

Prognosis and management of polymyalgia rheumatica

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SUMMARY Polymyalgia rheumatica (PMR) is considered to be a benign disease by some, while others think it is a more serious illness which requires similar treatment to giant cell arteritis (GCA). The progress of 85 patients with PMR who presented to a district general hospital has been studied in an attempt to study this relationship. Thirty-eight patients had PMR alone, and 14 developed PMR and GCA within 1 month. Five patients presented with GCA and then developed PMR, and 28 patients developed symptoms of GCA after presenting with PMR (PMR→GCA). Arteritis and complications developed up to 9 years after the onset of PMR (mean 1 year). Twenty-two patients (26%) developed some cerebral or visual complication. Fifteen of these patients were in the PMR→GCA group. All 6 patients with permanent loss of vision were in this group. Seven patients developed complications while on corticosteroids. 97% of patients required corticosteroids for at least 1 year; 32% of patients still required 10 mg of prednisone or more after 1 year. PMR is not a benign disease.

It is well recognised that polymyalgia rheumatica (PMR) is often a manifestation of giant cell arteritis (GCA), and in some myalgic patients biopsy of an asymptomatic and apparently normal temporal artery may reveal the classical histological appearances of GCA.

The true relationship between PMR and GCA remains uncertain. Some^{1,2} consider that polymyalgia is always a manifestation of GCA. Others disagree with this view; they point out that most patients with PMR followed up for many years never develop evidence of cranial arteritis and consider it to be a benign condition.³ Fauchald *et al.*¹ found that 40% of patients with myalgia alone had a positive biopsy, and other studies suggest that this occurs in 6%⁴ to 50%⁵ of patients. The cause of this variation is uncertain but may be explained in part by the selection of cases. The interpretation of temporal artery biopsies can be complicated by the presence of skin lesions, which were identified in 28% of patients with temporal arteritis.⁶ The true incidence of arteritis in polymyalgia is probably higher than reported. The onset of myalgic symptoms may precede, coincide with, or follow that of the arteritic symptoms. No difference has been found between the characteristics of those myalgic patients with a positive biopsy and those with no histological evidence of arteritis.¹

GCA can lead to blindness, deafness, and cerebral

infarction. These complications are largely preventable by treatment of the disease with adequate doses of corticosteroids.^{7,8} While the accepted initial dosage for treatment of GCA is 45-60 mg of prednisone a day,⁹ opinions differ on the treatment of patients with PMR alone. Some authors^{1,2} consider that, as all patients with PMR probably have an underlying arteritis, they should be treated as though they had GCA, that is, with high doses of corticosteroids. Others^{10,11} consider a lower dose of prednisone (10-15 mg a day) is adequate treatment for those with PMR and no signs of arteritis.

There is also a divergence of views about the length of time for which steroids should be continued. Russell⁷ suggested 6 months' treatment was usually sufficient, and more recently Huston *et al.*¹² found that it was possible to withdraw steroids within 1 year from 23 out of 43 patients with positive temporal artery biopsies. Hamilton *et al.*,² however, showed that disabling vascular occlusive episodes may occur from 6 months to 2 years after initiating treatment. Fauchald *et al.*¹ recommend treatment for 2 years, and Coomes *et al.*¹³ found that treatment with corticosteroids was necessary for 5 years or longer in 84% of their patients with PMR.

This study sets out to investigate the association between PMR and GCA in a district hospital population and also attempts to ascertain the incidence of complications and how long corticosteroid therapy is required.

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Patients and methods

Eighty-five patients presenting at Addenbrooke's Hospital between January 1974 and March 1979 have been reviewed. The patients were collected from four sources: (1) from those who underwent temporal artery biopsy; (2) the inpatient diagnostic index; (3) the Polymyalgia Clinic in the Department of Rheumatology; (4) referral from other departments.

A detailed history and examination was carried out if patients met the following criteria.

CRITERIA FOR DIAGNOSIS OF PMR

(1) Shoulder and pelvic girdle pain which was primarily muscular in the absence of true muscle weakness. (2) Morning stiffness. (3) Duration of at least 2 months unless treated. (4) ESR over 30 mm/h 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 to systemic corticosteroids.

CRITERIA FOR DIAGNOSIS OF GCA

(1) Positive temporal artery biopsy or cranial artery tenderness noted by a physician. (2) One or more of the following: visual disturbance, headache, jaw pain, cerebrovascular insufficiency. (3) ESR over 30 mm/h or CRP over 6 µg/ml. (4) Response to corticosteroids.

If a patient with PMR receiving corticosteroids developed symptoms of GCA, a raised ESR or CRP was not considered necessary for diagnosis of GCA.¹⁴

The initial treatment for patients with GCA was 40–60 mg prednisone a day, and in those patients with no clinical evidence of arteritis 10–15 mg prednisone a day was prescribed. The sedimentation rate was used as a guide to disease activity.

Results

Patients were divided into 4 groups depending on their clinical symptoms and signs (Table 1). Thirty-

Table 1 *Diagnosis of patients and results of temporal artery biopsy*

| | Temporal artery biopsy | | | | % positive |
|-----------|------------------------|----------|----------|---------------|------------|
| | No. of patients | Positive | Negative | Not performed | |
| PMR alone | 38 | 4 | 11 | 23 | 27 |
| PMR/GCA | 14 | 10 | 2 | 2 | 83 |
| PMR→GCA | 28 | 7 | 14 | 7 | 33 |
| GCA→PMR | 5 | 1 | 4 | 0 | 20 |
| Total | 85 | 22 | 31 | 32 | 41 |

eight of the 85 patients had symptoms of PMR with no clinical evidence of GCA. Fourteen patients developed signs of both conditions within a month of onset of illness. Twenty-eight patients developed clinical evidence of GCA 1 month or longer after the onset of PMR, and in 5 cases PMR occurred for the first time during treatment for GCA. Thus 28 (42%) of the 66 patients who suffered from PMR alone for at least 1 month developed clinical evidence of GCA. The results of the temporal artery biopsy when performed (Table 1) were positive in 4 (27%) of 15 patients who did not develop clinical evidence of GCA. Three patients in the PMR→GCA group (see Table 1) had negative biopsies early in the disease.

The clinical details of the 28 patients who later developed symptoms of GCA are shown (Table 2). Headache was the most prominent symptom. The length of time from onset of PMR to the development of GCA is shown in Fig. 1 (mean interval 1 year; range 1 month–9 years).

Table 3 lists the neurological and visual complications seen in the 4 groups of patients. A serious or potentially serious complication of GCA occurred in 22 (26%) of all 85 patients and in 15 (53%) of 28 patients in the PMR→GCA group. Exclusion of the

Table 2 *Clinical features of PMR→GCA group*

| Symptoms | Number |
|-----------------------------------------|------------------------------|
| Headaches | 23 (12 with visual symptoms) |
| Meteorism with flare PMR | 1 |
| Jaw pain | 2 (1 with visual symptoms) |
| Swollen face and tender temporal artery | 1 (with visual symptoms) |
| Prominent tender temporal artery | 1 |

Table 3 *Neurological and visual complications of 22 patients with PMR*

| | All patients | PMR/GCA | PMR→GCA | GCA→PMR |
|--------------------------------|--------------|---------|---------|---------|
| Permanent visual loss | 6 | | 6 | |
| Temporary visual loss | 7 | | 6 | 1 |
| Temporary visual blurring | 5 | 2 | 3 | |
| Diplopia | 3 | | 3 | |
| Permanent lateral rectus palsy | 1 | | 1 | |
| Transient third nerve lesion | 1 | 1 | | |
| Meteorism | 1 | | 1 | |
| Hemiparesis | 4 | | 3 | 1 |
| Vertebrobasilar ischaemia | 1 | 1 | | |
| Vertigo | 2 | | 2 | |
| Deafness | 1 | 1 | | |
| Number of patients | 22 | 5 | 15 | 2 |

Some patients suffered more than one complication.

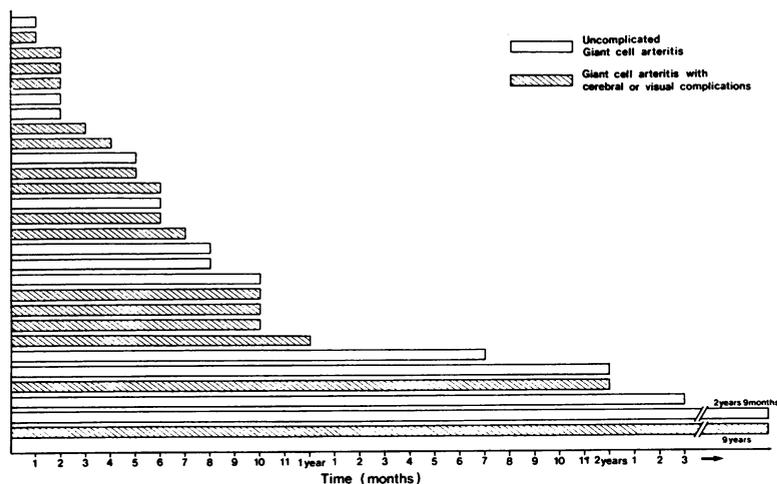


Fig. 1 Interval from onset of PMR to onset of GCA

Table 4 Details of visual and neurological complications

| Patient no. | Diagnosis | Complication | Time after disease onset | | Daily dose prednisone | Duration of treatment | | ESR |
|-------------|-----------|-----------------------------|--------------------------|-----|------------------------|-----------------------|-----|-----|
| | | | Yr | Mth | | Yr | Mth | |
| 1 | PMR → GCA | Hemiparesis, Transient LOV* | 6 | | 12.5 mg | 2 | | 60 |
| 2 | PMR → GCA | Permanent LOV | 4 | | | | | 105 |
| | | Lateral rectus palsy | 4 | | | | | |
| 3 | PMR → GCA | Hemiparesis | 1 | 0 | 10 mg | 7 | | 20 |
| 4 | PMR → GCA | Permanent LOV | 8 | | 8 mg | 2 | | 3 |
| | | Transient LOV | 4+ | | 2½ mg | 4 | 0 | 42 |
| 5 | GCA → PMR | Vertigo | | | | | | |
| 6 | GCA → PMR | Transient LOV | 2 | 6 | 30 mg | 3 | | 36 |
| 7 | PMR/GCA | Diplopia | 1 | 6 | 7.5 mg | 9 | | ? |
| 8 | PMR → GCA | Blurring | 2 | | 15 mg | 1 | | ? |
| 8 | PMR → GCA | Meteorism | 10 | | 15 mg | 3 | | 13 |
| 9 | PMR → GCA | Hemiparesis | | | Stopped 6 month before | 8 | 6 | 100 |
| | | Transient LOV | 9 | 0 | | | | |
| | | Blurring | | | | | | |

*LOV = Loss of vision.

patients who presented with clinical signs of GCA shows that 15 of 66 (23%) patients who had PMR alone for 1 month or longer went on to develop neurological or visual complications. All 6 patients with permanent visual loss were in this group. Seven out of 19 (37%) patients with clinical evidence of GCA at the onset of their illness developed complications. Eight of the 22 patients developed complications 1 year after disease onset and only 7 patients did so within the first 3 months. Complications occurred in 8 patients while receiving corticosteroids (Table 4 (patients 1–8)). Five of these complications occurred less than 4 months after initiation of treatment, while 1 occurred 4 years after starting prednisone. A rise in ESR occurred prior to the onset of complications in 4 out of 7 patients. Patient 9 received 8½ years' treatment with prednisone for uncomplicated PMR; 6 months after withdrawal of prednisone the patient was

Table 5 Details of visual and neurological complications

| Patient no. | Diagnosis | Complication | Time after disease onset | |
|-------------|-----------|-------------------------------|--------------------------|-----|
| | | | Yr | Mth |
| 10 | GCA → PMR | Hemiparesis | | 1 |
| 11 | PMR/GCA | Vertebrobasilar insufficiency | | |
| | | Deafness | | 2 |
| 12 | PMR → GCA | Permanent LOV* | | 10 |
| 13 | PMR → GCA | Permanent LOV | | 3 |
| 14 | PMR → GCA | Permanent LOV | | 8 |
| 15 | PMR → GCA | Permanent LOV | | 6 |
| 16 | PMR → GCA | Transient LOV | | |
| | | Diplopia | | 7 |
| 17 | PMR → GCA | Permanent LOV | 1 | 0 |
| 18 | PMR → GCA | Transient LOV | | |
| | | Vertigo | 1 | 7 |
| 19 | PMR/GCA | Transient III Nerve lesion | | 0 |
| 20 | PMR → GCA | Diplopia | | |
| | | Blurring | 1 | 7 |
| 21 | PMR → GCA | Blurring | | 2 |
| 22 | PMR/GCA | Blurring | | 1 |

*LOV = Loss of vision.

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Table 6 Details of patients able to stop steroids

| Patient no. | Diagnosis | Initial ESR | Biopsy | Disease duration before prednisone | | Duration of prednisone | | Time off prednisone | | Symptoms |
|-------------|-----------|-------------|--------|------------------------------------|-----|------------------------|-----|---------------------|-----|----------|
| | | | | Yr | Mth | Yr | Mth | Yr | Mth | |
| 23 | PMR/GCA | 117 | ND | | 9 | | 9 | 2 | 6 | 0 |
| 24 | PMR | 33 | ND | | 4 | 1 | 7 | 2 | 9 | 0 |
| 25 | PMR | 130 | + | | 2 | 1 | 5 | 3 | 0 | S |
| 26 | PMR | 74 | ND | | 3 | | 9 | 2 | 6 | 0 |
| 27 | PMR/GCA | 77 | ND | | 1 | 1 | 9 | | 6 | S |
| 28 | PMR/GCA | 80 | + | | 4 | 3 | 1 | | 2 | 0 |
| 29 | PMR/GCA | 40 | + | | 2 | 3 | 8 | | 6 | S |

Pred.=prednisone. Biopsy results: + = positive; ND=not done. Symptoms: 0=No symptoms; S=symptoms (see text).

admitted to hospital with bitemporal headaches, hemiplegia, and transient blurring of vision. The ESR was elevated at 100 mm/h and a temporal artery biopsy was positive. Reintroduction of corticosteroids controlled the symptoms, and 2 years later 10 mg of prednisone was still required.

Six patients did not receive corticosteroids because the symptoms were mild or they had a history of previous gastrointestinal haemorrhage or tuberculosis. Only 7 of the remaining patients had been able to discontinue corticosteroid therapy (Table 6). Two patients stopped treatment at 9 months and have remained free of symptoms. Three patients stopped treatment after 1 year, and treatment was withdrawn after 3 years in the other 2 patients. The clinical and laboratory features of those 7 patients at onset were similar to the rest of the group. Three patients still have some stiffness or occasional tender scalp nodules. Corticosteroids were withdrawn in 7 further patients, but recurrence of their symptoms necessitated reinstitution of treatment. In 2 cases this was less than 1 year after starting treatment, in 3 after 1 year of treatment, and in the other 2 it was after 3½ and 8½ years of treatment respectively.

Seventy-two patients were taking prednisone at the time of interview. Thirteen patients had received treatment for less than 1 year, 59 patients for over 1 year, 34 had been treated for 2 years, and 21 for at least 3 years. Interpretation of these figures is made difficult by the varying duration of follow-up, but 21 of the 59 patients who received treatment for at least 1 year required 10 mg of prednisone a day or more. Thirty-three patients were taking between 5 and 9 mg a day, and only 5 patients received less than 5 mg of prednisone a day.

Only 11 patients had not suffered a definite relapse on reduction of corticosteroid dosage. Forty of the 55 patients who developed a definite relapse on reduction of their prednisone did so at least 1 year after starting treatment, and 23 patients had relapsed 2 years or more after beginning treatment.

Discussion

In this group of hospital patients PMR does not appear to be a benign disease. Clinical evidence of GCA was seen in 55% of all patients with PMR, and serious or potentially serious neurological or visual complications occurred in 26% of cases. 44% of myalgic patients with no clinical evidence of GCA in the early stages of the disease developed GCA, and 23% of these patients suffered complications. All 6 patients with permanent loss of vision were in the latter group, as were the 3 of the 5 patients who developed cerebrovascular ischaemia. Arteritis and complications developed up to 9 years after the onset of PMR (mean 1 year; range 1 month to 9 years).

The complication rate in this group of hospital patients is high and may exaggerate the morbidity of the disease in the community. While some general practitioners refer all patients with PMR to hospital, others treat straightforward cases at home and refer only the more complicated ones to hospital. Thus any series of hospital patients is likely to contain more patients with complications than a series produced from general practice. On the other hand, the definition of PMR used in the series (involvement of both upper and lower limbs) is more stringent than in other series, which include patients with involvement of the upper or lower extremities alone. Our definition is more likely to exclude those patients with degenerative joint disease, capsulitis of the shoulders, or spinal disorders and may reflect a more classical disease pattern. This group of patients has been drawn from all departments of the hospital, which removes the bias of a series from 1 specialty. For example, a series from an ophthalmology department will have more patients with visual complications than a series from a rheumatology unit. Even when these considerations are taken into account, a complication rate of 26% is surprisingly high.

Complications developed at least 3 months after the onset of illness in 13 of the 15 cases without

initial evidence of arteritis. Harrison and Bevan¹⁵ described 9 patients who developed GCA at least 1 year after onset of PMR. One case suffered some visual loss and another developed a hemiplegia. Seven out of 15 cases reported by Olhagen¹⁶ developed localised changes of arteritis 3 to 27 months after the onset of PMR, and in 3 cases visual impairment was present. Unlike those cases who present with symptoms of GCA, where complications usually develop under 3 months,^{7,8} it appears that complications often develop at longer intervals in patients with PMR.

Temporal artery biopsy was of no value in predicting which patients would be likely to develop signs of GCA. Three patients with PMR who later developed GCA had negative biopsies before the onset of clinical evidence of GCA, and 4 out of 15 biopsies were positive in myalgic patients who never showed clinical evidence of arteritis.

Corticosteroid therapy did not prevent the development of arteritis in 8 cases, though signs of GCA did occur for the first time after withdrawal of corticosteroids in 2 cases. Complications developed in 8 patients while on corticosteroids, and in 3 of these patients the ESR was not raised when the complication occurred. Five of these patients developed complications less than 3 months after beginning corticosteroids. While 1 patient was taking 30 mg of prednisone a day, the other 4 were taking less than 15 mg a day. If these patients had been receiving a high-dose prednisone programme of treatment, it is possible that these episodes might not have happened. It is noteworthy that 1 patient permanently lost vision, and other patients suffered a hemiparesis.

The high incidence of complications in this series tends to support the belief of Hamilton *et al.*² and Fauchald *et al.*¹ that all patients with PMR should be treated with high doses of corticosteroids as though they had GCA. However, it should be emphasised that 58% of patients who presented with PMR and received low doses of prednisone have showed no evidence of GCA. The side effects caused by high dose corticosteroids in this elderly group of patients will produce a morbidity and mortality of their own, and this must be weighed against severity of the disease itself.

The disease relapsed in 40 patients a year after starting therapy, and we found that 97% of patients required corticosteroids for at least 1 year. Although the dosage of corticosteroids was kept as low as possible, 32% of patients still required 10 mg of prednisone or more after 1 year's treatment.

This study supports the view that PMR is not a benign disease. Patients require regular follow-up and should be instructed to report to their doctor if there is any exacerbation of their myalgia or if there are visual symptoms. The clinician should be alert to the development of signs of GCA at any time in the long course of this disease and not become complacent in the management of the apparently fit corticosteroid-treated patient. At present there is no method of predicting those patients who will develop complications of their disease.

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References

- 1 Fauchald P, Rygvold O, Oystese B. Temporal arteritis and polymyalgia rheumatica. Clinical and biopsy findings. *Ann Intern Med* 1972; **77**: 845-52.
- 2 Hamilton C R, Shelley W M, Tumulty P A. Giant cell arteritis including temporal arteritis and polymyalgia rheumatica. *Medicine (Baltimore)* 1971; **50**: 1-27.
- 3 Ettlinger R E, Hunder G G, Ward E L. Polymyalgia rheumatica and giant cell arteritis. *Ann Rev Med* 1978; **29**: 15-22.
- 4 Hunder G G, Allen G L. The relationship between polymyalgia and temporal arteritis. *Geriatrics* 1973; **28**: 134-42.
- 5 Malmvall B E, Bengtsson B A. Giant cell arteritis: clinical features and involvement of different organs. *Scand J Rheumatol* 1978; **7**: 154-8.
- 6 Klein R G, Campbell R J, Hunder G G, *et al.* Skip lesions in temporal arteritis. *Mayo Clin Proc* 1976; **51**: 504-8.
- 7 Russell R W R. Giant cell arteritis—a review of 35 cases. *Q J Med* 1958; **28**: 471-89.
- 8 Hollenhorst R W, Brown J R, Wagner H P, Schick R M. Neuralgic aspects of temporal arteritis. *Neurology* 1960; **10**: 490-8.
- 9 Hunder G G, Allen G L. Giant cell arteritis: a review. *Bull Rheum Dis* 1978-9; **29**: 980-6.
- 10 Healey L A, Wilske K R. Manifestations of giant cell arteritis. *Med Clin N Am* 1977; **61**: 261-70.
- 11 Myles A B. Polymyalgia rheumatica and giant cell arteritis: a seven year survey. *Rheumatol Rehabil* 1975; **14**: 231-5.
- 12 Huston K A, Hunder G G, Lie J T, Kennedy R H, Elverback L R. Temporal arteritis: a 25 year epidemiologic, clinical and pathologic study. *Ann Intern Med* 1978; **88**: 162-7.
- 13 Coomes E N, Ellis R M, Kay A G. A prospective study of 102 patients with polymyalgia rheumatica syndrome. *Rheumatol Rehabil* 1976; **15**: 270-6.
- 14 Rynes R I, Mika P, Bartholomew L E. Development of giant cell (temporal) arteritis in a patient 'adequately' treated for polymyalgia rheumatica. *Ann Rheum Dis* 1977; **36**: 88-90.
- 15 Harrison M J G, Bevan A T. Early symptoms of temporal arteritis. *Lancet* 1967; **ii**: 638-40.
- 16 Olhagen B. Polymyalgia rheumatica a form of senile arteritis? *Acta Rheumatol Scand* 1963; **9**: 157-64.