AMYLOID DISEASE COMPPLICATING ANKYLOSING SPONDYLITIS

BY

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Wichmann (1893) first described amyloid disease complicating rheumatoid arthritis. Many further reports of this association have been published, and, with the decline in the incidence of severe pulmonary tuberculosis, rheumatoid arthritis may become the commonest cause of amyloidosis in Great Britain. Thus, Fearnley and Lackner (1956) found eight cases of amyloidosis in a series of 183 patients with rheumatoid arthritis, Gedda (1955) found nine cases in a series of 45, and Teilum and Lindahl (1954) found seventeen cases in a series of 28. Teilum and Lindahl also included two cases of ankylosing spondylitis but no clinical details are recorded.

In the following case amyloid disease, diagnosed clinically, caused death as a result of renal involvement in a man with ankylosing spondylitis.

Case History

Symptoms of ankylosing spondylitis consisting of lumbar pain and stiffness began in 1942, when the patient was 16 years old. A year later typical radiological changes were present in the sacro-iliac joints (Fig. 1, opposite). The erythrocyte sedimentation rate was 65 mm. in 1 hour. He was immobilized in a plaster bed for a year. In 1945 radiotherapy was given to the thoracic and lumbar spine (750 r) and to each hip joint (1,000 r) with some improvement. In 1950 the patient was admitted to hospital for herniorrhaphy; at this time he had ankylosis of the spine with severe involvement of both hips, proteinuria was noted, and the blood pressure was 140/85 mm. Hg. A year later the blood pressure had risen to 160/100 mm. Hg. A further course of radiotherapy to the lumbar spine (750 r) and the sacral and cervical areas (750 r) gave relief of symptoms, but the proteinuria persisted, and by June, 1953, the clinical picture of malignant hypertension with left ventricular failure had developed. The blood pressure was now 225/145 mm. Hg and there was bilateral papilloedema with severe retinal changes. The blood urea was 71 mg. per cent. After a period of rest in bed and salt restriction the papilloedema, retinal exudates, and haemorrhages disappeared, and the cardiac asthma was relieved. The hypertension and uraemia persisted and cardiac asthma recurred a year later.

Laboratory Findings.—Blood urea 78 mg. per 100 ml., serum albumin 3.4 g. per 100 ml., serum globulin 3.37 g. per 100 ml. Thymol turbidity 1 unit, thymol flocculation 0, serum colloidal gold reaction 0 zinc sulphate turbidity 3 units, ammonium sulphate turbidity 2 units.

Congo red test positive with 78 per cent. dye removed from serum after 1 hour.

Urine contained 32 mg. per 100 ml. protein.

Nausea and vomiting were followed by epileptiform convulsions and a sudden left hemiplegia. The blood pressure fell to 160/100 mm. Hg and secondary optic atrophy developed. Death occurred suddenly in March, 1955, from a right cerebral haemorrhage.

There was no significant fever or oedema at any stage of this illness. The urine showed moderate or large amounts of protein on seven occasions, but not when examined in 1950 before the patient’s re-admission to hospital for herniorrhaphy. The centrifuged deposit showed a few red blood cells on three occasions, granular casts on three occasions, and no abnormality on four occasions.

Autopsy Findings.—The body was that of a well-nourished young man. There was extensive haemorrhage in the right frontoparietal region with rupture into the lateral ventricle. A few enlarged lymph nodes showed follicular hyperplasia but no amyloid. The lungs showed early bronchopneumonia. The heart (480 g.) showed left ventricular hypertrophy. The heart valves and coronary arteries appeared normal. There was early atheroma of the aorta. The liver (1,380 g.) was small and showed deposits of amyloid around the hepatic arteries only. The spleen (120 g.) was contracted and showed a mild diffuse amyloid change.

The kidneys (left 95 g.; right 110 g.) showed the appear-
Fig. 1.—X ray showing bony ankylosis of both sacro-iliac joints and of left hip joint on January 27, 1953.

ance of amyloid contracted (or "small amyloid") kidneys. The capsules were lightly adherent; the surface was a mottled grey-white and was granular. The cut surface showed prominent glomeruli throughout the cortex. The corticomedullary junction was blurred and the medullary fat increased. The vessels were prominent. Microscopically there were deposits of amyloid around the afferent arterioles, and glomerular and intertubular capillaries, and in the basement membrane of the tubular epithelium (Fig. 2, overleaf).

There was irregular interstitial fibrosis with alternating areas of tubular atrophy and dilatation. The tubules contained hyaline material and altered blood pigment.

The adrenal glands showed amyloid substance around the cortical capillaries with atrophy of the cells of the zonae reticulosa and fasciculata. The cells of the zona glomerulosa were vacuolated and contained lipoid. The medulla was normal. The thyroid showed a moderate increase in stroma with marked lymphocytic infiltration and some atrophy of vesicles. The pituitary, pancreas, and testes showed no abnormality. The hip, sacroiliac, and intervertebral joints showed advanced changes with bony ankylosis. There was calcification of
the interspinous ligaments in the thoracic region. Sections of the 11th costovertebral and costotransverse joints showed no ankylosis. The anterior and posterior longitudinal spinal ligaments appeared normal.

The presence of deposits of amyloid was confirmed by staining fresh material with a watery solution of iodine, and by staining sections prepared from tissues fixed in formal-saline with Congo red and with methyl violet, using the method described by Missen and Taylor (1956).

Discussion

Several points are illustrated by this case. The importance of proteinuria as an early sign of amyloid disease is again shown. It was noted 8 years after the onset of symptoms of ankylosing spondylitis and was unaccompanied by hepatic or splenic enlargement. Malignant hypertension developed in the next 3 years and death occurred after thirteen years illness.

The Congo red test gave useful clinical confirmation of the diagnosis, but a negative result does not rule out the possibility of amyloid disease (Selikoff, Paterson, and Herschfus, 1949). The importance of histological confirmation of the diagnosis has been stressed by Teilum and Lindahl (1954) and Missen and Taylor (1956) have pointed out the importance of using a metachromatic staining reaction in addition to the Congo red method. In histological preparations the latter dye may be taken up by materials other than amyloid.

Renal involvement is a common mode of death in secondary amyloidosis. Of the seventeen cases analysed by Teilum and Lindahl, death was due to renal amyloidosis in seven, and in the series reported by Gedda (1955), the nine cases of amyloidosis all died as a result of renal involvement.

The development of hypertension in amyloidosis is rare. Fishberg and Oppenheimer (1930) confirmed this and noted that hypertension did not occur in cachectic subjects. They suggested that cachexia might prevent the development of hypertension, even when many other factors predisposing to this condition were present. They also found that hypertension due to amyloidosis is invariably associated with the amyloid contracted kidney. In the case here reported, hypertension developed in a non-cachectic patient who was found at autopsy to have amyloid contracted kidneys. The blood pressure in our patient fell during the last few months of life; Liedholm (1940) suggested that adrenal involvement might prevent hypertension, but the adrenal changes were probably insufficient to account for the fall in pressure.

It has been suggested that the occurrence of the amyloid contracted kidney is related to the late stages of amyloid nephrosis and that hypertension may occur once this lesion is fully established, although the coexistence of fever and infection may reduce the intensity of the hypertension or even prevent it (Pickering, 1955).
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Gedda found that nine of his series of eleven cases died of renal amyloidosis; of these seven had contracted amyloid kidneys, and three of the seven had hypertension. He suggested that hypertension acted as a compensatory mechanism in renal insufficiency due to amyloidosis by increasing the filtration pressure.

If the contracted kidney were the result of hypertension it would appear to be reasonable to expect to find cases in which hypertension was accompanied by little or no contraction (as in essential hypertension). This is not so, except in late renal failure in the non-contracted kidney (Zuckerbrod, Rosenberg, and Kayden, 1956), nor is the contracted kidney invariably associated with raised blood pressure. It is possible that both contraction and hypertension are the result of progressive renal ischaemia, the occurrence of hypertension being dependent on additional factors which are either not present or are inhibited in the majority of cases.

In our case there were changes in other organs, namely the liver and spleen, which showed atrophy and fibrosis in the absence of chronic venous congestion, suggestive of a similar process.

Renal insufficiency, although constantly found when the kidneys are contracted, can occur in the absence of this change (Noble and Major, 1929).

The absence of cachexia in our case would seem to confirm that hypertension is more likely to occur in well-nourished subjects, but a study of the literature shows that cases have been reported in amyloidosis associated with cachexia (Noble and Major, 1929), including one described by Fishberg and Oppenheimer (1930).

The association of amyloidosis and ankylosing spondylitis must be rare. In rheumatoid arthritis a link has been suggested between the hyperglobulaemia and plasmacytosis, and the occurrence of amyloid disease. Pillers and Marks (1956) found an increased plasma cell content of the bone marrow in ten out of 28 cases of ankylosing spondylitis, but no serum protein estimations were made. Our case showed hyperglobulaemia on the one occasion that the serum proteins were estimated, but examination of the bone marrow from several sites showed no increase in plasma cells.

In the differential diagnosis, irradiation nephritis followed by secondary amyloidosis was considered to be an unlikely course of events owing to the relatively small dose of x-rays employed. Kunkler, Farr, and Luxton (1952) stated that a homogeneous dose of 2,300 r to the whole of both kidneys may lead to the development of hypertension and renal failure. The total dosage given here was 1,750 r in 1945, and 1,500 r in 1951 (after the onset of albuminuria), but only a very small amount arising from scatter of x-rays to the lumbar spine would have reached the kidneys. The latent period preceding the development of irradiation nephritis is only 6 to 12 months, and not several years as in this case.

Summary

The clinical and pathological features of fatal amyloid disease in a case of ankylosing spondylitis are described and discussed.

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REFERENCES


Maladie amyloïde complicant la spondylarthrite ankylosante

RÉSUMÉ

On décrit et on discute les caractères cliniques et anatomo-pathologiques de la maladie amyloïde mortelle dans un cas de spondylarthrite ankylosante.

Enfermedad amiloide complicando la espondilartritis anqulosante

SUMARIO

Se descreben y discuten los rasgos clínicos y anatomo-patológicos de la enfermedad amiloide con terminación fatal en un caso de espondilartritis anqulosante.
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