Giant cell arteritis in general practice

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SUMMARY. The clinical syndrome of polymyalgia rheumatica is reviewed. The relationship of this disease with temporal arteritis is discussed, and I consider both syndromes have a pathological basis of generalised giant cell arteritis.

Seven cases of polymyalgia and four cases of temporal arteritis were recorded during the six-year period (1969–1975) in one general practice.

The outlines of management are discussed, with a plea for earlier recognition of the syndromes of polymyalgia rheumatica and temporal arteritis in general practice.

Polymyalgia rheumatica syndrome

Definition

In 1970, at a conference at the Mason Clinic, Seattle, Washington, polymyalgia rheumatica was defined as: " a syndrome affecting older patients, characterised by pain and stiffness in the shoulder and pelvic girdle muscles, without weakness or atrophy; these symptoms persisting for at least a month, with erythrocyte sedimentation rate (ESR) greater than 50 mm in one hour and dramatic relief of symptoms with the use of steroids " (Healey, Parker, and Wilske, 1971).

Polymyalgia rheumatica is a disease complex seen in general practice which often passes unrecognised for several months and may even run its course undiagnosed. It is a disease of later life, the average age of onset being 65 years. It runs a protracted course, lasting between six months and six years. The average duration is between two and three years (Fernandez-Herlihy, 1971). Women are affected twice as often as men; there is no apparent seasonal incidence and so far the cause of the disease is unknown.

It is important that the disease is recognised, diagnosed, and treated in its early stages to save the patient from pain, misery, and some sinister complications.

Incidence

The incidence of polymyalgia rheumatica has been variously quoted. Ostberg (1972) suggested from his large study that it occurred with a frequency of 12/100,000 population per year. Others have stated that it is not a rare disease and have compared the incidence to that of gout (Dixon *et al.*, 1973). In my own series studied over a six-year period the incidence has been seven cases per 3,000 population over five years, which is considerably higher than expected.

Clinical features

The typical early symptoms are pain and stiffness in the muscles at the back of the neck, around the shoulders and upper arms and thighs. The stiffness is usually worse in the mornings and in damp weather, often resembling the prodrome of rheumatoid arthritis.

There is no muscle atrophy or weakness inherent in the disease, but the pain and

stiffness render the patient unwilling to move the limbs, so producing a secondary weakness.

Transient joint swelling and pain due to synovitis and effusion occurs, commonly in the knees and sterno-clavicular joints, less often in the hands, wrists, and shoulders.

The outstanding feature of the disease in its early stages is the degree of constitutional upset the patient suffers. The onset of symptoms can usually be recalled accurately and are often described as an attack of ' 'flu '.

Night sweats and intermittent pyrexia occur in most patients, accompanied by anorexia, fatigue, depression, and weight loss. The weight loss can be considerable, some patients losing as much as 20 kg before treatment (Hamrin, 1972). The average weight loss before treatment is approximately six kilograms.

Surprisingly, physical examination of the patient, who looks and feels so unwell, reveals little. The clinician will detect the anaemia, weight loss, and general debility but, apart from the occasional findings of effusions in the knees and wrists, often little else.

Laboratory findings

The most important clue to the diagnosis is the erythrocyte sedimentation rate (ESR). This is generally raised often exceeding 100 mm in one hour, rarely below 50 mm in an hour. The haemoglobin level is decreased, the anaemia being either normocytic or hypochromic. The remainder of the peripheral blood picture is unremarkable, although some workers have drawn attention to the moderate eosinophilia and leucocytosis (Gordon, 1960).

With this collection of sinister symptoms and the finding of a grossly elevated ESR, one must obviously be alert to exclude malignant disease and other serious diseases.

In uncomplicated polymyalgia rheumatica the routine laboratory tests reveal few biochemical abnormalities (table 1).

TABLE 1

LABORATORY TESTS WHICH ARE WITHIN NORMAL LIMITS IN UNCOMPLICATED POLYMYALGIA RHEUMATICA

Rheumatoid factor in blood and synovial fluid	
Culture and microscopy of synovial fluid	
L.E. cells and anti-nuclear factor	
Serological tests for syphilis and gonorrhoea	
Urine analysis and culture	
Serum creatinine	
Blood urea	
Brucella agglutinins	
Muscle enzymes:	Serum glutamic oxaloacetic transferase (S.G.O.T.)
	Lactic acid dehydrogenase (L.D.H.)
	Creatine phosphokinase (C.P.K.)

X-rays of the affected joints show changes commensurate with age. A common non-specific finding is elevation of the alpha 1 and alpha 2 globulin fractions and decrease of the serum albumin. Abnormal liver function tests have been reported in some patients. Moderate elevations of serum alkaline phosphatase and increase of bromsulphthalein retention has been described. In those patients liver biopsy showed non-specific fatty changes only (Dickson *et al.*, 1973). These biochemical changes were found to be reversible after treatment with corticosteroids. Biopsy of the painful, stiff muscles has been reported as yielding only normal results by most authorities (Wilske and Healey, 1967;

Fernandez-Herlihy, 1971), but others (Dixon *et al.*, 1966) likened the changes found in the muscle cells to those seen in chronically ischaemic muscle tissue—a finding of considerable interest.

Relationship to other diseases

Polymyalgia rheumatica is often confused with polymyositis. Although both have muscle pain in common, intrinsic muscle weakness is absent in polymyalgia and disease of the muscles, as seen in polymyositis, can be excluded in polymyalgia by muscle enzyme estimations, electromyograms, and biopsy.

Polyarteritis nodosa may be associated, but the clinical picture is different. In polyarteritis nodosa the smaller arterioles are affected and their histological picture is quite unlike the changes seen in the arteries in polymyalgia rheumatica.

Andrews (1965) thought that polymyalgia rheumatica was a marker sometime for occult malignancy, particularly bronchial carcinoma. This must always be considered, but subsequent work has not supported the association.

By far the most important association is the close relationship of polymyalgia with temporal arteritis and the syndrome now often called giant cell arteritis.

Giant cell arteritis

In 1956 Paulley drew attention to the close similarities of the symptoms and laboratory findings of the two conditions. Later, with Hughes (1960), he demonstrated classical changes of giant cell arteritis in specimens of temporal artery removed from patients suffering from uncomplicated polymyalgia rheumatica. Hamrin, in 1964, as a result of his own large study concluded that the two diseases were manifestations of the same basic arteritis affecting the large to medium sized arteries. He suggested the name polymyalgia arteritica to tidy up the controversy. Since then, others have confirmed these findings by showing that in up to 30 per cent of patients diagnosed as suffering from uncomplicated polymyalgia rheumatica, changes of giant cell arteritis are detected in biopsy specimens of the temporal artery (Hunder *et al.*, 1969; Fernandez-Herlihy, 1971).

This may be misleading, since although the giant cell arteritic process has a predilection for the temporal arteries, this is not always the case. Even in arteries so affected the disease is patchy in distribution, making a biopsy a hit or miss affair. It is likely that the figures may understate the case.

Further support came from Ostberg (1972) who performed post-mortem studies on 16 patients who had been diagnosed as having uncomplicated polymyalgia rheumatica before death. In 14 cases he discovered, after painstaking histological examination of the arterial vascular system, that there were changes of giant cell arteritis in the aortic arch, subclavian, and carotid vessels. A few had similar changes in the ileofemoral vessels. The changes in the aortic arch and associated vessels were not only microscopic. In some there was part occlusion of the lumen by intimal proliferation and thrombus.

This raises an important issue. If, as appears to be the case, the two syndromes (polymyalgia rheumatica and temporal arteritis) form part of a spectrum of generalised arteritis, then the former must be recognised early and treated with the same urgency as the latter. The reasons for this are clear. The clinical symptoms of both occur from ischaemic and other changes not fully understood as a result of an occlusive arteritis. No arteries appear to be exempt from this process, but the temporal, occipital, and retinal arteries are frequently affected. The latter is the most serious of all.

It has been reported that in 50 per cent of patients suffering from untreated giant cell arteritis there is a degree of visual loss. Of these 15–20 per cent become totally

blind. When blindness occurs, it is rapid, complete, and irreversible; and in 30 per cent of cases bilateral (Bonventre, 1974).

In untreated polymyalgia the risk of visual involvement has been estimated at 15 per cent (Fernandez-Herlihy, 1971).

The mysterious Takayashu's disease or " pulseless " disease has been suggested to be a manifestation of giant cell arteritis. Alestig and Barr (1963) concluded from their series that polymyalgia rheumatica, temporal arteritis, and Takayashu's disease were all different manifestations of the same basic arteritis.

One case in particular is of interest (Duthie and Chalmers, 1963). The patient, a 62-year old woman, had been diagnosed as having uncomplicated polymyalgia. She developed blue, cold hands and arms with diminished radial pulses. There were bruits to be heard in both infra-clavicular areas and aortography confirmed bilateral occlusion of the subclavian arteries. The ESR was found to be 100 mm in one hour and a temporal artery biopsy was positive. She was treated with prednisolone 40 mg daily and her radial pulses returned to normal and the ESR fell to normal. The relationship has been aptly described as " the unholy Trinity " (Hall, 1973).

Experience in general practice

In 1969 I recorded two patients who were diagnosed as having polymyalgia rheumatica and one patient with temporal arteritis. This unusually high incidence in comparison with available data (Ostberg, 1972; Dixon *et al.*, 1966) prompted me to examine the disease more closely.

TABLE 2
GIANT CELL ARTERITIS IN ONE GENERAL PRACTICE DURING SIX YEARS

Case number	*Patient*	*Sex*	*Age at diagnosis*	*Duration of symptoms before diagnosis (months)*	*Date of diagnosis*	*ESR mm 1 hour*	*Biopsy*	*Presenting syndrome*
1	L.L.	F	68	2	27.6.69	113	+ve	TA
2	K.G.	F	55	2	23.7.69	48	0	PMR
3	W.A.	M	76	1	17.12.69	78	−ve	PMR
4	E.P.	F	61	6	22.2.71	49	−ve	PMR
5	V.J.	F	71	24	14.12.71	105	+ve	TA
6	K.O'B.	F	63	3	18.7.71	69	−ve	PMR
7	G.W.	M	75	1	17.9.71	32	Equiv.	PMR
8	E.W.	F	78	2	4.4.72	68	0	PMR
9	D.W.	F	64	1	5.5.73	62	0	PMR
10	D.N.	F	70	2	31.7.74	101	+ve	TA
11	T.J.	M	73	2	18.10.74	96	−ve	TA

PMR = Polymyalgia rheumatica
TA = Temporal arteritis

During the period from January 1969 to January 1975, all cases of giant cell arteritis have been recorded and followed. There were 11 cases in all (seven with polymyalgia rheumatica and four with temporal arteritis). The age and sex distribution is in accordance with a group of 243 cases of polymyalgia reviewed by Herlihy (1971). The cases of temporal arteritis showed a three to one female to male ratio.

Of the 11 patients included in the study period, four have died. The remainder are alive and well, none so far having developed malignant disease or other serious,

unrelated diseases. Diagnosis was made on clinical grounds, supported by the finding of an elevated ESR and exclusion as far as possible of other diseases (table 1).

All but cases 8 and 9 were referred to a consultant rheumatologist for confirmation of the diagnosis and, where appropriate, for temporal artery biopsy. The patients were seen at monthly intervals by me and every three months at the rheumatology unit. By this means a critical clinical and biochemical assessment was made of the patients' progress.

TABLE 3
OUTCOME OF 11 PATIENTS WITH GIANT CELL ARTERITIS TREATED IN A GENERAL PRACTICE

Case number	*Presenting syndrome*	*Duration of steroid treatment (months)*	*Outcome*
1	TA	3	Died 3 months after diagnosis—Gastric ulcer: myocardial infarction
2	PMR	36	Well; asymptomatic. No treatment at present
3	PMR	18	Died. Myocardial infarct 30.4.74
4	PMR	36	Well: no steroid treatment for 3 months but has developed aortic incompetence and aneurysm
5	TA	36	Well; asymptomatic. Prednisolone continued
6	PMR	42	Well; asymptomatic. Prednisolone continued
7	PMR	36	Well, but ESR has risen to 76 mm. ?Progression to GCA. Continuing prednisolone
8	PMR	18	Died 7.1.74. Myocardial infarct
9	PMR	16	Well; asymptomatic. No treatment
10	TA	3	Died 26.10.74. Tuberculous bronchopneumonia
11	TA	4	Well. Treatment continuing

Treatment, duration, and outcome of patients included in study period January 1969—January 1975.

Case histories

Case 6. This 63-year old lady first attended on 23 April 1971. She was complaining of multiple aches and pains and was generally unwell. She returned often during the next three months, gaining no relief from the analgesics prescribed for her ' rheumatism'. On 31 July 1971 the pains across her shoulders had become so severe that she was unable to sleep and rising from bed and dressing in the mornings had become almost impossible. She had also developed pain and stiffness in her thighs and complained that she had to change her nightdress frequently because of drenching sweats. She had lost six kilograms in weight and began to look ill.

Physical examination was entirely non-contributory. Examination of the peripheral blood picture revealed an ESR of 69 mm in one hour; haemoglobin 12·6 g. Other routine tests were returned as normal (table 1).

A diagnosis of polymyalgia rheumatica was made and treatment started with a single bedtime dose of prednisolone 5mg. She described the effect as ' miraculous '. Within one week she started to gain weight, sleep undisturbed and her well-being was returning to normal. By October 1971 her ESR had fallen to 5 mm in one hour and her Hb. had risen to 14·8 g.

Prednisolone in a maintenance dosage of 7·5 mg daily was continued until August 1972. By this time she had received continuous steroid treatment for 13 months and was completely asymptomatic.

The dosage was gradually tapered, but by January 1973 she had a complete relapse with return of all her original symptoms. Prednisolone was restarted followed by the same rapid response and continued until February 1974. At this time another attempt at dosage reduction resulted in relapse. She still continues on prednisolone 7·5 mg at bedtime and is asymptomatic (figure 1).

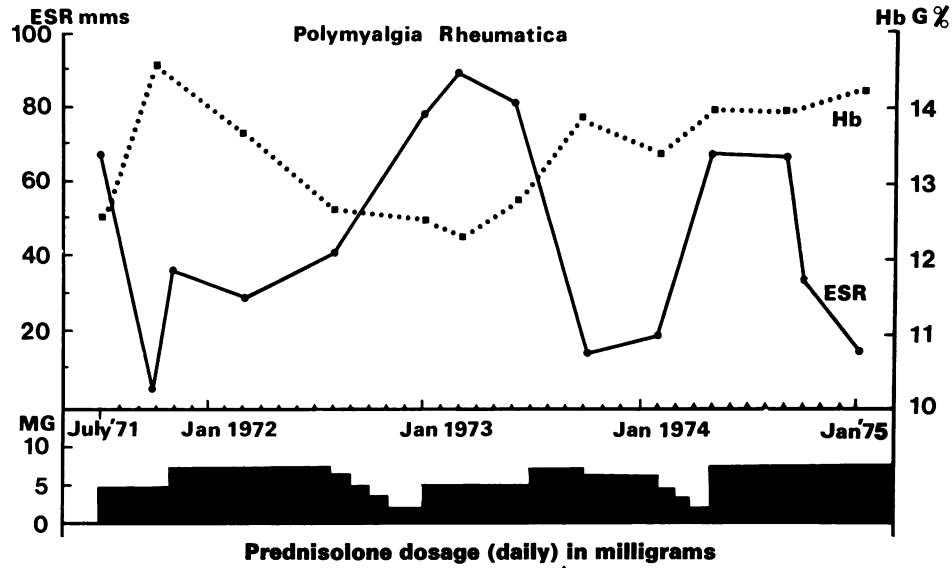

Figure 1

Case 6. Mrs K. O'B. To demonstrate the protracted course of polymyalgia rheumatica (P.M.R.) and the inverse relationship of the erythrocyte sedimentation rate (E.S.R.) and haemoglobin (Hb).

The main points of interest here are the delay of three months before diagnosis and the protracted course of the illness—at present 3½ years and still apparently active. The rapid response of symptoms to steroids can with caution be used as supporting evidence for the diagnosis.

Case 5. This 74-year old lady had been suffering from ' arthritis ' of her knees and shoulders associated with lethargy and malaise for nearly two years before she attended. The symptoms which finally prompted her to seek advice on 14 December 1972 were diminishing vision, diplopia, pain in the cheeks when chewing, and the inability to brush her hair because of scalp tenderness. She looked dreadful. The diagnosis was clear; the temporal arteries were thickened, red, tortuous, non-pulsatile cords, very tender to the touch.

Prednisolone 20 mg daily was started immediately. Examination of the blood revealed an ESR of 105 mm in one hour and haemoglobin of 11·3 g/100 ml. Temporal artery biopsy showed the classical features of giant cell arteritis (plate 1). Her response to treatment was rapid and successful. She had no worsening of her visual problems, but gradually lost her senses of taste and smell.

She has remained on prednisolone since diagnosis, but this has been cautiously tapered to a single dose of 7·5 mg daily on which she remains fit and active, although her ESR remains at 80 mm in one hour (figure 2).

In this case it is tempting to suggest that the two-year period of ' arthritis ' and malaise was in fact polymyalgia rheumatica. Certainly it has been shown that some patients with temporal arteritis have proven polymyalgia as a prodrome (Wilske and Healey, 1967).

Management

The keystone of treatment is corticosteroids. Prednisolone by the oral route in either divided or a single bedtime dosage is claimed to be the medication of choice (Fernandez-Herlihy, 1971). The dose and length of treatment varies.

Having once accepted that the syndromes of polymyalgia rheumatica and temporal arteritis (and possibly Takayashu's disease) are all part of a syndrome of giant cell arteritis, one must be constantly alert.

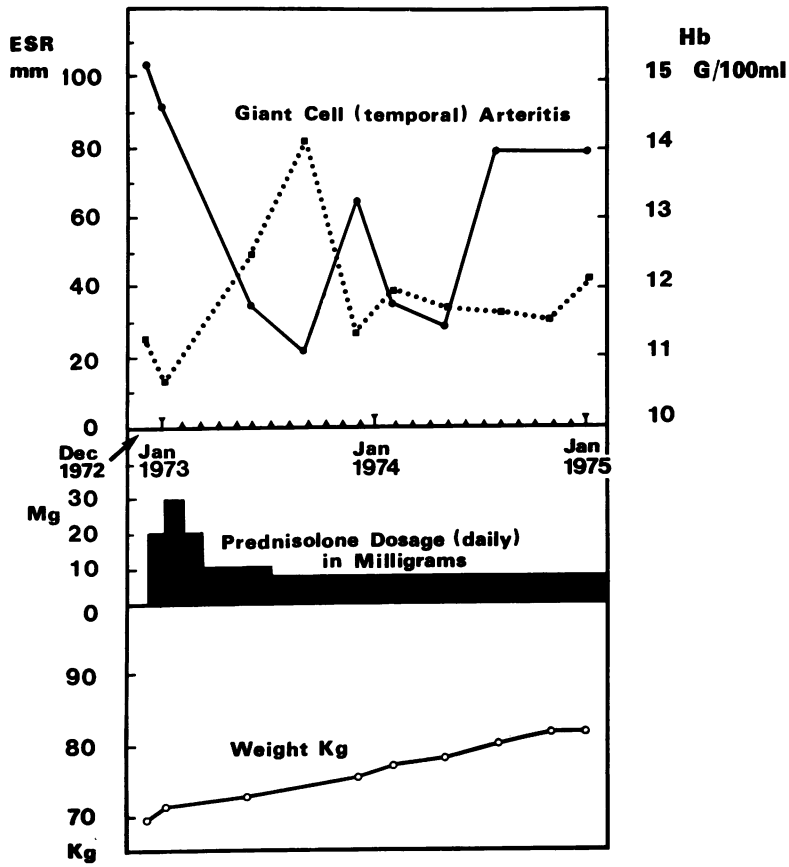

Figure 2

Case 5. Miss V. J. Temporal (Giant Cell) arteritis (GCA) and the effect of steroid treatment on erythrocyte sedimentation rate (ESR), haemoglobin (Hb) and body weight.

For this reason, in apparently uncomplicated polymyalgia, a temporal artery biopsy is a wise procedure. If the biopsy is negative, it does not exclude temporal arteritis and so clinical and haematological evidence must be considered as well. If the biopsy is positive in polymyalgia, then treatment must be started as for temporal arteritis.

For polymyalgia with negative biopsy and moderate elevation of the ESR, a single bedtime dose of 10 mg prednisolone is a reasonable start to treatment. In overt temporal arteritis a daily dosage of prednisolone between 40–60 mg has been recommended (Fernandez-Herlihy, 1971). This should be continued for seven to ten days and the dosage then maintained according to the clinical response and ESR.

One must be prepared to continue for two or three years and so a regular and careful follow-up of the patient, to exclude complications or the onset of other diseases, must be carried out.

Although the relief of symptoms can be remarkably effective with the use of corticosteroids, there is no evidence that they shorten the natural history of the disease (Hamilton *et al.*, 1971).

There must be a close liaison between family doctor and rheumatologist. The diagnosis must be well founded before embarking upon a long period of treatment with corticosteroids and their inherent dangers.

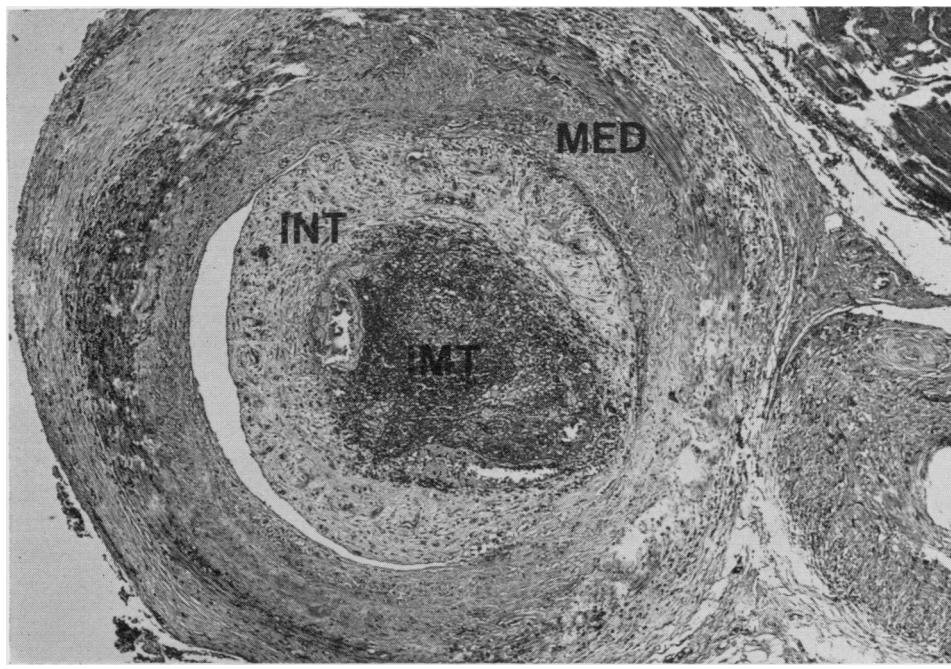

Plate 1

Section of temporal artery from case 5 (Miss V. J.), demonstrating the medial thickening (MED), the intimal proliferation (INT) and the intramural thrombus (IMT) Magnification × 64.

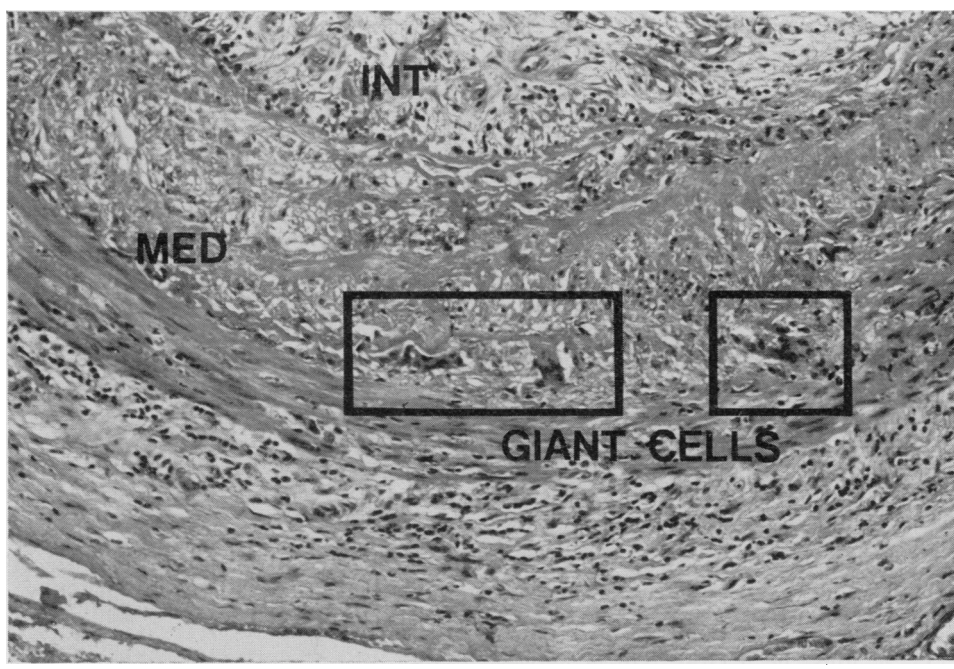

Plate 2

Higher power view of the same section (×160). The giant cells can be seen in the media (MED).

Complications

If all possible avenues of care are explored in diagnosis, the treatment and follow-up carefully maintained, few complications should be met. Even then tragedies occur.

Case 1. This 68-year old lady presented with florid temporal arteritis in July 1969. This was confirmed by temporal artery biopsy. Prednisolone 30 mg daily was started immediately. In spite of this she developed marked impairment of vision of her left eye due to ischaemic optic neuritis. The prednisolone was increased to 80 mg daily for two weeks and then reduced to 60 mg daily and then slowly tapered. Her vision improved a little and she was well and active.

I saw her on 8 September 1969. She was in a diabetic coma. Soon after admission she had a massive haematemesis and eventually died ten days later from a myocardial infarct.

This illustrates the fine line between adequate steroid dosage (in this case to save the vision of her left eye) and the tragedy of cortisone poisoning.

Case 10. This 70-year old lady had for six months suffered pain across her shoulders, neck and in her groins. She had also described a ' bursting ' sensation in both temples and occiptal region of the scalp. She had overt signs of polymyalgia with inflamed temporal and occipital arteries. Biopsy of the left temporal artery confirmed the diagnosis. Immediate relief of symptoms was obtained from a daily dose of 40 mg prednisolone. Three months later she developed signs of a chest infection and within a few days, despite intensive therapy, she died from fulminating tuberculous bronchopneumonia.

The pre-treatment chest x-ray had revealed a small calcified opacity in the lower middle zone of the left lung which was considered to be an old calcified primary focus. This stresses the need for routine chest x-ray and careful follow-up. In such cases, with old calcified foci visible on the chest x-ray, concurrent antituberculous therapy may well be indicated.

Discussion

These cases, collected during six years, are interesting in that they have occurred with a frequency higher than expected from current data (Dixon *et al.*, 1966; Ostberg, 1972).

Apart from two patients, the remainder all lived in one fairly small part of the village. Case 1 lived in the same house as case 6. Cases 8 and 4 lived as neighbours in an old people's housing development. Cases 5 and 7 were close friends.

It is tempting to draw conclusions from such associations, but there is no evidence at present to suggest that this disease is due to a transmissible agent, although some have drawn an association with the keeping of pet birds, especially parakeets (Healey, Parker and Wilske, 1971).

It is better to accept ignorance of the cause and admit that polymyalgia rheumatica, temporal arteritis, and Takayashu's disease appear to be related in some basic way, not yet fully proven or understood.

One fact is clear; polymyalgia is recognised too slowly in general practice. Temporal arteritis with florid signs is easier to recognise, but often can present in cryptic, confusing fashion, leading to delay in diagnosis and serious consequences.

The situation has been summarised neatly: " Giant cell arteritis . . . if untreated may progress slowly with pain, palsy, blindness, deafness and madness in its train, or sometimes more rapidly to a fatal termination . . . when elderly people begin to fail mentally and physically, giant cell arteritis is one of the first diseases to be considered, not the last " (Paulley and Hughes, 1960).

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