	"	Yes	β	20
	M 72	2	"	"	γ	26
Wilde and Hitzelberger (1954)	M 72	8	"	"		16.6
	F 51	6	No	"		19
	F 71	3	Yes	"		16
Mandema <i>et al.</i> (1955)	M 69	1	"	"	γ	15.8
	M 71	8.12	"	"	γ	19.2, 30.9
Mackay <i>et al.</i> (1956)	M 67	14	Yes	"	γ	15, 20
Jim and Steinkamp (1956)	F 79	4	"	"	γ	17, 24
Present case	M 60	2	"	"	Between β and γ	18

such as the Bence Jones proteins, which have molecular weights of the order of 25,000 to 75,000. Cryoglobulins—that is, globulins which coagulate or precipitate in the cold—vary greatly in molecular weight and in other ways. The macroglobulins found in the cases mentioned appear to be a group of proteins rather than a single entity. The Table shows that the sedimentation constants are not identical, and that the electrophoretic mobilities have lain in the β or γ globulin ranges or sometimes in between. Six have been described as cryoglobulins; such cryoglobulin could not be detected in the blood of our patient. Some macroglobulins give a 'positive "water" test—that is, copious precipitates are formed when the serum is dropped into large volumes of distilled water—but this property is not invariably present, and was absent in our case. A feature of this group of cases is the large amount of macroglobulins found in the blood. In our case as much as 2 to 3 g. per 100 ml. was present. Small quantities of macroglobulin may be present in normal serum (Pedersen, 1945), and therefore pathological macroglobulinaemia may be due to a derangement of normal mechanisms.

Pathogenesis.—The presence of an excess of globulin and of abnormal globulins is characteristic of various disorders involving the reticulo-endothelial system. The similarity of the 17 cases here discussed suggests that a clinical entity is being described, but its nature remains uncertain. The lymphocytosis in the peripheral blood is paralleled by lymphoid hyperplasia in bone-marrow smears, but an excess of plasma cells has also been found in the latter on occasion. Lymphoid or plasma-cell hyperplasia, or both, have been observed in sections from lymph nodes, spleen, bone marrow, and other organs obtained on biopsy or at necropsy. The condition therefore has affinities with both lymphatic leukaemia and multiple myelomatosis, but final elucidation of its nature must await further evidence. In any event, it is unlikely that macroglobulinaemia will be found confined to any one disease, any more than Bence Jones proteinuria is exclusively associated with multiple myelomatosis. The second case reported by Schaub (1952) may be a case in point.

Treatment.—Cortisone, amidines, urethane, and nitrogen mustard have been used by others without seeming effect on the underlying process, though the last-mentioned drug appeared to be of value in our case.

Summary

A case of macroglobulinaemia is described. The rather characteristic features of this and similar cases from the literature are reviewed.

We wish to thank Dr. J. F. Heggie for laboratory facilities; Dr. A. H. T. Robb-Smith for a report on the bone-marrow smears and for advice on pathological aspects of these cases; Dr. A. S. McFarlane for the ultracentrifuge study; Mr. J. H. Dobree for ophthalmological reports; Mr. T. R. Tarrant, of the Institute of Ophthalmology, for the retinal drawing; and Dr. R. G. Macfarlane and Professor N. H. Martin for assistance.

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Medical Memoranda

Anterior Tibial Syndrome after Acute Arterial Occlusion, Treated by Decompression

In his report of instances of an anterior tibial syndrome following arterial embolism, Watson (1955) suggests that surgical decompression of the ischaemic muscles should be attempted. The present communication reports the successful use of this treatment in a case of acute arterial occlusion which was probably due to arterial thrombosis rather than embolism (Jepson, 1955).

CASE REPORT

A man aged 68 was admitted as an emergency case at 11.15 p.m. on July 20, 1955. Five hours previously he had experienced a sudden severe pain in his right leg, which rapidly became cold, numb, and paralysed. For several months before admission he had suffered from angina of effort and intermittent claudication.

On examination his general condition was good and his temperature normal. A loud blowing systolic murmur was heard all over the praecordium, maximal at the aortic area, but there was no other evidence of cardiac disease. The left lower limb appeared healthy and the usual pulses could be felt in it. The right was pale, and felt cold from a level just above the knee. No pulsation could be felt distal to the femoral artery. Voluntary movements of the ankle were absent and there was complete sensory loss distal to the knee.

Medical treatment for arterial embolism was instituted with tolazoline, papaverine, heparin, and phenindione. Within 24 hours the whole limb, except the outer side of the foot, felt as warm as the left. No pulses had returned, but motor and sensory functions had greatly improved.

On the next morning the patient complained of pain down the front of the right leg. The pain increased during the day, and could be controlled only by morphine. By the evening the antero-lateral part of the leg was swollen and the skin over it reddened. Dilated veins could be seen here, and the maximum calf circumference was $\frac{1}{2}$ in. (1.3 cm.) more than on the left side. Sensory loss was demonstrable in this area and in that corresponding with the cutaneous distribution of the anterior tibial nerve. In view of the patient's good general state and severe pain, the anterior tibial compartment was explored.

Under general anaesthesia, a linear incision some 8 in. (20 cm.) long was made over the reddened skin area. When the deep fascia was incised the anterior tibial muscles bulged outwards and were seen to have a well-marked patchy yellowish discoloration. This faded during the next five minutes, and the muscles by that time appeared normal.

Small portions were cut from the anterior tibial and peroneal muscles. The skin was sutured over the open fascia. A plaster back slab was applied for a week.

After operation the pain in the leg was dramatically relieved. Movements of the foot improved during the following week, extension of the great toe being the last to recover. The wound healed slowly, with some sloughing of its edges.

The patient was discharged on August 25, and when examined a month later had no symptoms referable to his leg. Recovery of muscle power was complete except for some persistent weakness of the extensor hallucis longus.

The muscle fragments showed, in the case of tibialis anterior, interstitial oedema and leucocytic infiltration with extensive degeneration and early necrosis of muscle fibres. The control specimen from the peronei showed only some fatty infiltration.

The delay in the healing of the operation wound, which might be more serious in a limb with a greater degree of ischaemia, suggests that a case can be made for performing decompressions of this sort through a small incision, using Gallie's fasciotome.

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Enteritis and Polyarthritis following Partial Gastrectomy

Examples of severe diarrhoea following major abdominal surgery were reported by many observers long before the use of antibiotics, and particularly since. Finney in 1893 first described a fatal case following pylorotomy and gastro-enterostomy, and Riedel in 1902 described two fatal cases following gastrectomy. Penner and Bernheim (1939) extensively reviewed the subject just prior to the antibiotic era. From a study of the clinical records and post-mortem material in 40 cases, following a variety of operations, including gastrectomy, appendectomy, and lobectomy, they concluded that the vasomotor mechanisms known to occur in shock were responsible for the enteritis and that infection was only of secondary importance. Penner and Druckerman (1948), Dixon and Weismann (1948), Williams and Pullan (1953), and Fowler (1955) have all described cases subsequent to the use of antibiotics, many of which were fatal.

It is accepted that the use of antibiotics may lead to enteritis. Fairlie and Kendall (1953) described five examples following the use of a mixture of penicillin and streptomycin, and Fowler (1955) described three fatal cases following the use of mixed antibiotics. It is believed that the use of antibiotics allows a resistant organism, usually a staphylococcus, to start up the enteritis, but Fairlie and Kendall suggested that the aetiology was more complex; they postulated that, in view of the early onset of diarrhoea in some cases, there may be a direct stimulation of toxin production by the antibiotics.

In the following case severe diarrhoea developed on the fifth day after partial gastrectomy and was accompanied by a rigor and auricular fibrillation; the diarrhoea persisted for 48 hours, ceased, and polyarthritis developed. The diagnosis of enteritis causing pyaemia was made and the patient recovered on erythromycin.

CASE REPORT

A fit man aged 45 underwent partial gastrectomy for a chronic duodenal ulcer 48 hours after admission to hospital, and his bed was next to that of an old man who had developed enteritis. "Distaquine" penicillin, 300,000 units twice

daily, and streptomycin, 0.5 g. twice daily, were given post-operatively for four days. On the third post-operative day he complained of some abdominal discomfort and pain in the left loin. He vomited 30 ml. of bile-stained fluid and a further 1,400 ml. was withdrawn on passing a Ryle tube. His temperature was 99° F. (37.2° C.) and his abdomen a little distended. Next day he felt better and his temperature returned to normal.

On the fifth day he passed eight very loose and slightly offensive stools and complained of backache and feeling cold. His temperature was 99° F. (37.2° C.) and he was sweating profusely. There was moderate abdominal distension with generalized tenderness, and the pulse was 120 a minute and irregular, owing to auricular fibrillation. Next day his temperature was normal, pulse 100 a minute and regular, and blood pressure 120/85. He complained of backache and pains in all the large joints, and the diarrhoea gradually ceased. The white blood count was 31,000, and examination for subphrenic abscess, pelvic abscess, and pus at other sites was negative. On the seventh day his temperature was 100.4° F. (38° C.) and pulse 120. Marked distension of the abdomen had developed, with effusions into both knees.

Enteritis causing pyaemia was diagnosed and the abdominal distension was thought to be due to ileus. However, discussion led to laparotomy the same day, and this showed the whole of the small intestine and caecum to be distended and injected; there were many enlarged mesenteric glands, some of which were haemorrhagic. The left knee-joint was aspirated and purulent fluid sent for culture.

A course of 250 mg. of erythromycin intravenously four-hourly was started, changed to six-hourly after 24 hours, and given six-hourly orally after 48 hours. The total dose was 4.5 g. Bacteriological examination of the stools did not reveal a pathogen, the blood culture was negative, and the purulent fluid from the knee was sterile on culture.

On the following day he was much improved and he made an uneventful recovery, the effusions in the knees disappearing in a week and the bowel action slowly returning to the passage of one or two normal stools a day.

COMMENT

The importance of this case is that the patient developed enteritis following partial gastrectomy, that penicillin and streptomycin were used post-operatively for four days, and that arthritis developed as a further complication. Arthritis as a pyaemic lesion subsequent to peritonitis is not seen; enteritis causing arthritis is, however, common in the infectious fevers, and this fact made the clinical diagnosis possible.

A leak at one of the anastomoses was regarded as a cause of the abdominal signs and symptoms, particularly in view of the leucocytosis of 31,000; pancreatitis was excluded by a serum amylase estimation, though this condition does not cause clinical arthritis, anyway. Arthritis may be caused by penicillin and streptomycin therapy, but a skin rash would almost certainly be present. Whilst the correct diagnosis was made clinically, it was not so firmly made that laparotomy was avoided.

It was disappointing that the joint effusion was sterile and that we do not know what organism caused the enteritis. However, in view of the fact that the polyarthritis developed soon after the severe diarrhoea, it is reasonable to think that an organism resistant to penicillin and streptomycin produced this dangerous picture.

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