Polymyalgia rheumatica and giant cell arteritis — a difficult diagnosis

J. G. JONES, MB, FRACP
Senior Registrar, Addenbrooke's Hospital, Cambridge

B. L. HAZLEMAN, MA, MB, FRCP
Consultant Physician, Department of Rheumatology, Addenbrooke's Hospital, Cambridge

SUMMARY. This five-year study of 108 patients with giant cell arteritis and/or polymyalgia rheumatica drawn from all departments of a district general hospital emphasizes the difficulties of diagnosis. A correct diagnosis was made by the referring doctor in 33 per cent of patients and on initial attendance at hospital in 67 per cent of patients. Symptoms were present for more than three months before referral to hospital in 39 per cent of patients, and the delay before diagnosis at hospital was greater than one month in 20 per cent. Systemic illness (present in 83 per cent of cases), anaemia (33 per cent), elevated alkaline phosphatase (73 per cent) and raised immunoglobulin levels (48 per cent) caused diagnostic problems in 28 patients at primary care level and in 23 patients at hospital.

Introduction

POLYMYALGIA rheumatica is a clinical syndrome in which severe pain and stiffness of the shoulder and pelvic girdle muscles are the main features. In many patients an underlying vasculitis can be demonstrated; clinically there is no clear distinction between giant cell arteritis (GCA) and polymyalgia rheumatica (PMR).

Polymyalgia rheumatica has received increasing attention in recent years. It can lead to considerable morbidity, including sudden irreversible blindness, but effective treatment is available. Unfortunately, there is often considerable delay in making the diagnosis, partly because of the frequent absence of physical signs and lack of specific laboratory tests (Mowat and Hazleman, 1974).

Although GCA and PMR both have their typical presentation, there are other features which, though well described, are less well recognized and tend to complicate the diagnosis. There is commonly a constitional disturbance in both conditions (Harrison and Bevan, 1967; Fauchald *et al.*, 1972) consisting of weight loss, malaise, anorexia, night sweats, fever and depression. Myalgia may sometimes start in one group of muscles before spreading to involve the remainder of the proximal musculature (Bulgen and Hazleman, 1976), suggesting a local, rather than a systemic disorder. GCA can involve any large or medium-sized arteries, giving rise to local arterial tenderness and ischaemia in the area supplied by that artery (Mowat and Hazleman, 1974). Thus, arteritis of the coronary, cerebral, brachial, femoral and aortic vessels occurs in addition to the better known ophthalmic artery involvement. Myalgia, symptoms of arteritis and the constitutional effects can be present or absent in any case, while any one of these three features can dominate the clinical picture. Indeed, cases of systemic disease without myalgia or symptoms attributable to arteritis have been described (Ghose *et al.*, 1976).

Laboratory abnormalities often seen in GCA and PMR include anaemia (Wilske and Healey, 1967), raised alkaline phosphatase level (McCormack *et al.*, 1978) and raised immunoglobulin levels (Bacon *et al.*, 1975). All these features tend to obscure the diagnosis. Paulley and Hughes (1960) reported 14 modes of presentation of GCA and Hamilton and colleagues (1971) suggested 33 ways in which the condition may present.

Aim

Early diagnosis and, as a consequence, early treatment are desirable if vascular complications are to be minimized. We reviewed a group of patients with the intention of exploring the difficulties of diagnosis.

Methods

One hundred and eight patients with GCA and/or PMR presented at Addenbrooke's and Newmarket General Hospitals between January 1974 and March 1979. The patients were drawn from four sources:

1. Temporal artery biopsy records.
2. Inpatient diagnostic index.
3. Polymyalgia clinic of the Department of Rheumatology.
4. Referral from other departments.

The criteria for the diagnosis of PMR were:

1. Bilateral shoulder and pelvic girdle pain which was primarily muscular in the absence of true muscle weakness.
2. Morning stiffness.
3. Duration of at least two months.
4. ESR over 30 mm/hr or C-reactive protein (CRP) over 6 μg/ml.
5. Absence of rheumatoid or inflammatory arthritis or malignant disease.
6. Absence of objective signs of muscle disease.
7. Prompt and dramatic response (i.e., by the next day) to systemic corticosteroids.

The criteria for the diagnosis of GCA were:

1. A positive temporal artery biopsy, or
2. Cranial artery tenderness noted by a physician and
3. One or more of the following:
   a) Visual disturbance.
   b) Headaches.
   c) Jaw pain.
   d) Cerebrovascular insufficiency.
4. ESR over 30 mm/hr or CRP over 6 μg/ml.
5. Response to corticosteroids.

Details of the patient's symptoms and signs were compiled from the case records and personal interview. The presenting features and the initial diagnosis of both general practitioner and hospital doctor were documented. In an attempt to define which features of the disease were responsible for misdiagnosis, the reasons for general practitioner referral and initial hospital diagnosis were assigned to five categories according to their most prominent feature. This depended on whether myalgia, arteritis, systemic symptoms or abnormal laboratory tests caused the major diagnostic problem; a small number were assigned into a miscellaneous group. This division was somewhat artificial because several cases would fit into more than one category, but it does help to demonstrate the disease characteristics most responsible for diagnostic difficulties. The results of the initial values for full blood count, alkaline phosphatase and immunoglobulins were also recorded.

Table 1. Constitutional disturbance (total patients 108).

Weight loss (3-20 kg)	63
Anorexia	64
Malaise	73
Night sweats	52
Fever (>37.5°C)	31
Depression	28

Results

Thirty-four patients fulfilled the criteria for diagnosis of PMR alone, 23 patients for GCA and 51 had features of both disorders. The frequency of systemic symptoms is listed in Table 1. Ninety patients had one or more features.

Laboratory findings

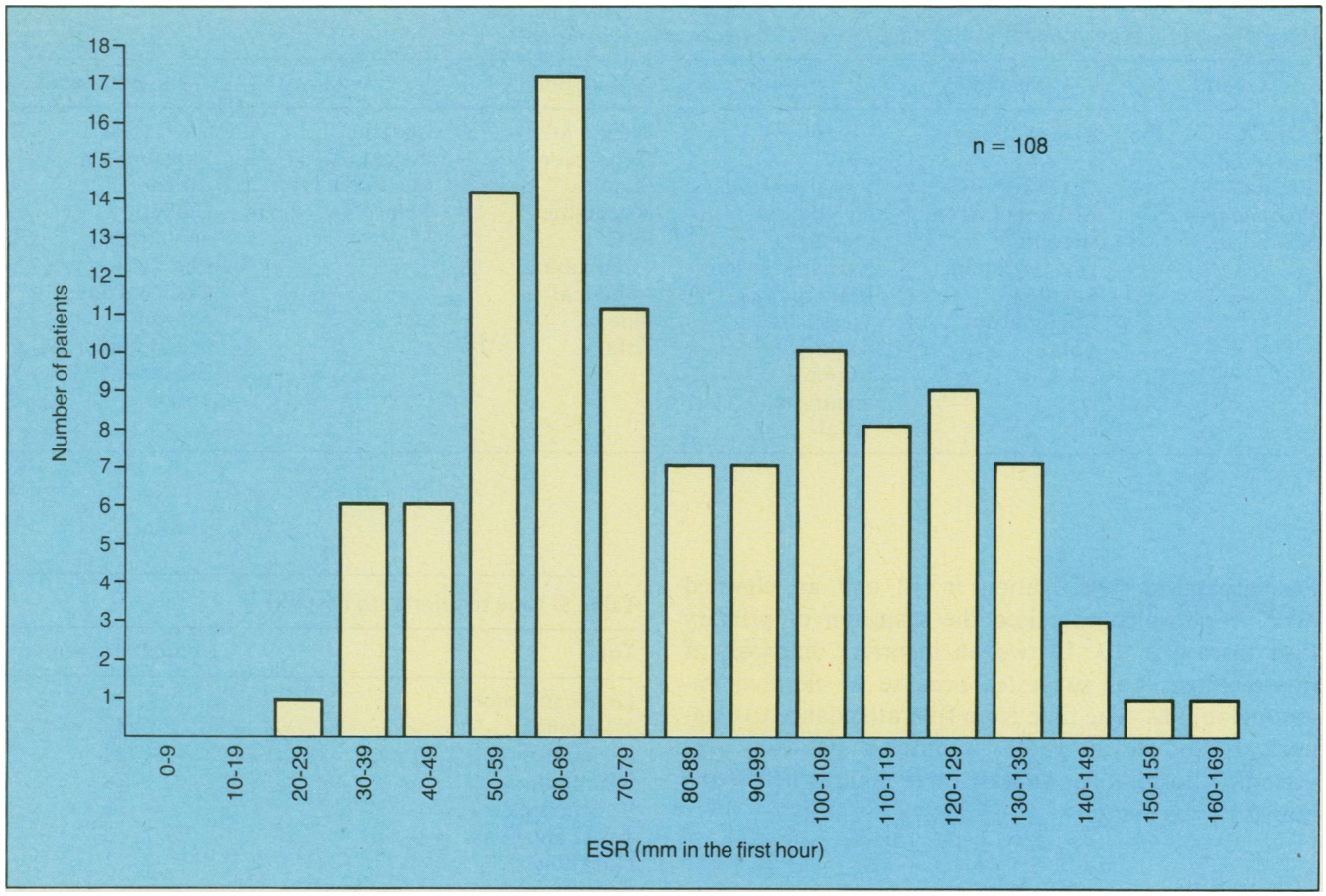
Thirty-six (33 per cent) of the 104 patients were anaemic (Hb less than 11 g/dl). In 28 cases the anaemia was normochromic, in six hypochromic and in two the type was not recorded. Eight patients had been given iron. The ESR was raised in all patients, sometimes to a very high level. The figure shows the ESR at presentation; in the one patient with an ESR less than 30 mm/hr, the test later became abnormal. The alkaline phosphatase level was found to be raised in 56 (73 per cent) of the 77 patients in whom it was estimated (Table 2). Immunoglobulin levels were estimated in 37 patients; the IgG level was raised in 16 (in five cases there was an accompanying elevated IgA and in three cases an elevated IgM), and IgM and IgA alone were each raised in one case.

Hospital departments

Table 3 lists the hospital departments to which the patients were referred; most patients attended either the rheumatology or general medical departments. Three patients initially went to their dentist with jaw pain and two went to an optician.

Initial diagnosis

The initial diagnosis on referral is listed in Table 4. In 13 cases two diagnoses were suggested and both are included. Thirteen patients presented while attending hospital for another condition. In three cases no diagnosis was offered by the referring physician; of the remaining 105 referrals, the correct diagnosis was made in 34. Fourteen patients were referred with a diagnosis of rheumatism and in 15 further cases myalgia appeared to be the major cause of diagnostic difficulty. Six patients who had predominantly arteritic symptoms were sent to hospital with diagnoses other than GCA. Systemic symptoms were responsible for a further 14 attendances, and 14 cases were referred as a conse-



ESR at presentation.

Table 2. Alkaline phosphatase level in 77 patients (international units/l).

Level	Patients	Level	Patients
0-92 (normal)	21	241-270	1
93-120	26	271-300	1
121-140	11	301-330	0
141-170	6	331-360	1
171-210	6	680	1
211-240	2	1150	1

Table 3. Hospital department at presentation.*

Rheumatology	46
General physicians	42
Ophthalmology	8
Orthopaedic	6
Neurology	5
Dermatology	1
Diabetic clinic	1
Chest physicians	2
Vascular surgeons	1
General surgeons	1
Physiotherapy	1
Total	114

*Six of the 108 patients presented twice.

quence of abnormal laboratory tests. Eight other patients attended with miscellaneous diagnoses. The interval between onset of the disease and referral to hospital is shown in Table 5; 79 patients were seen within three months.

The correct diagnosis was made at the first hospital visit in 70 patients. The diagnosis in the remaining 38 patients is given in Table 6. In six patients this was revised and both diagnoses have been included. In 14 patients the systemic symptoms resulted in an incorrect diagnosis, and in nine abnormal laboratory tests were responsible. Complications of anti-inflammatory therapy (a rash and a gastro-intestinal haemorrhage) were responsible in two instances for referral, the underlying illness not being recognized in either case.

Difficulty was caused by the systemic symptoms suggesting neoplasia in 11 patients, and in two further patients a myositis secondary to neoplasia was the initial diagnosis. A fever suggested infection in nine cases, and the presence of headache with or without ophthalmoplegia led to investigation to exclude an intracranial lesion in four. The presence of anaemia led to further

Table 4. General practitioners' initial diagnoses (121 diagnoses in 108 patients).

Overall		"Myalgic"		Arteritic		Systemic		Laboratory		Miscellaneous	
PMR/GCA	34	Rheumatoid arthritis	4	Visual loss: why?	1	Weight loss	3	Anaemia	8	Thyrotoxic	1
Presented at hospital	13	Osteoarthrosis	4	Visual loss and high blood pressure	1	Depression	2	Raised ESR	4	Reassure not cancer	1
No diagnosis offered	3	Bilateral frozen shoulder	3	3rd nerve lesion	1	Malaise	2	Myeloma	2	Diabetic amyotrophy	1
		Low back pain	2	Brain tumour	1	Meningitis	3	Total	14	Chest pains: why?	1
		Sciatica	2	Trigeminal neuralgia	1	PUO	1			Diabetes out of control	1
		Rheumatism	14	Femoral aneurysm	1	? Carcinoma	2			Second opinion	2
		Total	29	Total	6	? Physical illness	1			Bilateral DVT	1
						Total	14			Total	8

haematological investigation in 12 and an elevated alkaline phosphatase raised the suspicion of primary liver disease in 10. In two an incorrect diagnosis of myelomatosis was suggested because of elevated immunoglobulins. The time from first attendance to diagnosis is shown in Table 7. Fifteen patients were attending hospital for at least three months before the diagnosis was made.

Table 5. Time to referral to hospital.

Time	Number of patients
Less than 1 month	21
1-3 months	43
3-6 months	21
6-9 months	14
9-12 months	5
1 year and over	3
Not known	1

Discussion

Many patients with PMR and GCA are managed by their general practitioner and not referred to hospital. Those who are referred are more likely to be those with an atypical presentation and will consequently be more likely to cause diagnostic difficulty. Thus no series of patients from hospital practice alone can be considered to present a typical picture of the disease. Other recent series come from a single department of a hospital and reflect the interests of the specialty. For example, comparison of Coomes and colleagues' series (1976) from a rheumatology/general medicine clinic with Meadows' series (1966) from the National Hospital and Westminster Hospital shows the incidence of visual symptoms to be one per cent in the rheumatology/general medicine department and 75·5 per cent in the ophthalmological department.

This survey, giving the experience of the disease in a district general hospital, is more likely to give a truer overall picture of the condition than a series from one department, but does not include all patients who attended during the study period. Not all patients underwent temporal artery biopsy and therefore do not appear on the temporal artery list, and the diagnostic index does not cover outpatients.

The incidence (26 per cent) of ocular and neurological complications (Jones and Hazleman, 1981) demonstrates the potential complications of this condition. There was a delay of over three months in 43 (39 per cent) patients before referral to hospital. In some cases the patient attributed her aches and pains to family tensions or other problems; in others, patients and doctors ascribed the symptoms to degenerative joint disease. At hospital it took more than one month to reach the correct diagnosis in 22 (20 per cent) patients. The delay was in some cases due to lack of familiarity with the more unusual laboratory and clinical presentations of this condition; not surprisingly, the departments which saw the occasional case found diagnosis more difficult.

The diagnosis of this condition by Cambridgeshire general practitioners compares favourably with that found by Coomes and colleagues (1976) in Central London; they found that, over a 10-year period, the rate of correct diagnosis rose from four per cent to 10 per cent.

Thirty-three per cent of patients were found to be anaemic. The anaemia, which often posed a diagnostic problem that led to extensive investigation, is that seen in inflammatory disease and is readily corrected by corticosteroids. The presence of a normochromic anaemia in an unwell elderly patient should suggest the diagnosis of GCA or PMR.

The alkaline phosphatase level was raised in 73 per cent of patients, and led to the suggestion of a primary liver disease or of infiltration on 10 occasions. Forty-eight per cent of patients showed a rise in immunoglobulin level which led to the suspicion of myelomatosis in two cases.

Table 6. Initial hospital diagnoses (PMR/GCA = 70).

"Myalgia"		Arteritis		Systemic symptoms		Laboratory		Miscellaneous	
Low back pain	2	Headaches and raised blood pressure	1	Subacute bacterial endocarditis	1	Chronic liver disease	1	Hypothyroid	1
Rheumatoid arthritis	3	Inguinal lymphadenitis	1	Meningitis	1	Collagen disease	1	Hyperthyroid	1
Osteoarthrosis	3	Retinal artery thrombosis	1	Viral illness	1	Collagen disease and liver involvement	1	Uraemia	1
Post-gastrectomy malabsorption	1	Total	3	Unwell, refer physicians	1	Anaemia	6	Congestive heart failure	1
Polymyositis secondary cancer	1			Cancer	6	Total	9	Malaena—Ca. colon	1
Clofibrate myopathy	1			Depression	3			Malaena—Ketoprofen	1
Total	11			"Compensationitis"	1			Rash—Naproxen	1
				Total	14			Total	7

Systemic effects and abnormal laboratory investigations caused difficulty with the referring doctor's diagnosis in 26 patients and with diagnosis at hospital in 23 patients. Weight loss, malaise and anorexia (along with anaemia, elevated ESR and raised alkaline phosphatase) raised the suspicion of malignancy. Night sweats and fever suggested infection, including subacute bacterial endocarditis, viral illness and meningitis. Endogenous depression was diagnosed in three cases.

Arteritis caused headache, ophthalmoplegia suggested a brain tumour and jaw pain a dental problem or trigeminal neuralgia. Femoral arteritis with local pain was diagnosed as inguinal lymphadenitis.

When myalgia dominated the clinical picture, the diagnosis of clofibrate myopathy, post-gastrectomy vitamin D deficiency and polymyositis secondary to carcinomatosis were all considered. It is worrying that 14 patients should have been referred with the very non-specific diagnosis of "rheumatism". Letters of referral are often graded as to urgency: a suggestion of PMR would lead to an urgent appointment, whereas a patient suffering from "rheumatism" may be given a routine appointment. Local myalgia led to the mistaken diagnoses of osteoarthrosis, frozen shoulder, cervical spondylosis and lumbar spinal disease.

In 1960 Paulley and Hughes stated that "Diagnostic failure is due to many diverse presentations, some of which are little known, and to continued acceptance of a too rigid profile of the disease, despite the fact that the literature is replete with clinical and pathological evidence of its systemic nature." This statement appears as pertinent today as it was 20 years ago.

Table 7. Delay in diagnosis at hospital.

Time	Number of patients
Under 2 weeks	7
2 weeks-1 month	6
1-2 months	8
2-3 months	2
3-4 months	4
4-5 months	3
5-6 months	2
6-7 months	2
7-12 months	1
12-24 months	2
More than 24 months	1
Total	38

References

Bacon, P. A., Doherty, S. M. & Zuckerman, A. J. (1975). Hepatitis-B antibody in polymyalgia rheumatica. *Lancet*, **2**, 476-478.

Bulgen, D. Y. & Hazleman, B. L. (1976). Polymyalgia rheumatica. *Hospital Update*, January, 39-46.

Coomes, E. N., Ellis, R. M. & Kay, A. G. (1976). A prospective study of 102 patients with the polymyalgia rheumatica syndrome. *Rheumatology and Rehabilitation*, **15**, 270-279.

Fauchald, P., Rygvold, O. & Oystese, B. (1972). Temporal arteritis and polymyalgia rheumatica. Clinical and biopsy findings. *Annals of Internal Medicine*, **77**, 845-852.

Ghose, M. K., Shensa, S. & Lerner, P. I. (1976). Arteritis of the aged (giant cell arteritis) and fever of unexplained origin. *American Journal of Medicine*, **60**, 429-436.

Hamilton, C. R. Jr., Shelley, W. M. & Tumulty, P. A. (1971). Giant cell arteritis, including temporal arteritis and polymyalgia. *Medicine* (Baltimore), **50**, 1-27.

Harrison, M. J. G. & Bevan, A. T. (1967). Early symptoms of temporal arteritis. *Lancet*, **2**, 638-640.

Jones, J. G. & Hazleman, B. L. (1981). Prognosis and management of polymyalgia in rheumatism. *Annals of Rheumatic Diseases*, **40**, 1-5.

McCormack, L. R., Astarita, R. W. & Foroozan, P. (1978). Liver involvement in giant cell arteritis. *American Journal of Digestive Diseases*, **23**, (5), Suppl. 72S-74S.

Meadows, S. P. (1966). Temporal or giant cell arteritis. *Proceedings of the Royal Society of Medicine*, **59**, 329.

Mowat, A. G. & Hazleman, B. L. (1974). Polymyalgia rheumatica—a clinical study with particular reference to arterial disease. *Journal of Rheumatology*, **1**, 190-202.

Paulley, J. W. & Hughes, J. P. (1960). Giant-cell arteritis or arteritis of the aged. *British Medical Journal*, **2**, 1562-1567.

Wilske, K. R. & Healey, L. A. (1967). Polymyalgia rheumatica. A manifestation of giant-cell arteritis. *Annals of Internal Medicine*, **66**, 77-86.

Acknowledgements

We thank the Arthritis and Rheumatism Council for their continuing support and are grateful to the doctors at Addenbrooke's Hospital who kindly referred cases.

Address for reprints

Dr B. L. Hazleman, Department of Rheumatology, Addenbrooke's Hospital, Cambridge.