The Changing Clinical Presentation of Temporal Arteritis in Israel: a Multicenter Study

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Abstract

Objectives: To evaluate whether the increasing incidence of temporal arteritis in Israel is associated with a changing clinical presentation.

Methods: The demographic data and clinical manifestations of 144 TA[1] patients in this large multicenter study were recorded and compared with data obtained in a previous study.

Results: The patient population was older, with 24% ≥ 80 years compared to 6% in the previous study. There was an increase in the number of nonspecific presenting symptoms, and less patients presented with the "classical" manifestations of headache (81% vs. 71%), fever (83% vs. 40%), jaw claudication (21% vs. 13%), and visual symptoms (47% vs. 24%). The median time from presentation to diagnosis was significantly reduced, from 5 to 1.5 months.

Conclusions: There were substantial changes in the clinical presentation of TA patients in Israel during 1980–95 compared to patients diagnosed prior to 1978. It is suggested that these changes may be attributed not only to the influence of aging of the population, but are due largely to increasing physician awareness to the spectrum of manifestations of TA, which leads to earlier diagnosis.

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Temporal arteritis is a vasculitis of medium-sized and large arteries that usually affects people above the age of 50. A previous population-based study of TA in Israel showed a very low incidence of the disease compared to its occurrence worldwide [1]. It is our impression that there has been a change in the incidence and the nature of this condition in recent years [2,3]. The purpose of this multicenter study was to describe the changes in the clinical presentation of TA in Israel.

Patients and Methods

We conducted a computer-assisted search of the archives of several hospitals for patients diagnosed as having TA. These included the two Hadassah hospitals in Jerusalem (Ein Kerem and Mount Scopus) for the years 1980–1992; the Shaare Zedek Medical Center, Jerusalem, 1980–95; and the Sheba Medical Center, Tel-Hashomer, 1984–94. Altogether, 156 Jewish patients were identified, and 144 charts (53 from Hadassah hospitals, 52 from Shaare Zedek, and 39 from Sheba Medical Center) had sufficient data for review.

All patients met the American College of Rheumatology criteria for the classification of giant cell arteritis [4]. Symptoms at diagnosis, laboratory parameters, time from onset of symptoms to diagnosis, and demographic data were recorded. These were subsequently compared with data obtained from previous studies on the Israeli population [1,5]. For the purpose of the study we defined Ashkenazi Jews as those born in Europe and America, and Sephardic Jews as those born in Asia and Africa. For those born in Israel, the father's country of birth was taken as their ethnic origin.

The Chi-square test with Yates' correction was used for comparison of proportions of different variables in the two periods, and the Wilcoxon rank sum test for comparison of means between the two groups.

Results

The study group comprised 93 women and 51 men (ratio of 1.8:1). Temporal artery biopsy was performed in 142 cases. Arteritis was diagnosed histologically in 125 cases (88%), based on the presence of inflammatory infiltrates within the vessel wall — with or without giant cells — and disruption of the internal elastic membrane. The median time from onset of symptoms to diagnosis was 1.5 months (range 1 day to 1 year). Treatment with prednisone resulted in rapid improvement of symptoms in all cases, except for those with irreversible ischemic complications such as visual loss or stroke.

Altogether, there were 96 Ashkenazi and 48 Sephardic patients (ratio 2:1). The ratio was higher among the Sheba Medical Center patients than among the patients from Jerusalem (3.3:1 compared to 1.6:1, respectively). The mean age at diagnosis was 73 years. The age distribution is presented in Figure 1. Patients whose biopsy was negative were younger than those with a positive biopsy (70 versus 74 years, respectively), but this difference was not statistically significant.

Trends in the clinical presentation of TA are presented in Figure 2. The "classical" symptoms and signs at the time of diagnosis, such as headaches, visual disturbances and jaw claudication, were less common in the present study, but more patients presented with symptoms of po-

[1] TA = temporal arteritis

Table 1. Unusual presenting symptoms of temporal arteritis among the 144 patients

Symptoms	No. of patients
Respiratory symptoms*	10
Central nervous system symptoms**	7
Peripheral neuropathy	2
Skin rash	2
Raynaud's symptoms	1
Nephrotic syndrome	1

* Including nonproductive cough (7 cases), lung infiltrates on chest radiography (2 cases), pleural effusion (2 cases), and hemoptysis (1 case). All resolved following steroid therapy.

** Including recurrent strokes (2 cases), hearing loss (2 cases), and one case each of nonpsychotic visual hallucinations, confusion, psychosis, and behavioral changes. Except for stroke, all resolved with steroid therapy.

Table 2. Laboratory studies in 144 patients with temporal arteritis compared to 47 patients in a previous study *

Laboratory parameter	Percent of patients		
	1980–95	1960–77	*P*
Elevated ESR (> 40 mm/h)	97	100	NS
Anemia (Hb < 12 g/dl)	70	71	NS
Thrombocytosis (> 400,000)	46	25	< 0.05
Leukocytosis (> 10,000)	18	37	< 0.05
Liver enzyme abnormalities	36	60	< 0.05
Hyperglobulinemia (> 3.5 g/dl)	29	46	< 0.05

* Ref. 5

lymyalgia rheumatica. However, only the decrease in the proportion of patients presenting with fever or visual symptoms reached statistical significance ($P < 0.01$).

Nonspecific symptoms as the sole manifestation (low grade fever, fatigue and weight loss — the so-called occult presentation) — were present in 11% of the patients. PMR[2] only (without headaches, jaw claudication or visual symptoms) was the presenting symptom in an additional 4% of the cases, and 16% of the patients had unusual presenting symptoms [Table 1]. Altogether, one-third of the patients presented with "non-classical" TA symptomatology. There were no significant differences in presenting symptomatology between men and women or between Sephardic and Ashkenazi Jews.

Laboratory studies are presented in Table 2. Elevated erythrocyte sedimentation rate was the most common laboratory abnormality. However, it should be noted that 4 patients (3%) had normal ESR (< 40 mm/h). Mild normocytic anemia, leukocytosis, liver enzyme abnormalities (mostly mild elevation of alkaline phosphatase levels) and hyrerglobulinemia were less common. Compared to the previous study, there was a statistically significant decrease in the proportion of patients with leukocytosis, liver enzyme abnormalities and hyperglobulinemia, and an increased proportion of patients with thrombocytosis.

Discussion

Temporal arteritis has been diagnosed more frequently in Israel over the last decade compared to previous data [1,2]. We noticed a marked increase in TA prevalence, with recent rates of biopsy-proven TA for 100,000 population older than 50 years being 7.7 and 12.1 for men and women, respectively [2], compared to only 0.5 and 0.47 for

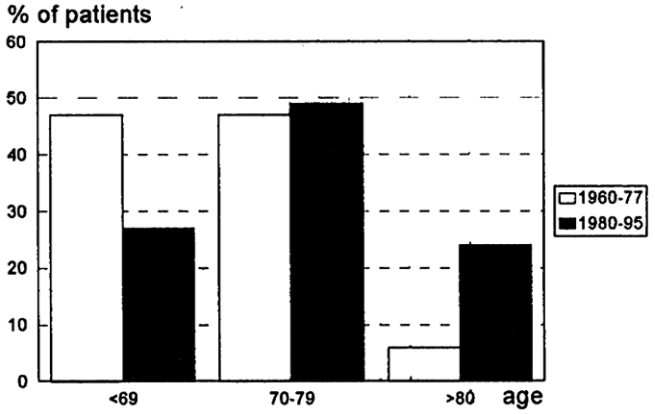

Figure 1. Age distribution of 144 temporal arteritis patients in the present study compared to 47 patients reported previously (ref. 5).

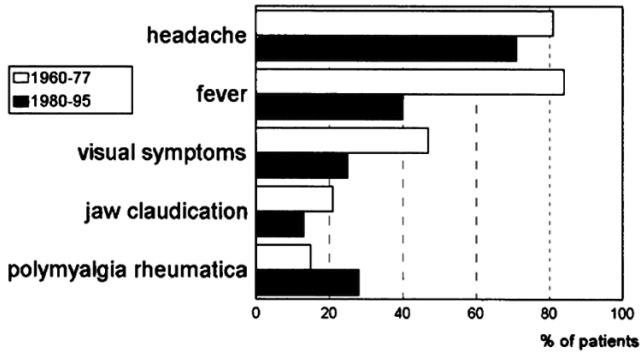

Figure 2. Clinical symptomatology in 144 temporal arteritis patients compared to 47 patients reported previously (ref. 5).

the period 1960–78 [1]. There are probably multiple reasons for this striking increase, such as a true increase in the occurrence of TA, increased awareness of physicians, and aging of the population. The aim of this study was to examine whether this increasing incidence of TA in Israel is associated with changing clinical manifestations.

This is the largest study on TA ever reported in Israel. A previous study on the clinical findings of 47 patients was reported in 1979 [5]. On comparing the data, it becomes clear that the age distribution and clinical symptomatology of TA have changed considerably. In the earlier study only 6% of TA patients were 80 years or older compared to the current 24%. Conversely, fewer patients now are younger than 70 years.

We noticed a trend toward a lower frequency of the classical manifestations of TA such as headaches, visual symptoms and fever, and increased presentation with nonspecific ("occult") manifestations, PMR and unusual symptoms. It is not clear whether the age shift was one of the reasons for the changing clinical presentation of TA. The earlier diagnosis of TA in the present study (median time 1.5 months compared to 5 months previously) may have also contributed to this change by "preventing" some disease manifestations from developing. This may also explain the lower frequency of leukocytosis, hyperglobulinemia and liver abnormalities in the present study. Varied manifestations of TA may have contributed as well to this changing nature of TA in our population.

Similar trends were shown in another longitudinal study, from Olmsted County, Minnesota [6]. There, the incidence of TA increased fourfold — from 6.2/100,000

[2] PMR = polymyalgia rheumatica

population ≥ 50 years in 1950–59 to 24.1/100,000 during 1980–85. In addition, it is possible that the heightened awareness of physicians to the increase was mostly with regard to women; however, it should be noted that in our population the increase in TA incidence was also of larger magnitude in women (26-fold) compared to men (15-fold). In the Olmsted County study the frequency of the "classical" presenting symptoms also declined over the years, with the occurrence of headaches decreasing from 96% to 71%, jaw claudication from 73% to 42%, and blindness from 19% to 6% [6]. The proportion of cases with "nonspecific" presentation of TA in our population was also similar to data presented in other recent studies [6,7].

The ratio of Ashkenazi to Sephardic patients in Jerusalem (1.6:1) was lower than that among the Sheba patients (3.3:1), which was similar to the 3:1 ratio reported previously in Israeli patients [1]. In that study 46% of the patients were from the Tel Aviv area and only 26% from Jerusalem [5]. The reason for these differences is not clear and could be related to population structure in different parts of the country, or to the different prevalence of TA among subpopulations in these ethnic groups. For the Jerusalem population, the age-adjusted incidence rates were calculated by the direct standardization method from data obtained from the yearly publications of the Central Bureau of Statistics. Rates were found to be similar for both ethnic groups: 11.1/100,000 in Ashkenazi Jews (95% Confidence Interval 7.9–14.1), and 11.9/100,000 in Sephardic Jews (95% CI 7.9–15.6) [2]. It suggests that at least in the Jerusalem area the prevalence is similar in these two ethnic groups.

In conclusion, the incidence of TA in Israel is higher than previously reported. Over the years, the clinical presentation has changed in that more cases present with nonspecific and non-classical symptoms. Increased physician awareness and aging of the population may have contributed to both of these changes. It is important that physicians be aware of the various manifestations of TA [8] in order to make an early diagnosis and prevent serious complications.

References

1. Friedman G, Friedman B, Benbassat J. Epidemiology of temporal arteritis in Israel. *Isr J Med Sci* 1982;18:241–4.
2. Sonnenblick M, Nesher G, Friedlander Y, Rubinow A. Giant cell arteritis in Jerusalem: a 12-year epidemiological study. *Br J Rheumatol* 1994;33:938–41.
3. Gur H, Rapman E, Ehrenfeld M, Sidi Y. Clinical manifestations of temporal arteritis: a report from Israel. *J Rheumatol* 1996;23:1927–31.
4. Hunder GG, Bloch DA, Michel BA, Arend WP, Calabrese LH, Edworthy SM, Fauci AS, Leavitt RY, Lie JT, et al. The American College of Rheumatology 1990 criteria for the classification of giant-cell arteritis. *Arthritis Rheum* 1990;33:1122–8.
5. Fainaru M, Friedman G, Friedman B. Temporal arteritis in Israel. A review of 47 patients. *J Rheumatol* 1979;6:330–5.
6. Machado EBV, Michet CJ, Ballard DJ, Hunder GG, Beard CM, Chu CP, O'Fallon WM. Trends in incidence and clinical presentation of temporal arteritis in Olmstead County, Minnesota, 1950-1985. *Arthritis Rheum* 1988;31:745–9.
7. Desmet GD, Knockaert DC, Bobbaers HJ. Temporal arteritis: the silent presentation and delay in diagnosis. *J Intern Med* 1990;227:237–40.
8. Sonnenblick M, Nesher G, Rosin A. Nonclassical involvement in temporal arteritis. *Semin Arthritis Rheum* 1989;19:183–90.

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