SCIENTIFIC REPORT

Epidemiology of giant-cell arteritis in an Arab population: a 22-year study

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Objective: To study the epidemiology of biopsy-proven giant-cell arteritis (GCA) in an Arab population with clinical features suggestive of GCA.

Methods: Clinical records of 102 patients who underwent temporal artery biopsy (TAB) at King Khaled Eye Specialist Hospital, Riyadh, Saudi Arabia from January 1983 to December 2004 were reviewed.

Results: Among the 56 men and 46 women who had TAB, 7 (6.8%) had biopsy-proven GCA. The mean (SD) age of the biopsy-positive group (71.7 (8.6) years) was higher than in the biopsy-negative group (65 (9.8) years; $p=0.005$). None of the untreated patients with a negative TAB developed additional symptoms that are typical of GCA.

Conclusion: The small absolute number of biopsy-proven cases of GCA implies a relatively low incidence of GCA in Arab population, confirming previous observations that GCA occurs primarily in the Caucasian population.

Giant-cell arteritis (GCA) is a systemic vasculitis that affects large-sized and medium-sized arteries. Giant-cell-based inflammatory reaction destroys the media of the artery wall with fragmentation of the elastic lamina.^{1–3} Ocular symptoms in most of the patients with GCA are usually associated with acute blindness and may occur in a substantial number of patients with untreated disease. The epidemiological characteristics of GCA have been studied in populations from the US, Scotland, Sweden and Denmark.⁴ Most of these studies have focused on the incidence of GCA in the white population of European origin and the epidemiology of this disease in the Arab population was not known. This study was undertaken to evaluate the incidence of GCA in patients from Saudi Arabia who attended King Khaled Eye Specialist Hospital (KKESH), Riyadh, Saudi Arabia, a tertiary referral eye centre in Saudi Arabia and the largest ophthalmological facility in the Middle East. The referral population is the entire Kingdom of Saudi Arabia and eligibility criteria require that patients be Saudi Arabian citizens and that they have tertiary ophthalmological problems. The Saudi Arabian government transports patients free of charge to the Hospital in Riyadh from anywhere in the Kingdom. Over 100 000 outpatient examinations and >10 000 surgical procedures are performed annually.

METHODS

Clinical and histopathological records of all patients who had undergone temporal artery biopsy (TAB) for suspected GCA at KKESH from January 1983 until December 2004 were reviewed. Information from the clinical records was reviewed regarding demographics such as age, gender and presenting symptoms. Associated systemic medical conditions such as diabetes, hypertension and coronary artery disease were reviewed along with diagnostic laboratory tests and the results

of TABs performed. One of the authors (FCR) reviewed each biopsy specimen and reported that none had been classified incorrectly. Patients were considered to have biopsy-proven GCA if the histological examination of the temporal artery revealed arteritis, characterised by mononuclear cell infiltration in the arterial wall granulomatous reaction and interruption of the internal elastic lamina (figs 1–3). The group of patients with biopsy-proven GCA was compared with the biopsy-negative group. Variables studied included gender, age at diagnosis, associated medical conditions and final outcome of the treatment. A two-sample *t* test was used to compare mean age and Fisher's exact test was used to compare frequencies.

RESULTS

There were 102 patients (56 men, 46 women) who underwent TAB during the study period between January 1983 and December 2004. In all, 83 (81%) patients had loss of vision in one eye, 15 (14.8%) in both eyes; and 33 (32%) patients described it as "sudden loss of vision". Totally 39 (38%) patients had associated headache, 18 (17.6%) patients had temporal area tenderness, 10 (9.8%) patients had pain, 10 (9.8%) patients had cranial nerve palsy (3rd, 6th, 7th) and 9 (8.8%) patients had jaw claudication. Documented weight loss was noted in 4 (3.9%) patients, myalgia and joint pain in 5 (4.9%) and fever in 5 (4.9%) patients (table 1). Systemic conditions in the patients included diabetes mellitus in 47 (46%) patients, hypertension in 25 (24.5%), cardiac diseases in 13 (12.7%), asthma in 4 (3.9%), renal failure in 3 (2.9%) and arthritis and thyroid dysfunction in 2 (1.9%) patients each.

Presenting visual acuity (VA) in the 202 eyes (two patients having only one eye each) was: no light perception in 15 eyes (7.4%); hand-motion to light perception in 35 (17%), 20/200 to counting fingers in 74 (36.6%); 20/50 to 20/100 in 39 (19%); and 20/20 to 20/40 in 33 (16%) eyes (table 2). The cause of visual loss was anterior ischaemic optic neuropathy (AION) in 59 (29%) eyes, optic atrophy in 30 (14.8%), central retinal artery occlusion in 4 (2%), central retinal vein occlusion in 4 (2%), ocular ischaemic syndrome in 3 (1.5%) and branch retinal artery occlusion in one eye (table 3).

From the 106 temporal artery biopsies (4 bilateral) performed during the 22-year period, only 7 (6.8%) were positive for GCA (table 4). Mean (SD) age of the biopsy-positive group (71.7 (8.6) years) was higher than the biopsy-negative group (65 (9.8) years; $p=0.005$). Average (range) erythrocytes sedimentation rate (ESR) 62 (45–112) mm/h in the biopsy-positive group was higher than that 49 (6–124) mm/h in the biopsy-negative group ($p<0.05$). One patient with an ESR of 124 and negative TAB had a history of arthritis. All 60 (58.8%) patients

Abbreviations: AION, anterior ischaemic optic neuropathy; ESR, erythrocytes sedimentation rate; GCA, giant cell arteritis; KKESH, King Khaled Eye Specialist Hospital; TAB, temporal artery biopsy; VA, visual acuity

Figure 1 All temporal artery biopsies were performed by identifying an artery in the temporal area and obtaining a minimum segment of 2–3 cm and closing the skin wound. Informed consent was obtained for publication of this figure.

were systemically treated either with intravenous (17; 28%) or oral (43; 72%) corticosteroids before or after obtaining the results of TAB. Duration of treatment with systemic corticosteroids in the patients was 3 days to 6 years; most patients required only short-term treatment except ten patients who were treated from 1 month to 6 years. Patients were treated longer if their VA or systemic conditions improved with systemic corticosteroids. In two patients systemic corticosteroids were discontinued due to recurrent gastritis without any further loss of vision.

The average follow-up on the patients was 21.3 months (range 1 month to 11 years). Recorded VA was available for 197 eyes on patient's last follow-up visits. The VA had improved in 58 (29%) eyes, deteriorated in 59 (30%) eyes, and remained unchanged in 80 (41%) eyes. On the last follow-up, 22 (11.1%) eyes had VA of no light perception; hand-motion to light perception in 26 (13.2%) eyes, 20/200 to counting fingers in 64 (32.5%), 20/50 to 20/100 in 53 (27%) and 20/20 to 20/40 in 32 (16.2%). There were two patients who had evidence of anterior ischaemic optic neuropathy (AION) and biopsy-proven GCA (table 4). Among the seven patients with biopsy-proven GCA, only three had improvement in their presenting VA ranging from 1 to 4 lines. There were no particular characteristics of patients who had improvement in their VA. In patients whose VA did not improve after systemic corticosteroids, their non-ocular symptoms such as headaches and temporal area tenderness improved in addition to the normalisation of their ESR. For example, in a man age 70 years with biopsy-proven GCA who presented with simultaneous loss of vision in both

eyes, his ESR decreased from 55 to 10 after systemic administration of corticosteroids despite no gain in his visual loss. No untreated patient with a negative TAB went on to develop additional symptoms typical of GCA that would have implied a falsebiopsy-negative result.

DISCUSSION

Ocular symptoms in GCA are most typically associated with acute blindness. Severe visual loss may occur in up to 40% of patients with untreated GCA and is most often caused by some type of infarctive process within the terminal blood supply of the ophthalmic artery to the optic nerve and retina.^{5–8} As suggested by the current study, there is also high frequency of the second eye involvement in untreated patients. Approximately 65% of those untreated for AION caused by GCA were found to have their second eye involved within 10 days.⁵ Among the seven patients who had biopsy-proven GCA, only two patients had evidence of AION; in one patient VA improved (HM to 20/100) after treatment, whereas in other, final VA worsened (CF to HM). The other common visual symptoms were diplopia due to cranial nerve palsies and transient visual loss which was found in up to 10% of our patients. The most common non-ocular symptoms found in a significant number of our patients with presumed GCA were headache, temporal scalp area tenderness, myalgias and arthralgias, fever, weight loss, jaw claudication and anorexia. (table 1). The most common systemic conditions in patients with negative TAB and elevated ESR were diabetes mellitus, hypertension and cardiac diseases.

Figure 2 Histopathology of a temporal artery biopsy taken from an 80-year-old man with diabetes who presented with decreased vision in both eyes (OU), fever, ptosis, 3rd cranial nerve palsy, weight loss, jaw claudication and temporal area tenderness. (A) Cross-section of a temporal artery showing inflammatory infiltrates and a narrow lumen (H&E, $\times 10$); (B) at higher magnification giant cells are visible (H&E, $\times 40$); (C) Periodic acid-Schiff staining, $\times 10$; (D) elastin staining showing disruption of elastic lamina by inflammatory infiltrates, $\times 10$.

Table 1 Presenting symptoms of patients undergoing temporal artery biopsy (n = 102)

Symptoms	n (%)
Vision loss	83 (81)
Headache	39 (38)
Scalp tenderness/pain	28 (27)
Cranial nerve palsy	10 (9.8)
Jaw claudication	9 (8.8)
Weight loss	4 (3.9)
Myalgia/joint pain	5 (4.9)
Fever	5 (4.9)

Table 2 Presenting visual acuities of patients undergoing temporal artery biopsy

Vision	n (%)
20/20–20/40	33 (16)
20/50–20/100	39 (19)
20/200–CF	74 (37)
HM-LP	35 (17)
NLP	15 (7.4)

CF, counting fingers; HM, hand motion; LP, light perception; NLP, no light perception.

The incidence of GCA increases from approximately 2/100 000/year at ages 50–59 years to 33/100 000/year at ages 60–69 years; by the age of 80 years, the incidence is 844/100 000 or ~1%.² This age difference was found in our patients with biopsy-proven GCA compared with those patients in the biopsy-negative group. In addition, there have been reported differences among the patients of different ethnicities. The disease is found to be more common in white patients—eg, in one report the incidence of biopsy-proven GCA was compared with biopsy-negative group and study variables such as age, ESR and ethnic background.⁴ In this report, a patients who underwent TAB the mean age of those in the biopsy-positive group was higher than that of those in the biopsy-negative group; there were statistically higher numbers of white patients with raised ESR compared with non-white patients. Among those suspected of GCA, 29% of white patients had biopsy-proven disease, whereas 11% of Asian patients, and none of the Hispanic patients had positive biopsy.

At present, the true incidence of GCA in an Arab population is difficult to estimate as no nationwide prospective, population-based study has been undertaken in any of the Arab countries in Middle East, including Saudi Arabia.⁹ However, seven positive TABs were reported at KKESH in 22 years

Table 3 Aetiology of visual loss in patients undergoing temporal artery biopsy

Aetiology	n (%)
AION	59 (29)
Optic atrophy	30 (14.8)
CRAO	4 (2)
CRVO	4 (2)
Ocular ischaemic syndrome	3 (1.5)
BRAO	1 (<1)

AION, anterior ischaemic optic neuropathy, BRAO, branch retinal artery occlusion; CRAO, central retinal artery occlusion, CRVO, central retinal vein occlusion.

compared with substantially larger numbers of positive TABs reported from North American referral eye centres with similar, or smaller, ophthalmologic patient population size. For example, the Bascom Palmer Eye Institute, Miami, Florida, USA recorded 185 positive biopsies over a 13-year period,⁵ the Ochsner Clinic, New Orleans, Los Angeles, USA, had 97 positive biopsies over a 19-year period¹⁰ and the Bowman Gray School of Medicine, Winston-Salem, North Carolina, USA, reported 30 positive biopsies over a 5-year period.¹¹

The Saudi Arabian population is close to 17 million with approximately 100 000 patient visits annually at KKESH. Among the 1.5 million patient visits, a total of 450 000 different patients have been seen since the hospital opened in 1982. Since KKESH is the only specialised tertiary care referral centre in Saudi Arabia, in all likelihood >90% of the tertiary care of the 1980s took place here, about 80% of that in the 1990s, and >70% during the last five years. It is difficult to quantify the number of Saudi Arabian adult individuals at risk of GCA. However, considering that for other ocular conditions such as uveal melanoma and retinoblastoma, there is a high capture rate for these diseases at KKESH—for example, during the 22-year study period, there were 60 cases of uveal melanoma and 567 cases of retinoblastoma diagnosed and treated at KKESH.¹² Similar observations have been reported from Shanghai Eye, Ear, Nose and Throat Hospital in Shanghai, China in which 65 cases of uveal melanoma and 631 cases of retinoblastoma were diagnosed and treated during a 23-year study period.^{13 14} These results are in agreement with the observations that incidence rates of uveal melanoma are very low in non-Caucasian populations although incidence rates of retinoblastoma are similar across all races.¹⁵

The average life expectancy of the Saudi Arabian population (men 74 years; women 78 years) is not much different from the life expectancy in the US (men 75 years; women 80 years), UK (men 76 years; women 81 years) and Denmark (male 75 years; female 80 years) (http://www.intute.ac.uk/sciences/worldguide/html/1012_people.html). The ratio of

Figure 3 Temporal artery biopsy of a 78-year-old woman who presented with loss of vision, temporal area tenderness and elevated erythrocyte sedimentation rate. There are no inflammatory infiltrates but evidence of arteriosclerosis is found. (A) H&E, $\times 10$; (B) periodic acid-Schiff staining, $\times 10$.

Table 4 Characteristics of patients with biopsy-proven GCA

Patient no	Age/gender	Vision (OD:OS)		Aetiology	ESR	Corticosteroids
		Presenting	Last F/U			
1	71/F	CF:OU	CF:20/200	—	45	Oral
2	70/M	NLP:OU	NLP:OU	PION	55	Oral
3	81/M	CF:NLP	HM:NLP	AION	65	IV
4	55/F	20/80:20/60	20/40:20/125	—	48	Oral
5	70/M	NLP:HM	NLP:20/100	AION	60	Oral
6	75/M	20/50:HM	20/50:HM	OA	47	Oral
7	80/M	20/100:20/100	Patient died	—	112	Oral

AION, anterior ischaemic optic neuropathy; CF, counting fingers; ESR, erythrocyte sedimentation rate; F, female; F/U, follow-up; HM, hand motion; IV, intravenous; M, male; NLP, no light perception; OA, optic atrophy; OD, right eye; OS, left eye; PION, posterior ischaemic optic neuropathy.

ophthalmologists relative to population size is similar in Saudi Arabia (1/27 389 persons) and the US (1/20 802 persons).¹⁶ At present there is no information available regarding specific referral patterns to KKESH for patients with symptoms typical of GCA from various parts of Saudi Arabia, but the large number of referrals to this hospital confirms that ophthalmologists in Saudi Arabia both recognise serious ophthalmologic problems and refer them frequently.⁹ The small percentage of positive biopsies (7/102 or 6.8%) at KKESH indicates that ophthalmologists at this tertiary eye care centre have been sensitive to the potential of GCA to cause serious ophthalmological problems, and have not treated patients presumptively for GCA without biopsy-proven disease. The small absolute number of positive biopsies over a period of 22 years probably implies a relatively low incidence of GCA in the Arab population of Saudi Arabia. These results are in agreement with previous observations that GCA seems to be more common in northern European and North American populations.¹⁷ Clinical suspicion is the keystone to the diagnosis; immediate Westergren sedimentation rate should be obtained, but TAB is still the definitive diagnostic study.

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