British/Italian Interchange

Language is a major problem here. As there are no language requirements for Italian medical training, most young Italian doctors, like their British counterparts, know no language other than their own. Those with a burning interest in international medicine make it their business to learn English, but scholarships in the United Kingdom and the United States usually involve some financial sacrifice, and are not likely to improve career prospects at home, so only an exceptional Italian graduate will have the determination and thirst for knowledge to pursue this course.

Likewise conversational Italian is essential for the British doctor intending to work in Italy, though it might be possible to scrape by in a pure research laboratory without it. Most British doctors wishing to work in Italy will already have a centre in mind, and are likely to gain most benefit in a research institute, either in a university or more likely outside it. They can be confident of a warm welcome, for Italians like visitors to feel at home and have a great admiration for British institutes and medical practice.

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Hospital Topics

Tuberculosis as a Continuing Cause of Renal Amyloidosis

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Summary

In 40 patients with renal amyloidosis seen in a ten-year period tuberculosis was the major preceding disease in 20, though it was active in only two at diagnosis. Most patients presented with renal failure, and only two survived for five years. This experience (at least, in the west of Scotland) conflicts with the generally accepted view that rheumatoid arthritis is the commonest cause of renal amyloidosis.

Introduction

Early papers on amyloidosis quoted incidences of tuberculosis as a preceding disease of over 80%,[1-6] but more recent texts on renal disease[7-9] state that rheumatoid arthritis is now the main cause of secondary amyloidosis. This opinion seems to be widespread, reflecting the view that with the introduction of effective antituberculous chemotherapy the incidence of amyloidosis as a secondary complication would decline. Since our experience is that tuberculosis remains the major antecedent of renal amyloidosis we thought it important to record our data.

Patients and Methods

The case records of 40 patients known to have renal amyloid disease in Glasgow Royal Infirmary in 1963-73 were available for analysis. Thirty-three patients had been under the direct care of the renal unit and the remaining cases were found from the hospital's necropsy records. The diagnosis was confirmed in all cases by histological examination. Kidney tissue, obtained by percutaneous renal biopsy (20 cases) or at necropsy (nine cases), was diagnosed as containing amyloid by the presence of classical green birefringence in sections stained with Congo red and viewed under a polarizing microscope. In 11 patients the finding of considerable amyloid deposition in biopsy specimens of rectal mucosa or liver together with clinical evidence of renal involvement led to the diagnosis of renal amyloidosis without recourse to renal biopsy.

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Results

The clinical, biochemical, and pathological findings in the 40 patients are grouped according to aetiology in the table. There were 21 males and 19 females ranging in age from 12 to 75 years (mean 48). Most (72%) were in the 40-60 age group. In 37 patients there was evidence of an antecedent chronic illness permitting a diagnosis of secondary amyloidosis. Tuberculosis (15 pulmonary, three bone, one renal, and one abdominal) was the major preceding disease, accounting for 54% of those with secondary amyloidosis. The tuberculosis was considered active in only two of these patients at the time of diagnosis of amyloid disease. Ten patients (27% of those with secondary amyloid) had polyarthropathy (seven rheumatoid arthritis, one Still's disease, one psoriatic arthropathy, and one ankylosing spondylitis) but three of these patients also had a history of pulmonary tuberculosis. Nine patients (24% of those with secondary amyloid) had histories of chronic suppurative disease (seven pulmonary, one bone, one skin). In the three patients classified as having primary amyloid disease no preceding cause was identified despite thorough investigation. One patient had amyloidosis associated with a tumour of the bronchus.

The estimated interval between the onset of the predisposing illness and the diagnosis of renal amyloidosis varied from 6 months to 43 years (mean 17 years). There was no great difference between the time of diagnosis of amyloidosis after tuberculosis (21 years) or after chronic suppurative disease (17 years),

Pathological and Clinical Data in 40 Patients with Renal Amyloidosis. Cases are grouped according to Common Predisposing Factors

Case Nos.	Age or Age Range	Nature and Duration of Antecedent Disease	Presentation of Amyloid (No. of Cases)	Means of Diagnosis (No. of Cases)	Blood Pressure (mm/Hg)	Urea (mg/100 ml)	Serum Albumin (g/100 ml)	Urine Protein (g/24 hr)
1-12	44-54	Tubercle lung, average 20 years	Nephrotic (5), proteinuria (3), C.R.F. (3), liver biopsy at vagotomy and pyloroplasty (1)	Renal biopsy (6), liver biopsy (3), rectal biopsy (2), necropsy (1)	95/60-220/110	24-171	1·1-3·8	2·2-23·7
13-15	27-40	Tubercle bone, average 24 years	Nephrotic (2), A.R.F. (1)	Renal biopsy (3)	90/60-135/85	23-312	1·2-2·2	6·4-13·8
16, 17	53-55	Tubercle lung, rheumatoid arthritis	Nephrotic (1), C.R.F. (1)	Renal biopsy (1), liver biopsy (1)	170/120 110/90	59 114	2·5 3·4	9 8
18	48	Tubercle lung 24 years, ankylosing spondylitis	Haematuria	Renal biopsy	190/120	40	3·7	3·7
19	34	Tubercle kidney 3 years	C.R.F.	Necropsy	110/70	375	—	0·3
20	51	Tubercle abdomen	Haematuria	Renal biopsy	100/60	103	1·3	3·2
21-25	44-71	Rheumatoid arthritis, average 14 years	Proteinuria (2), comatose (1), C.R.F. (1), U.T.I. (1)	Renal biopsy (1), rectal biopsy (2), necropsy (2)	75/0-180/105	46-300	1·7-2·7	+ to 4·7
26	12	Still's disease 2 years	Nephrotic	Rectal biopsy	105/70	13	1·4	+ + +
27	37	Psoriatic arthropathy	Nephrotic	Necropsy	130/85	100	1·0	9·0
28	44	Pustular psoriasis 26 years	Proteinuria	Renal biopsy	100/70	12	2·1	2·8
29-35	19-63	Chronic suppuration lung, average 17 years	Nephrotic (2), C.R.F. (2), A.R.F. (2), proteinuria (1)	Renal biopsy (3), necropsy (3), rectal biopsy (1)	95/70-160/115	28-440	1·0-3·0	5·7-18
36	75	Bronchial carcinoma 6 months	Ascites, hepatomegaly	Necropsy	140/70	24	2·3	+
37	46	Osteomyelitis 12 years	Anaemia, R.T.A.	Renal biopsy	170/90	70	2·7	3·2
38-40	45-64	None identified	Nephrotic (3)	Renal biopsy (2), rectal biopsy (1)	95/65-105/70	13-56	1·4-3·2	6·7-8·7

C.R.F. = Chronic renal failure. A.R.F. = Acute renal failure. U.T.I. = Urinary tract infection. R.T.A. = Renal tubular acidosis.

but amyloid tended to be evident earlier (after 11 years) in those with polyarthropathy. In the 12-year-old patient with Still's disease the time interval was only two years.

The presenting features were as follows (numbers of patients are given in parentheses): nephrotic syndrome (15), chronic renal failure (8), proteinuria (7), "acute" renal failure (3), painless haematuria (2), urinary infection (1), terminal coma (1), iron deficiency anaemia, hyperkalaemia, and renal tubular acidosis (1), hepatic disorder (1), and ascites and hepatomegaly (1). Thirty-seven patients presented with symptoms and signs strongly suggestive of renal disease. All had significant proteinuria and in the 28 cases in which proteinuria was quantified, losses ranged from 0·3 g to 23·7 g/day (average 7·5 g/day). Fifteen patients presented with a classical nephrotic syndrome with proteinuria above 5 g/day, serum albumin less than 2·5 g/100 ml, and oedema. Of the eight patients who presented with chronic renal failure (blood urea 85 mg to 375 mg/100 ml) five died shortly after admission, the diagnosis of renal amyloid being confirmed at necropsy. Three patients presented with acute renal failure after infective illnesses leading to dehydration. Case 37 initially presented with iron deficiency anaemia related to chronic osteomyelitis in the left tibia and fibula but was found to have hyperkalaemia which proved to be renal in origin. Renal biopsy showed widespread amyloidosis of both cortex and medulla, with considerable peritubular deposition of amyloid, and it was postulated[10] that the peritubular amyloid deposition caused interference with distal tubular potassium and hydrogen ion exchange leading to potassium and hydrogen ion retention.

Only eight patients (20%) were hypertensive (diastolic blood pressure of 100 mm Hg or over). Accurate assessment of kidney size was possible in 28 patients and in 15 the size was normal. Of the six patients with large kidneys five had chronic renal failure of severe degree (blood urea >100 mg/100 ml) and only one was hypertensive, while of the seven patients with small kidneys two had severe renal failure and three had significant hypertension.

Eleven patients had clinical evidence of hepatic or splenic enlargement and two had biochemical evidence of incipient liver failure. One patient had diarrhoea, leading to dehydration and acute renal failure (case 15), while a further patient was admitted comatose with features strongly suggestive of long-standing malabsorption (case 23).

In only two patients (cases 27 and 34) was evidence of renal vein thrombosis detected and in both of these the complication was noted at necropsy; one of these (case 34) became dehydrated before the terminal hospital admission.

Eight patients died shortly after admission to hospital and a total of 20 patients had died within one year of diagnosis of amyloid disease. Only two patients are known to have survived for five years and eight patients survived for intervals between one and five years.

Discussion

In earlier decades it was widely recognized that 80-90% of amyloid disease was found in association with a past history of tuberculosis or chronic suppurative disease.[1-6] Much of the evidence for the belief that rheumatoid arthritis is now the commonest preceding illness is derived from careful post-mortem studies in patients with rheumatoid arthritis. An incidence of secondary amyloidosis at necropsy as high as 61% in patients with rheumatoid arthritis has been reported by Teilum and Lindahl[11] but the incidence varies widely, and others have quoted incidences of 13·3%,[12] 26%,[13] 12%,[14] and 20%.[15] Ennevaara and Oka[16] diagnosed amyloidosis by renal biopsy in 70·8% of patients with rheumatoid arthritis but this was in a selected group of individuals who were known to have significant proteinuria. Boyle and Buchanan[17] while stating that rheumatoid arthritis is now the commonest cause of amyloidosis in the United Kingdom qualify this by saying that "it is rarely clinically significant during life. Occasionally it may cause hepatic and splenic enlargement or the nephrotic syndrome with renal failure." Hence apparently there is a high incidence of amyloid deposits in various sites on careful necropsy studies of patients with rheumatoid arthritis, but the overall incidence of amyloidosis of sufficient severity to cause renal failure in patients with rheumatoid arthritis is relatively low when one considers the prevalence of rheumatoid arthritis. In discussing the incidence of amyloidosis in rheumatoid arthritis more careful distinction should be made between clinical and necropsy data.

In the present series antecedent tuberculosis was present in 54% of the patients while 24% had polyarthropathy. The centre for rheumatic diseases, like the renal unit, is closely linked to the university department of medicine at the Royal Infirmary so that it is unlikely that the present series was unrepresentative. Hence probably tuberculosis remains the leading cause of amyloidosis in the west of Scotland. This experience no doubt reflects the previously high incidence of tuberculosis in this area but the recent publication by Triger and Joekes[18] from London also shows that tuberculosis was the commonest antecedent illness though to a lesser degree than in our series. Thus the statement that tuberculosis is no longer the major antecedent of renal amyloidosis needs qualification.

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Beclomethasone Dipropionate and Oropharyngeal Candidiasis

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Summary

A survey of 936 patients attending a respiratory diseases unit outpatient department was performed to assess the incidence of oropharyngeal candidiasis in patients inhaling beclomethasone dipropionate in daily doses of 400 μg or less. Throat swabs from 209 (41%) patients treated with beclomethasone were positive on culture for yeasts compared with positive swabs from 77 (27·2%) patients not receiving corticosteroid therapy either orally or by inhalation. Clinical oropharyngeal thrush, confirmed by culture, was detected in 28 (5·5%) patients inhaling beclomethasone, one (0·7%) patient receiving treatment with oral prednisolone, and two (0·7%) patients not being treated with corticosteroids.

Introduction

Inhalation of beclomethasone dipropionate is now an established and effective treatment of chronic asthma.[1 2] Beclomethasone therapy is free from systemic side effects unless high doses are given.[3] Local complications of treatment are not unexpected, however, since high concentrations of the drug are inevitable in certain sites. One such complication of beclomethasone aerosol therapy is fungus infection of the mouth and throat.[1 4 5] The incidence of this side effect is not known, though McAllen *et al.*[6] reported candidal infection of the pharynx or larynx in 13% of 120 patients treated with beclomethasone dipropionate or betamethasone valerate in varying doses. This investigation was planned to assess the incidence of fungal throat infection in patients with chronic asthma while being treated with beclomethasone in daily doses of 400 μg or less. Patients with chronic asthma receiving treatment with oral prednisolone alone and a group of patients with a variety of chest disorders but not being treated with corticosteroids of any type were used as control groups.

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Patients and Methods

All patients attending the outpatient department of the respiratory diseases unit, Northern General Hospital between July 1973 and December 1973 were questioned about sore throat and hoarseness of the voice and a throat swab was taken from each patient. One dry swab was used to sample both tonsillar areas. A record of beclomethasone, prednisolone, and antifungal therapy was kept (patients being treated with corticotrophin or tetracosactrin were included with those taking prednisolone and were not analysed separately). If lesions in the mouth or pharynx typical of thrush were seen when the swab was taken this was recorded. All patients treated with beclomethasone were inhaling a maximum dose of 400 μg daily (100 μg four times a day). A few patients whose chronic asthmatic symptoms had been well controlled had had their dose reduced to less than 400 μg a day.

MYCOLOGICAL METHODS

All throat swabs were inoculated on to malt peptone agar in Petri dishes within three hours of sampling. The growth of yeasts was recorded after incubation at 37°C for 48 hours. Identification of the yeasts was made primarily on the production of germ tubes (*Candida albicans*) and subsequently by conventional methods.

Results

During the survey 936 patients were investigated. Of these, 283 patients were not receiving treatment with corticosteroids (control group) and 143 patients were being treated with oral prednisolone, 333 with a combination of oral prednisolone and beclomethasone, and 177 with beclomethasone alone.

The isolation of yeasts from each treatment group is shown in table I. Seventy-seven swabs from patients in the control group and 47 from patients taking oral prednisolone yielded yeasts on culture. This difference was not statistically significant. Yeasts were isolated from 73 patients inhaling

TABLE I—*Isolation of Yeasts from 936 Patients*

Corticosteroid Treatment	No. of Patients	No. (%) in whom Yeast was Isolated
None	283	77 (27·2)
Prednisolone	143	47 (32·8)
Beclomethasone	177	73 (41·2)
Beclomethasone and prednisolone	333	136 (40·8)