Prognosis in giant-cell arteritis

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Abstract

In a study to assess the natural history of giant-cell arteritis, 90 patients with proved disease were followed up from the time of diagnosis. Early mortality was low and most commonly due to vertebral arteritis, but cerebral infarction did not appear to be a late complication. High maintenance dose steroids and visual loss were associated significantly with a shortened life span ($p=0.0003$ and $p=0.0024$). One-third of the patients developed chronic relapsing disease, but serious late complications were not encountered.

After the initial attack has been controlled steroid dosage should be reduced to the minimum needed to alleviate symptoms.

Introduction

Giant-cell arteritis (temporal arteritis) was recognised as a clinical entity 90 years ago,[1] yet is still not fully understood. It occurs almost exclusively in elderly patients, who present with temporal headache, scalp tenderness, proximal muscle pain, and stiffness (polymyalgia rheumatica). There is a considerable risk of loss of vision due to ischaemia of the optic nerve or retina.

The diagnosis is usually made clinically and confirmed by finding a raised erythrocyte sedimentation rate and arteritis on biopsy of a scalp artery. Treatment is by systemic corticosteroids, which produce a dramatic response. After treatment for weeks or months the disease in many cases is apparently cured, but some patients follow a more prolonged course, requiring long-term steroid treatment.

In this retrospective study of 90 patients we examined the clinical course of the disease to see how long it had been active and whether it affected life expectancy. We also investigated the cause of death at various stages in the disease and attempted to determine whether treatment altered the course of the disease or merely suppressed the symptoms.

Patients and methods

The patients had attended the ophthalmology and neurology departments of St Thomas's Hospital, the National Hospital for Nervous Diseases, or Moorfields Eye Hospital between 1968 and 1978. In all cases the diagnosis had been confirmed by temporal artery biopsy.

Clinical details were obtained from case notes; these included presenting symptoms and signs, initial erythrocyte sedimentation rate, and treatment regimens. All surviving patients were traced and most were seen again and examined. A further clinical history was taken with particular reference to headache, muscular pains, visual failure, and any other symptoms possibly attributable to arteritis, vascular disease, or treatment regimens. A full examination was carried out including visual acuity, visual fields, and fundoscopy. Blood was taken for cell count, erythrocyte sedimentation rate, and plasma protein and immunoglobulin concentrations. From the case notes of those patients who had died additional information on drug regimens and evidence of relapse was also obtained; the cause of death was established from death certificates. All patients were traced.

Survival curves were used to assess whether patients suffering from temporal arteritis had a different mortality rate from that of the normal population of similar age and sex. Assuming that the national death rate applied, we determined the expected number of deaths in the study using life tables[2] and the program MYCL.[3] For example, if a man aged 76 had been at risk for six months (0·5 of a year) his contribution to the expected number of deaths would be: time at risk $\times$ age-sex specific death rate $= 0{\cdot}5 \times 0{\cdot}05546 = 0{\cdot}02773$. The expected number of deaths was derived by summing each person's contribution for each pair of years. The survival curves were then calculated using standard life-table methods.[4]

The survival analysis computer program (Surv-C) (M C Pike, DHSS Cancer Epidemiology and Clinical Trials Unit, personal communication) was used to calculate survival curves and the log-rank test statistic,[5] which were then used in the analysis of the results to ascertain factors of prognostic significance.

Results

The study group consisted of 90 patients (64 women, 26 men). The youngest presenting age was 55 years and the oldest 88 years. The average duration of follow-up was five years (range 12 months to 12 years): 11 patients were followed up for up to a year, 48 for one to five years, 26 for six to 10 years, and five for over 10 years. All 58 surviving patients were traced; 50 patients were seen and the remainder returned questionnaires.

The erythrocyte sedimentation rate at time of diagnosis ranged from 15 mm to 148 mm (mean 81 mm) in the first hour (table I). The patient with an erythrocyte sedimentation rate of 15 mm had coexistent polycythaemia rubra vera, which presumably caused a falsely low sedimentation rate, but there were no additional factors to alter the erythrocyte sedimentation rates in the remainder of patients.

VISUAL SYMPTOMS AND SIGNS

The following symptoms and signs were present in all patients at presentation: headache (68 patients), scalp tenderness (50), visual loss (43), polymyalgia rheumatica (30), dizziness with double vision (16), ophthalmoplegia (11), and angina (9). Table II lists the visual symptoms. This information correlated well with past reports on hospital series.[6–8] Forty-four patients presented with visual loss, the cause of which was ischaemic papillopathy in 38 patients and central retinal artery occlusion in four. One patient developed upper retinal branch artery occlusion with consequent arterial sheathing (see table II). Three women who presented with ischaemic papillopathy recovered some vision. All these had lost vision within 24 hours of starting treatment, and on each occasion acuity declined to 6/60 with an altitudinal field defect. In one patient the vision recovered within one hour of treatment to 6/9, and in the others it improved over 48 hours.

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TABLE I—*Erythrocyte sedimentation rates at time of diagnosis in 90 patients with giant-cell arteritis*

Rate (mm in 1st h)	10–	20–	30–	40–	50–	60–	70–	80–	90–	100–	110–	120–	130–	140–	⩾150
No of patients	1	2	3	3	10	16	10	14	10	6	4	6	3	2	0

TABLE II—*Visual symptoms*

Type	No of patients	% of patients with visual symptoms	Improved
Ischaemic papillopathy:			
Unilateral	33	60	3
Bilateral	5	9	0
Central retinal artery occlusion	4	9	0
Branch retinal artery occlusion	1		
VI nerve palsy:			
Unilateral	4	7	3 (one died)
Bilateral	1	2	1
III and IV nerve palsy	6	11	5 (one died)
Cortical blindness	1	2	
Total	55	100	

TABLE III—*Outcome of 58 patients still alive*

	F	M	Total	Time of follow-up or until relapse
Off steroids, no recurrence	10	7	17	6 months to 7 years
Steady dose. Asymptomatic	13	3	16	1 year to 7 years
Relapse with raised erythrocyte sedimentation rate only	6	1	7	4 years to 10 years
Relapse with symptoms and raised erythrocyte sedimentation rate	13	5	18	6 months to 11 years
Total	42	16	58	

Eleven patients presented with ophthalmoplegia.[9 10] Two of these died in the acute illness, but the remainder rapidly responded to corticosteroids and the ophthalmoplegia recovered between two hours and four weeks from starting treatment. None of the third-nerve palsies affected the pupil.

TREATMENT REGIMENS

All patients received corticosteroids. Treatment was started with high-dose steroids, beginning with 80 mg daily and occasionally supplemented by 250 mg hydrocortisone intravenously in the casualty department. The daily dose was reduced as follows: 80 mg for two days, 60 mg for three days, 40 mg for four days, then reduction of the daily dose by 5 mg weekly until 10 mg was reached, provided that the patient remained asymptomatic. The daily dose of 10 mg was maintained for three months and then gradually reduced. The aim was to reduce the symptoms and prevent further visual loss. In three cases with amaurosis fugax and fluctuating visual loss during the first few days intravenous heparin and dextran were also given.

DEATHS

At the time of the study 32 patients had died and 58 were still alive. These patients fell into two groups: those who died early—that is, within six weeks of diagnosis during the initial acute illness (eight)—and those who died later (24). The causes of death of those who died within six weeks were brain-stem infarction (four cases), ruptured aortic aneurysm (one), myocardial infarction (one), perforated diverticula (one), and pulmonary embolism (one). Causes of late deaths were myocardial infarction (12 cases), bronchopneumonia (five), malignant disease (three), perforated peptic ulcer (one), pulmonary embolism (one), cor pulmonale (one), and cerebrovascular accident (one).

Four patients in the first group died from brain-stem infarction within one month of diagnosis. Necropsy was carried out in three of these patients, and in two confirmed the presence of arteritis in both vertebral arteries and posterior ciliary and ophthalmic arteries. In the third patient, who had also suffered right hemiplegia with dysphasia, the bifurcation of the left common carotid and both vertebral arteries were occluded by thrombosis. Necropsy was not carried out on the fourth patient. A fifth patient collapsed six weeks after admission due to rupture of an aortic aneurysm which was found at necropsy to contain giant-cell granulomas. The remaining three patients died from coronary thrombosis, pulmonary embolism secondary to deep vein thrombosis, and perforated diverticular disease. No histological report was available on the patient who died from coronary thrombosis.

TABLE IV—*Patients who relapsed while on steroids with raised erythrocyte sedimentation rate and associated symptoms*

No	Age at diagnosis (years)	Symptoms at relapse	Time after diagnosis	Steroid dose at time of relapse (mg/day)
1	77	Polymyalgia	2 years 6 months	10
6	77	Polymyalgia	2 years	6
7	68	Headache	4 years	1
11	62	Left hemiparesis	5 years	10
		Polymyalgia	6 years	0
		Depression	8 years	3
		Headache	11 years	0
15	59	Intermittent claudication	2 years	15
17	62	Intermittent claudication, right hemiparesis	1 year	10
31	61	Polymyalgia	11 years	0
32	65	Polymyalgia	3 years	5
34	72	Headache	1 year 3 months	2·5
36	80	Polymyalgia	1 year	20
37	77	Headache	9 months	15
38	73	Left nerve palsy	2 years	0
		Vascular cord lesion	5 years	5
39	75	Headache	6 months	20
		Polymyalgia	9 months	20
40	55	Jaw claudication	6 months	7·5
41	69	Headache	6 years	5
		Polymyalgia	7 years	0
66	72	Headache	4 years	10
67	66	Headache	6 months	10
73	67	Polymyalgia rheumatica	3 years	10

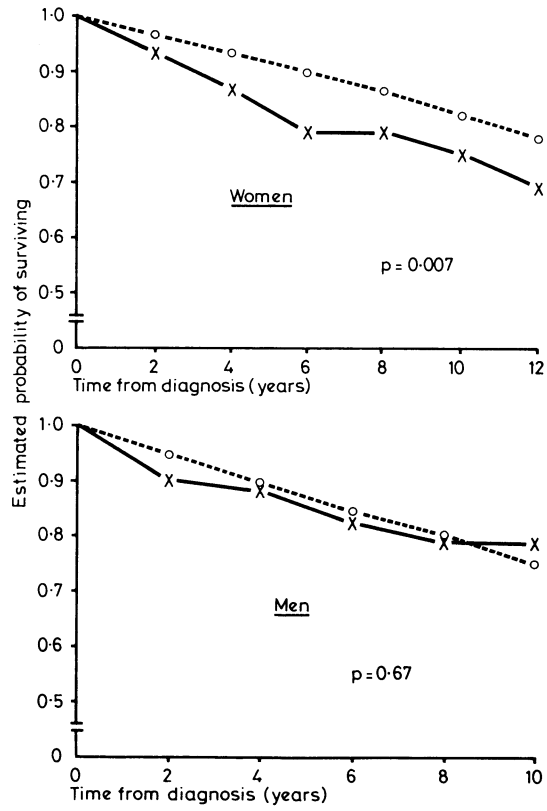

FIG 1—Erythrocyte sedimentation rate at diagnosis in 90 patients with giant-cell arteritis. Observed (X——X) and expected (O - - - O) survival from English age-sex specific death rates.[2] Top: women. Bottom: men.

TABLE V—*Prognostic significance of some clinical features*

	p Value		p Value
Sex	0·82	Season at presentation (Oct-March: April-Sept)	0·15
Headache	0·09		
Polymyalgia rheumatica	0·58	Erythrocyte sedimentation rate >75 mm/ in 1st h	0·44
Tender scalp	0·35		
Visual loss	0·0024	Haemoglobin ≤11 g/dl	0·98
Dizziness with diplopia	0·0291	White cell count >10 × 10^9/l	0·62
Angina	0·23	Daily steroid dose >10 mg	0·0003
Relapse	0·06		

The most common cause of death in the later group was myocardial infarction (12 patients). Two of these had stopped all treatment and four others were taking only 2 mg prednisone daily, so it was unlikely that either the disease or the drug was the main contributory factor. Bronchopneumonia accounted for five deaths, and three of these patients were maintained on a daily dose of over 10 mg prednisone, possibly increasing their susceptibility to infection. Only one patient in this group died from a cerebrovascular accident. No histological details were available from this group.

RELAPSE

Evidence of continuing activity was judged by recurrence of symptoms and raised erythrocyte sedimentation rate in the 58 patients who were still alive (table III). Seventeen were in clinical remission, having stopped steroids after periods of six months to seven years. Sixteen were asymptomatic and in clinical remission, taking a steady dose of prednisone ranging from 3 mg weekly to 10 mg daily for one to seven years. In seven patients the erythrocyte sedimentation rate rose while on a steady dose of corticosteroids, though with no relapse of symptoms. Four of these were subsequently found to have benign paraproteinaemia, suggesting that a raised erythrocyte sedimentation rate alone may not always indicate reactivation of disease. Eighteen patients relapsed with symptoms and a high erythrocyte sedimentation rate; most of these had developed headache or polymyalgia rheumatica; none had visual loss. The longest interval between initial illness and relapse was 11 years (table IV).

SURVIVAL

Life tables comparing the survival of the study group with the normal population showed that there was a significantly increased mortality among women ($p=0.007$) but no significant difference in men ($p=0.67$) (figure). Survival curves were plotted and the log-rank test statistic used to assess which clinical features had prognostic significance. The clinical features chosen were sex, age at diagnosis, maintenance steroid dose, and symptoms, including visual loss, angina, headache, tender scalp, polymyalgia rheumatica, and those of vertebrobasilar ischaemia. Initial erythrocyte sedimentation rate, white cell count, and haemoglobin concentrations were also considered. Table V summarises the results. Factors which had a significantly increased mortality rate were the presence of visual loss and a maintenance daily prednisone dose of over 10 mg. Age was not included, since patients who presented at over 80 years had a higher death rate than those in a younger age group. There was no evidence that the younger patients had a more severe form of the disease.

Discussion

Temporal arteritis mainly affects the external carotid, vertebral, and ophthalmic arteries. Four of our patients died early from brain-stem ischaemia thought to be due to embolisation of thrombus from affected vertebral arteries. Four others died within six weeks of diagnosis: one from a ruptured aortic aneurysm which at necropsy was found to contain giant-cell granulomas, and another from coronary thrombosis, though no histological details were available. Because our patients were a highly selected hospital series we estimate that overall early mortality is very low. Three patients developed cerebral infarction during the follow-up period, and in one this was fatal. None of these patients had evidence of active arteritis at the time, and we conclude that cerebral ischaemia is not a late complication of arteritis.

Leaving aside the mortality in the early stages of the disease, the women in the study had an increased mortality rate compared with the men and with national death rates for the female population after allowing for age. Moreover, in those who had apparently completely recovered from their illness there was a higher proportion of men to women than in the group where the disease was still active. In men who survived the first two years after diagnosis, life expectancy was as good if not better than the normal population.

Apart from this sex difference, a search for other factors influencing prognosis yielded two interesting findings. In the group as a whole both the presence of visual loss and the requirement of a higher maintenance dose of corticosteroids were significantly related to a shortened life span. Since visual loss occurs more commonly in patients over 75 years the prognostic significance of this feature may be more apparent than real. It is more difficult to explain the increased mortality rate of those patients taking a maintenance dose of prednisone greater than 10 mg daily. The possible reasons for this are that these patients were older, that they suffered from a more severe type of disease, or that high steroid dosage shortens life. Only eight of the 19 patients in the high-steroid group were older than 75 years, which suggests that age alone cannot account for the worse prognosis. In the higher steroid group the clinical features did not appear to be more severe than in those requiring less steroids, and the reasons for the high requirements are not clear. We suggest that steroid treatment itself contributed to the increased mortality, since the occurrence of side effects in this group was notable and pulmonary infections possibly aggravated by steroids caused death in three patients.

In one-third of our surviving patients the disease had "burnt out" in a period ranging from six months to seven years. These patients had no symptoms and were apparently in good health for their years. The temporal and scalp arteries were clinically normal on follow-up; pulsations which had previously been absent had returned.

A further third of our patients needed steroids indefinitely and appeared to suffer from a chronic form of arteritis with a tendency to relapse of headache and polymyalgia. Serious late complications were rare in this group and delayed visual loss was not encountered. No indication emerged for continuing steroids in high dosage longer than six months. After the initial attack has been controlled we suggest that the steroid dosage should be reduced to the minimum which will alleviate the symptoms of headache and polymyalgia rather than attempt to achieve a normal erythrocyte sedimentation rate. No evidence was found from this series that giant-cell arteritis commonly transforms into a more generalised severe arteritis requiring increased dosage of steroids, though occasional patients of this type have been described.[8 11 12]

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