

SHORT REPORT

Seasonal clustering of sarcoidosis presenting with erythema nodosum

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ABSTRACT: Seasonal clustering of sarcoidosis presenting with erythema nodosum (EN) has previously been reported only in the northern hemisphere.

Of 59 patients presenting to a single centre in New Zealand with a new diagnosis of sarcoidosis, 21 had EN and three more had acute arthralgia without EN. These patients were compared with the rest of the cohort.

The patients with EN or arthralgia alone presented exclusively between April and December, with peak clustering in the spring months of August, September and October ($p < 0.001$, Fisher's exact test). This cohort was more likely to have a stage I chest radiograph and to be female ($p < 0.05$), but there were no other differences between the groups.

This is the first report of seasonal clustering in the southern hemisphere suggesting a common environmental trigger in the aetiology of sarcoidosis.

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Seasonal clustering of erythema nodosum (EN) in association with sarcoidosis has previously been reported in the UK, Norway, Greece, Spain, Finland and Japan [1–7]. There have been no reports of seasonality of sarcoidosis from the southern hemisphere. This study reports the features of patients presenting to a single centre in New Zealand over 3 yrs in which it became apparent that there was seasonal clustering of cases of EN each spring.

Methods

All patients with newly diagnosed sarcoidosis were registered prospectively over a three-year period and followed for a minimum duration of 2 yrs. The diagnosis in all patients was based on the histological finding of noncaseating granulomata and/or the typical clinical appearance [8]. The month of presentation was determined as the month in which symptoms first appeared.

Statistical analysis was performed using SAS (SAS Institute, Cary, NC, USA) and Primer software. The Student's t-test and Chi-squared test were used to examine differences between the groups. The Fisher's exact test was used to examine clustering.

Results

Of the 59 patients, 21 presented with EN and a further three with acute arthralgia (A) but without EN. This latter group was analysed together with the patients with EN (EN/A, $n=24$) and compared with the remainder of the cohort (no EN, $n=35$). Fifty-two patients had a biopsy confirming the presence of noncaseating granulomata in affected tissue and seven were diagnosed on clinical grounds alone

(one had Heerfordt's syndrome and the other six had EN with hilar and mediastinal lymphadenopathy). All patients were Mantoux negative.

The mean age of the cohort was 30 (20–51) yrs and there were 32 females (table 1). There were no age or racial differences between the EN/A and no EN groups, but a

Table 1. – Characteristics of 59 patients presenting with a new diagnosis of sarcoidosis over 3 yrs

	EN/A $n=24$	No EN $n=35$
Age (mean) yrs	31	22
Sex	18 F (75)*	14 F (40)
Race	20 E, 3 I, 1 P	26 E, 5 I, 4 P
Chest radiographic stage		
0	1 (4)	
I	20 (83)**	13 (37)
II	3 (13)	10 (29)
III		12 (34)
Extrapulmonary disease	5 (23)	12 (34)
	Cardiac 1, skin 1, neuro 1, eyes 1, parotid 2	Liver 2, node 3, skin 2, spleen 2, eyes 1
EN	21	0
Acute arthralgia alone	3	0
Hypercalcaemia	0	3 (9)
Abnormal lung function	2 (8)	3 (9)
Required corticosteroid treatment	8 (33)	10 (29)

Patients are grouped according to whether they presented with erythema nodosum (EN) and/or acute arthralgia (EN/A) or not. Abnormal lung function was defined as forced expiratory volume in one second and/or vital capacity $< 85\%$ predicted. Chest radiographic stage according to SCADDING [8]. F: female; E: European; P: Polynesian; I: Indian. Data are presented as number with percentages in parentheses.

significantly greater number of patients with EN/A were female (18/24, $p < 0.05$). Likewise, patients with EN/A were more likely to have a stage I chest radiograph (21/24, $p < 0.001$). Nineteen patients presented with hypercalcaemia ($n=3$) and/or other extrapulmonary involvement. Although the no EN group tended to have more extrapulmonary manifestations (12/35) than the EN/A group (5/24) this did not reach statistical significance.

There was strong seasonal clustering of the EN/A group, with the majority of patients presenting in the second 6 months of the year (20/24, $p < 0.001$) (fig. 1) with a peak in the late winter to spring months. This was not observed for the no EN group. No apparent exposure accounting for the seasonality of presentation of the EN/A group could be identified. There was no difference in the numbers treated in each group, but the EN/A group generally received shorter courses of oral corticosteroids and were more likely to have a better outcome.

Discussion

This study shows that patients with sarcoidosis associated with EN or acute arthralgia are most likely to present in the spring months in New Zealand, a country in the

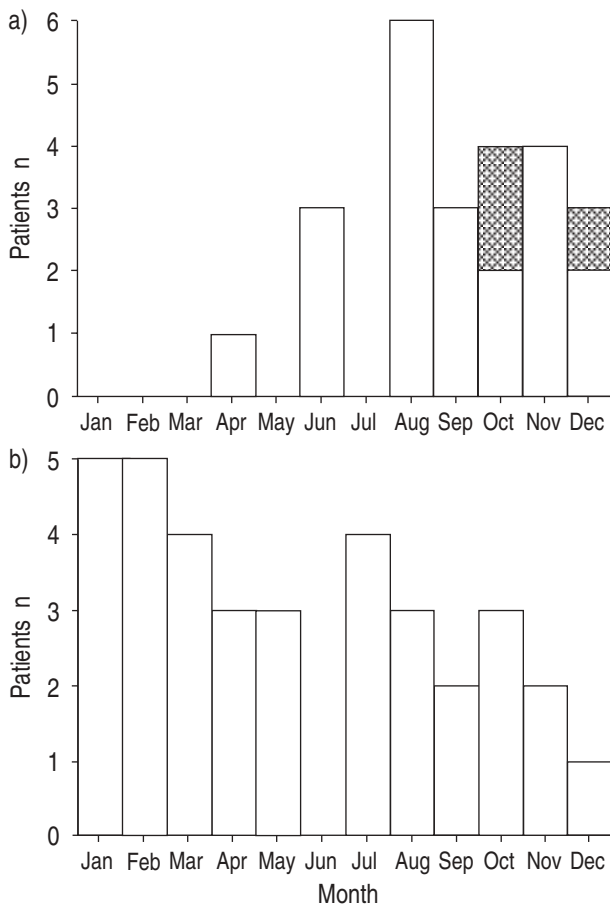


Fig. 1. — a) Monthly incidence of sarcoidosis presenting with erythema nodosum (EN; □, $n=21$) or acute arthralgia (▨, $n=3$) demonstrating clustering in the spring months ($p < 0.001$, Fisher's exact test). b) Monthly incidence of sarcoidosis presenting with other than EN or arthralgia. No evidence of seasonal clustering was apparent.

southern hemisphere just as reported for the northern hemisphere. These patients are more likely to be female and to have hilar and mediastinal lymphadenopathy on chest radiography without parenchymal infiltrates. They are also more likely to have a self-limiting illness.

A cluster of sarcoid arthritis in the spring, of which 10 out of 17 cases also had EN and lung involvement, was reported from Norway [1]. Unlike the present study there was no female preponderance but most had stage I chest radiography. In Greece, all 57 patients with asymptomatic bilateral hilar lymphadenopathy due to sarcoidosis who presented between 1980 and 1989 were diagnosed between December and June in each year [2]. An outbreak of six cases of acute sarcoid arthropathy in May was identified in Norfolk, UK [3]. Four of these cases had EN and all had bilateral hilar adenopathy. In a separate study from the UK EN due to sarcoidosis was noted to occur in every month of the year, but predominantly during February to May, when over half of the patients presented [4]. A striking female preponderance was noted (74%). In Greece 49% of patients presenting with Lofgren's syndrome between 1972 and 1986 noticed the onset of symptoms between April and June [5]. Most patients were female (89%). Sarcoidosis was diagnosed more often in the first half of the year in Finland, especially if patients had symptoms [6], and also in Japan, where a significant increase in cases presented in June and July [7].

Previous reports of seasonality of sarcoidosis in the northern hemisphere have not identified an environmental exposure, but clustering has been reported in firefighters [9] and a study of sarcoidosis in the Isle of Man demonstrated that one-third of the patients had been in contact with the disease before diagnosis, suggesting a transmissible agent [10]. The hypercalcaemia of sarcoidosis has been reported as having a peak seasonal incidence in the summer but this undoubtedly reflects exposure to sunlight and increased 1,25-dihydroxycholecalciferol production [11]. The present patients with hypercalcaemia likewise presented in the summer.

Many different environmental factors have been suggested as causing sarcoidosis including exposure to pine trees, farm animals, clay soil and natural well springs, but most studies reporting such associations do not stand up to epidemiological scrutiny [12]. Possibly the strongest association is with rural residence. All of the present patients were urban dwellers but more detailed exposure history is not available as the seasonal clustering was only identified retrospectively. A more systematic prospective study is underway.

In summary, seasonal clustering of sarcoidosis presenting with erythema nodosum has been identified in New Zealand, suggesting a common environmental trigger across the world.

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