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Lacrimal gland involvement in sarcoidosis

The clinical features of 9 patients

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Summary

Patients and Methods: Ocular disease is relatively common in sarcoidosis and can be the initial clinical manifestation in some instances. In this study, we retrospectively evaluated the clinical and demographic features of 9 (1.74%) patients with lacrimal gland (LG) involvement out of 516 sarcoidosis patients who were followed up at our centre over the preceding 36-years. In addition, the characteristics of patients with LG involvement were compared to those of other cases with eye involvement and to other sarcoidosis patients.

Results: In 5 subjects with LG involvement, the chest X-ray was normal. The number of stage 0 subjects among other sarcoidosis patients was significantly lower than among patients with LG involvement ($p < 0.001$). In 2 of these cases, the diagnosis of sarcoidosis was reached by LG biopsy. The mean age of patients with LG involvement was significantly lower than that of other sarcoidosis patients ($p < 0.001$). Also, sarcoidosis-related organ involvement – other than of the LG – was more frequent than in other sarcoidosis patients ($p < 0.001$).

Conclusions: It should be borne in mind that LG involvement might be the initial manifestation of sarcoidosis and the chest X-ray in these patients might be completely normal.

Key words: sarcoidosis; lacrimal gland; uveitis; ocular involvement

Introduction

Sarcoidosis is a granulomatous disease of unknown aetiology with various clinical manifestations. Ocular findings during the course of systemic sarcoidosis are observed in 25–60% of the patients [1]. Ocular disease might be the initial finding of sarcoidosis and can sometimes cause serious visual impairment and even blindness [2]. Although lacrimal gland (LG) and conjunctival involvement are frequent during the course of sarcoidosis, they are generally asymptomatic [2]. In this study, we evaluated the features of sarcoidosis patients with LG involvement being followed up at our centre. We also compared the clinical features of subjects with LG involvement to those of patients with other forms of eye involvement and to all sarcoidosis patients.

Patients and methods

In this study, we retrospectively evaluated the clinical and demograhic features of 9 sarcoidosis patients with LG involvement who were followed up at Cerrahpaşa Medical Faculty, Department of Internal Medicine between 1966–2002. The control group comprised 516 subjects diagnosed with sarcoidosis within the same period and 70 subjects with eye involvement. The age, sex, diagnostic methods, chest X-ray and disease stage at the time of diagnosis of sarcoidosis and extrapulmonary findings of the patients were obtained retrospectively from the hospital records.

The diagnosis of sarcoidosis was based on clinical, radiological and histopathological criteria. Other granulomatous diseases were excluded. Also, the presence of non-caseating granulomas in at least one tissue specimen; and absence of Mycobacteria and fungi in tissues and cultures were needed for diagnosis of sarcoidosis. The diagnosis of sarcoidosis was proven by biopsy in all 516 patients.

All 9 patients with LG involvement had routine eye examination (biomicroscopy, tonometry, fundoscopy), and also underwent peripheral examination of the retina by using a 3-mirror Goldman lens. When there was suspicion of retinal vasculitis, fundus fluorescein angiography (FFA) was performed. In patients found to have an orbital

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mass, computerised tomography (CT) of the orbit was performed in 6 patients, magnetic resonance imaging (MRI) in one patient, and both CT and MRI in 2 patients. A Gallium 67 scan was performed in only 2 of the patients with LG involvement; and, in both of these subjects the isotope concentrated in the hilar and orbital regions. The serum ACE levels were not measured in sarcoidosis patients with LG involvement. In addition, the diagnosis of LG involvement was confirmed by obtaining a biopsy from the patients by means of orbitotomy. In all patients with LG involvement, the Schirmer test was performed to evaluate tear production.

In 70 patients with eye involvement tissues for histopathological examination at the time of initial diagnosis were obtained by the following methods: transbronchial biopsy (34 cases), mediastinoscopic biopsy (15 cases), skin biopsy (14 cases), peripheral lymph node and LG biopsy (2 cases each), thoracotomy, parotid gland and open lung biopsy (one case each). The initial diagnostic methods in 9 patients with LG involvement were: transbronchial and skin biopsy (3 cases each), LG biopsy (2 cases), parotid gland biopsy (one case). During follow-up, all these 9 patients had histopathological proof of LG involvement by biopsy. Chest X-rays were classified into 3 stages according to De Remee [3]: stage I, bilateral hilar lymphadenopathy (BHL); stage II, BHL plus parenchymal infiltration; and stage III, parenchymal infiltration without BHL.

Comparisons were made between sarcoidosis patients with and without LG involvement regarding age, sex, general clinical and radiological features. Chi-square and Mann Whitney U tests were used for statistical evaluation of the data.

Results

Seventy (13.6%) of 516 patients had eye involvement, of whom 9 (1.74%) had LG involvement. The disribution of eye findings in the patients is seen in Table 1. The most frequent ocular finding was uveitis.

The clinical and demographic features of 9 subjects with LG involvement are seen in Table 2. It was an important finding that 7 of the patients with LG involvement were female and 5 (55%) had stage 0 disease.

The comparison of some of the clinical and demographic features of patients with LG involvement to those of other sarcoidosis patients is seen in Table 3. Patients with LG involvement and those with eye involvement were younger than other sarcoidosis patients (p values, respectively, <0.001 and <0.05). The frequency of extrapulmonary involvement – other than the LG – was higher in patients with LG involvement than in sarcoidosis patients without LG involvement (p <0.05).

Table 1

The distribution of various forms of eye involvement in sarcoidosis patients.

	N	% in patients with eye involvement	% in all sarcoidosis patients
Isolated anterior uveitis (iridocyclitis)	27	38.6	5.2
Isolated posterior uveitis	5	7.1	0.97
Panuveitis (anterior+posterior)	10	14.3	1.94
Isolated retinal vasculitis	7	10	1.36
Combined (vasculitis+uveitis)	1	1.4	0.2
Isolated lacrimal gland involvement	8	11.4	1.55
Lacrimal gland+anterior uveitis	1	1.4	0.2
Optic nerve involvement	7	10	1.36
Episcleritis	1	1.4	0.2
Conjuctival granuloma	2	2.8	0.4
Keratoconjunctivitis	1	1.4	0.2

Table 2

The clinical features of sarcoidosis patients with LG involvement.

Age/sex	Initial stage	Kveim test	Mantoux test	Extrapulmonary involvement
39/F	II	NA	+	LG
44/F	I	NA	–	LG, skin, lymph node
48/M	0	–	–	LG, skin
20/F	0	NA	–	LG
17/F	I	+	+	LG, uveitis
16/F	II	+	–	LG, lymph node
9/F	0	NA	–	LG
60/F	0	NA	–	LG, skin
44/M	0	NA	–	LG, parotid gland

F: female, M: male, NA: not available, LG: lacrimal gland.

Discussion

In our study, ocular involvement was diagnosed in 13.6% of the patients. In spite of the fact that histological LG involvement is frequent in sarcoidosis, it has been reported at lower rates in different series because it is generally asymptomatic [2, 4, 5]. In our study, 1.74% of the sarcoidosis patients were found to have clinically detectable LG involvement.

Ocular sarcoidosis has been reported to have 2 peaks of incidence: the first is around 20–30 years of age, and the second is around 50–60 years of age [6]. Although it is known that ocular sarcoidosis mainly affects young females, it was reported that patients with orbital sarcoidosis were generally females over 50 years of age [7]. Contrary to these data, we observed that our patients with LG and other ophthalmological involvement were younger than the remaining sarcoidosis patients. The ratio of female patients among those with LG and other eye involvement was higher than other sarcoidosis patients – although this was not significant.

LG involvement might present as an orbital mass in some sarcoidosis patients and be confused with a malignant tumour [8]. For the diagnosis of LG involvement in sarcoidosis, biopsy and histopathological confirmation are needed; however, MRI findings might demonstrate enlargement of the extraocular muscles thereby pointing to LG involvement [9]. As our study was retrospective, the presence of LG involvement was supported by MRI in only 3 of our patients. In the rest of our patients, LG involvement was diagnosed at a time when MRI was not in routine use. Still, all 9 patients included in our study had histopathological proof of involvement of the LG by sarcoidosis.

Isolated orbital involvement in sarcoidosis is rare and is generally limited to the LG [9]. In some cases, ocular involvement in systemic sarcoidosis might be observed years before lung and other organ involvement [10–12]. In our study, 5 of the 9 patients with LG involvement had no pathological finding on chest X-ray: that is the disease was radiologically at stage 0. Among other sarcoidosis patients, only 5.8% of the patients had stage 0 disease. Two of our 5 stage 0 patients with LG involvement also had skin involvement; and one of our stage 0 patients had parotid gland involvement (Table 3). In the first 2 patients the initial diagnosis of sarcoidosis was established after skin biopsy; and, in the latter patient by parotid gland biopsy. In 2 of our other stage 0 patients, the only presenting sign of the disease was LG involvement. Sarcoidosis in these 2 patients was initially diagnosed by means of LG biopsy; and, during follow-up bilateral hilar lymphadenopathy developed in both.

The most frequent ocular manifestation of sarcoidosis is uveitis and is reported as occurring in 30–70% of cases [1, 13, 14]. It was also stated that conjunctival nodule formation is observed in 40% of sarcoidosis patients [13, 14]. The most frequent form of ocular involvement in our study was uveitis. The frequency of conjunctival involvement, however, was lower than that reported in the literature.

In our patients with LG involvement, signs of extrapulmonary involvement – other than that of the LG – were more frequent than in other patients. Collison et al. [15] detected sarcoid involvement of the other organs in 14 of their 15 patients with histologically proven orbital involvement; and drew attention to investigating for the presence of other organ involvement in these patients.

LG sarcoidosis is usually treated with corticosteroids [2, 7]. In our study, subjects with LG involvement were given steroid therapy. In all patients, response to steroids was good. Although surgical extirpation has been tried in some cases in the past, results were unsatisfactory and the technique was quite difficult [16, 17].

Table 3

The comparison of some clinical features of our patients with LG and eye involvement to those of other sarcoidosis patients.

	Patients with LG involvement	patients with other eye involvement	all sarcoidosis patients
N	9	61	446
F/M	7/2	43/18	291/155
Age (mean ± SD)	33 ± 17.7*	40.3 ± 8**	44.5 ± 9.5
Stage 0, n (%)	5 (55.6)*	7 (11.5)**	26 (5.8)
Stage I, n (%)	2 (22.2)***	38 (62.3)	324 (72.6)
Stage II, III, n (%)	2 (22.2)	16 (26.2)	96 (21.5)
Extrapulmonary involvement, n (%)	5 (55.6)**	14 (23)	103 (23.1)
Skin involvement, n (%)	3 (33.3)	22 (36.1)	145 (32.5)
Parotid gland involvement, n (%)	1 (11.1)	6 (8.6)	26 (5.8)

* $p < 0.001$, different from all sarcoidosis patients.
** $p < 0.05$, different from all sarcoidosis patients.
*** $p < 0.01$, different from all sarcoidosis patients.

Eye involvement is quite common in sarcoidosis: it is encountered in 11 to 83% of the patients [18]. Although clinically detectable LG involvement is rare, it might be the initial clinical finding in some cases as was the condition in our study. Contrary to the data in literature, in this study LG and eye involvement were more frequent among younger patients. Similar to our study, chest X-ray in subjects with LG involvement can be normal (7); however, in these patients the presence of sarcoid involvement in other organs should be investigated.

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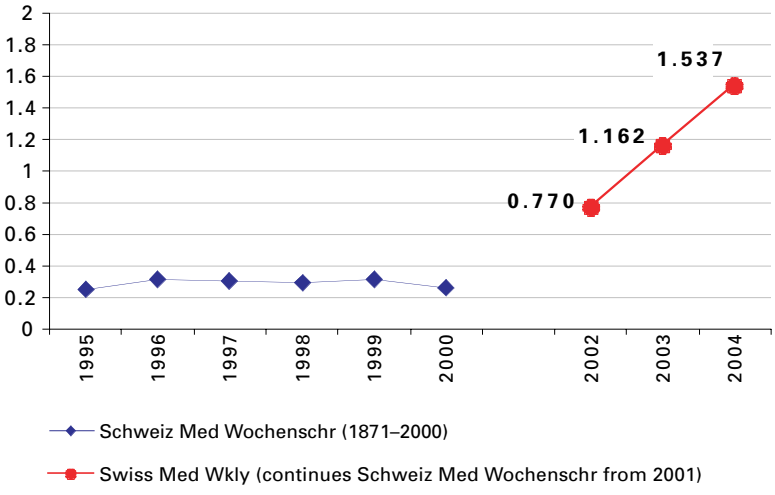

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