AMYLOIDOSIS PRESENTING AS LYMPHADENOPATHY

BY

D. H. MACKENZIE, M.A., M.D.

Senior Lecturer in Pathology and Honorary Consultant Pathologist, Westminster Hospital, London

Recent years have seen a revival of interest in amyloidosis, particularly the primary type. The very extensive literature describes involvement of virtually every organ in the body, and amyloidosis is now considered in the differential diagnosis of many obscure cases. Relatively few authors have described amyloid involvement of lymph nodes, and these include Binford (1940), Pearson *et al.* (1941), Lindsay and Knorp (1945), Eisen (1946), Massachusetts General Hospital (1949), and Symmers (1956). Amyloidosis presenting as lymphadenopathy is extremely rare. Miller (1929) described a case presenting with enlarged cervical nodes. In this case, however, they were involved not only by amyloid but by an anaplastic tumour of uncertain nature. In the case described by Dillon and Evans (1942) the patient had large masses in the left axilla and smaller ones in the right. These proved to be lymph nodes replaced by amyloid, and the patient died of primary amyloidosis. In view of the rarity of this presentation the following three cases are described. All sections were stained with thioflavine-T according to the method of Kurban (1960), with congo red, and with methyl violet.

Case 1

The patient, a man aged 32, was admitted to Westminster Hospital for investigation of a mass of enlarged glands in the left deep cervical chain. Five years and three years prior to admission he had had attacks of acute left-sided parotitis associated with cervical adenitis. On both occasions the parotitis had resolved, but after the second attack the cervical glands remained enlarged. At that time he was treated with deep x-ray therapy empirically, with some reduction in the size of the glands.

On clinical examination no abnormality was found apart from the enlarged glands, and, with the exception of a raised E.S.R. of 100 after one hour, haematological and radiological investigations were normal. The glands were removed surgically and the operation specimen consisted of eight enlarged lymph nodes varying from 1 to 4 cm. in diameter and together weighing 80 g. They were well encapsulated, firm in consistency, greyish white in colour, and not matted together or caseating. Histological examination showed numerous pale nodules resembling germinal centres scattered throughout the gland (Fig. 1). These nodules showed the staining reactions for amyloid with the stains mentioned above. The intervening tissue was composed of a fine amyloid matrix entangling lymphocytes and plasma cells and showed amyloid thickening of vessel walls. There was no evidence of any tumour of lymphoid tissue. Further investigations were then carried out. The congo-red test revealed that 67% of the dye was removed from the circulation after one hour, a result which suggested that the process was not wholly localized. The serum alkaline phosphatase was 21 King-Armstrong units and the urinary urobilinogen 3.3 units—high values suggesting liver involvement. There was persistent albuminuria, but the blood urea and urea-clearance tests were normal. The plasma proteins totalled 7.8 g./100 ml. (albumin 4.2 g., globulin 3.6 g.). The patient's health slowly deteriorated and he died two years later. A necropsy was performed elsewhere and the cause of death was given as generalized primary amyloidosis.

Case 2

The patient, a man of 56, presented with enlarged glands in the cervical, axillary, and inguinal regions. In addition he complained of loss of weight, pains in the limbs, and some

deterioration of vision. On examination he was found to have generalized lymphadenopathy, hepatomegaly, and gross proteinuria. A lymph node was removed from the axilla. It was about 2 cm. in diameter, dark red in colour, and soft in consistency. Histology showed almost complete replacement of lymphoid tissue with amyloid (Fig. 2). A congo-red test showed that 95% of the dye was removed from the circulation in 30 minutes. X-ray examination of the chest showed enlarged mediastinal glands. The blood count was normal. The Wassermann reaction and Kahn test were negative. The patient's condition steadily deteriorated and he died five months after the biopsy. At necropsy there was widespread amyloidosis of lymph nodes, liver, spleen, adrenal glands, kidneys, heart, peripheral nerves, ocular muscles, and optic nerves. There was no known predisposing cause for the amyloidosis.

FIG. 1.—Case 1. Amyloid "nodule" in lymph node. The amyloid material, fluorescent with violet light, appears white. (Thioflavine-T. $\times 80$.)

FIG. 2.—Case 2. Amyloid replacement of lymphatic tissue. (Haematoxylin and eosin. $\times 180$.)

Case 3

The patient, a woman of 49, complained of a lump in the left axilla which had been increasing in size for a year. Her general health was good but her right leg had been amputated below

FIG. 3.—Case 3. Amyloid deposition in lymph node. (Haematoxylin and eosin. $\times 125$.)

FIG. 4.—Case 3. Amyloid masses in lymph node. (Thioflavine-T. $\times 65$.)

the knee after an accident. At operation a lump 6 by 4 cm. was found attached to a chain of smaller lumps suggestive of enlarged lymph nodes. All these swellings were red or yellowish red in colour and soft in consistency. Histology showed small collections of lymphocytes widely scattered among eosinophilic anuclear material (Fig. 3). The possibility of amyloidosis was considered, but special stains gave inconclusive results. Thioflavine-T was not used on this occasion. The patient made an uneventful recovery.

Ten months later similar lumps appeared in the same axilla. At this time haematological investigations were normal. X-ray examination of the chest, an intravenous pyelogram, and serum protein investigations, including electrophoresis, were within normal limits. Histological examination of the lumps showed appearances identical with those seen previously. Special stains, however, including thioflavine-T, confirmed that the eosinophilic material was amyloid (Fig. 4). A congo-red test had not been performed, but a rectal biopsy showed no evidence of amyloidosis. The patient remains in good general health.

Discussion

The reports describing amyloid deposition in lymph nodes have all been dealing with primary amyloidosis. In the present series Case 1 had a history of acute parotitis, which may well have been coincidental. There was no known predisposing cause in Cases 2 and 3. In my opinion all three cases are examples of lymph-node involvement by primary amyloidosis. The reddish colour of the glands seen in Case 2 and at both operations in Case 3 may have diagnostic significance. Case 3 in particular illustrates the value of thioflavine-T, a fluorescent stain for amyloid.

Summary

Three cases are described in which amyloidosis presented with enlargement of lymph nodes. Two of these cases were fatal, but the third patient remains well although the gland masses have recurred. The literature is reviewed briefly.

I am indebted to my clinical colleagues for permission to study their cases and to Dr. J. R. Hobbs for the thioflavine-T preparations. I acknowledge the help of Professor A. D. Morgan, who presented Case 1 to the Pathological Society in 1946.

REFERENCES

- Binford, C. H. (1940). *Arch. Path.*, **29**, 314.
 Dillon, J. A., and Evans, L. R. (1942). *Ann. intern. Med.*, **17**, 722.
 Eisen, H. N. (1946). *Amer. J. Med.*, **1**, 144.
 Kurban, A. K. (1960). *Bull. Johns Hop. Hosp.*, **107**, 320.
 Lindsay, S., and Knorp, W. F. (1945). *Arch. Path.*, **39**, 315.
 Massachusetts General Hospital (Case 35141) (1949). *New Engl. J. Med.*, **240**, 572.
 Miller, J. (1929). *J. techn. Meth.*, **12**, 210.
 Pearson, B., Rice, M. M., and Dickens, K. L. (1941). *Arch. Path.*, **32**, 1.
 Symmers, W. St. C. (1956). *J. clin. Path.*, **9**, 187.

Preliminary Communications

Mild Nitrogen Narcosis?

Breathing compressed air has not been found to affect mental efficiency until a pressure has been reached of about 4 atmospheres absolute, or is 45 pounds per square inch (p.s.i.) (3.16 kg./sq. cm.) gauge pressure, which occurs at a depth of about 100 ft. (30 m.) of water (Kiessling and Maag, 1962; Barnard *et al.*, 1962). At the invitation of the M.R.C. Decompression Sickness Panel we recently looked for measurable changes in mental efficiency at lower pressures. When we used a test which had been practised first at normal atmospheric pressure we failed to find any effect on mental efficiency at a pressure of $3\frac{1}{2}$ atmospheres absolute (38 p.s.i.

(2.67 kg./sq. cm.) gauge pressure). But when the test was carried out first at pressure without any previous practice we found a statistically reliable change in performance at a pressure as low as 2 atmospheres absolute (16 p.s.i. (1.12 kg./sq. cm.) gauge pressure), as indicated in the Table.

Each man had to sort packs of cards for 10 minutes into boxes according to the suit. The time at which each card fell into a box was recorded automatically, and the occasional errors of classification were noted at the end of the

Effect of Compressed Air on Card Sorting

Absolute Pressure (Atmospheres)	No. of Men	Mean Age	Mean Percentage of Very Slow Responses*
$3\frac{1}{2}$	7	33	2.89
$2\frac{1}{2}$	10	27	3.15
2	10	29	2.74
1 (normal)	13	27	1.99

* 1 atmosphere reliably different from all higher pressures ($P < 0.05$).