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Scientific letter

Incidence of Cancer in Sarcoidosis Patients in a Tertiary Care Hospital in the UK

Incidencia de cáncer en una cohorte de pacientes con sarcoidosis de un hospital terciario en Reino Unido

Dear Editor,

Sarcoidosis is a multisystem chronic granulomatous inflammatory condition of unknown aetiology. It can affect almost any organ of the body. Over 90% cases, most commonly lung, including thoracic lymph nodes and/or parenchymal involvement occur.[1] Increased risk of cancer in sarcoidosis is a long-debated issue over half a century. It has been postulated that chronic inflammation and/or different immunological dysregulation in sarcoidosis may be associated with high risk of cancer incidence.[2,3] Few population-based study also revealed increased incidence of cancer in sarcoid patients.[4,5] Though the possibility of misclassification and selection bias cannot be excluded.[6] Series of case study found high incidence of lymphoproliferative disease[7] and lung cancer[8] in sarcoid patients; however, case report is inconclusive to establish any association.

We aim to confirm if incidence in our cohort and profile of cancer is similar to previous studies. We conducted a retrospective descriptive study, using individual patient's unique hospital number from the online intranet-based record system, of a cohort of sarcoidosis patients attending to Coventry University Hospital from 2002 to July 2021.

This study achieves the ethical requirements of retrospective descriptive studies where the data have been used anonymously.

The study group consist of 121 pulmonary sarcoidosis patients seen in a respiratory outpatient clinic at University Hospital Coventry & Warwickshire over the period of Jan 2002 to July 2021. Among these 121 patients 39 (32%) have extra-pulmonary involvement as well. 79 patients (65%) had histologically proven diagnosis of sarcoidosis. Table 1 shows the characteristics of the study population.

This cohort mean age is 48 years (SD 2) with female predominance (56%). A total of 14 patients (11.6%) were diagnosed with cancer over the follow up period. 6 patients were diagnosed with cancer before the diagnosis of sarcoidosis (43%). Among them 1 patient later on developed metastatic breast cancer after the diagnosis of sarcoidosis. 1 patient developed 2 different non-melanoma skin cancer lesions before and after the sarcoidosis diagnosis. This patient has been included in both groups. Therefore, total 10 cancer patients after the diagnosis of sarcoidosis have been further evaluated retrospectively using the hospital records. These patients were diagnosed with malignancy either simultaneously or after the diagnosis of sarcoidosis. Among 10 malignancy and sarcoidosis coexistence patients, 7 patients were male and only 3 patients were female, however the total number of female sarcoid patients (56%) were higher in this cohort. Patient with non-Hodgkin's lymphoma, one patient with breast cancer and prostate cancer were diagnosed within one year after the diagnosis of sarcoidosis.

Table 1
Characteristics of sarcoidosis patients.

Variable	*N*
Total sarcoidosis patients	121
Sex	
Male	53 (44%)
Female	68 (56%)
Age of diagnosis[a]	
20–39	33 (27%)
40–59	63 (52%)
≥60	24 (20%)
Radiological stage during diagnosis	
0-I	75 (62%)
II	23 (19%)
III	3 (3%)
IV	2 (2%)
No record	18 (15%)
Smoking history	
Current smoker	20 (16.5%)
Ex-smoker	28 (23%)
Never smoker	47 (38.8)
No record	26(21.5%)
Treatment	
Steroid (systemic & topical)	52 (43%)
Methotrexate	6 (5%)
Azathioprine	6 (5%)
Mycophenolate	3 (2.5%)
Hydroxychloroquine	4 (3%)
Infliximab	1 (0.8%)
Vital status at the end of follow up	
Dead	8 (6.6%)
Transfer to different hospital	1 (0.8%)
Alive	112 (92.5%)

[a] 1 patient-no information about the year of diagnosis.

Mean age of patients diagnosed with cancer was 60 years old (SD 15). In Table 2 both groups are described separately.

Our data show an incidence of cancer is 11.6% in our population that increases with age. The profile of cancers identified correlates with the most common malignancies in general population.

Association of malignancy and sarcoidosis is a controversial issue in the literature. The increased incidence of haematological malignancy and cancer of solid organs has been reported in population-based study. Brincker and Wilbek first did a large population-based study in 1973. They studied 2544 pulmonary sarcoidosis patients reported in Danish Institute of

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Table 2
Distribution of cancer patients by age, sex, number, type of malignancy, and duration of diagnosis.

Type of cancer	Male	Female	Mean age of cancer diagnosis (years)	Mean duration (days) of cancer diagnosis from the diagnosis of sarcoidosis
Cancer diagnosis after development of sarcoidosis (n = 10)				
Breast	1	1	63	1988
Prostate	1	0	56	231
Skin (non-melanoma)	2	1	55	1131
Colorectal	0	1	72	4322
Bladder	1	0	61	639
Non-Hodgkin's lymphoma	1	0	69	302
Tonsil	1	0	47	534
Total	7	3	60	1224
Cancer diagnosed before the diagnosis of sarcoidosis (n = 6)[a]				
Breast	0	2	42	1084
Lung	0	1	75	604
Non melanoma skin cancer	0	2	79	1752
Malignant Melanoma	0	1	58	439
Total	0	6	64	970

[a] 1 patient is included in both groups due to relapse of cancer after diagnosis of sarcoidosis.

Clinical Epidemiology and found the occurrence of malignant lymphoma 11 times and lung cancer 3 times more frequent in sarcoidosis patients.[4] However, Romer had revisited the same study group and excluded 14 patients due to diagnostic incorrectness and questioned the validity of the result.[9] Romer and colleague did another study on 555 Danish sarcoid patients, where 48 cancer patients were found[10]. However, this study did not find any increased occurrence of malignancy in sarcoidosis or any association of increase age at diagnosis of sarcoidosis with malignancy.

In our cohort, we noticed one non-Hodgkin's lymphoma but no incidence of lung cancer in patients who develop malignancy after sarcoidosis diagnosis. Though the number of the study group is too small for any conclusive statement. Another Swedish study in 1999 revealed increased relative risk of cancer in sarcoidosis patients including the risk for lung cancer, non-Hodgkin's lymphoma, melanoma, non-melanoma skin cancer, and liver cancer.

Chronic inflammation to the affected organ was proposed to be the putative mediator of high cancer risk.[5] We can observe 3 occurrence of non-melanoma skin cancer; although only one patient had skin involvement by sarcoidosis other two patients had no evidence of skin involvement. That one patient with sarcoid skin involvement was diagnosed with skin cancer simultaneously; therefore chronic inflammation could be the causative factor for the development of cancer in this case. Moreover, we found the mean age of sarcoidosis diagnosis in cancer patient was 9 years higher than the sarcoidosis without cancer cohort. A linkage analysis found aetiological relation in one fourth of cases of sarcoidosis and malignancy in whom both conditions co-exist.[11] Five of our patients had history of malignancy before the diagnosis of sarcoidosis. It is difficult to denote, whether both condition co-existed or a separate incidence, however all of them later on were diagnosed with sarcoidosis with histology proven evidence from different lymphatic distribution other than the cancerous site with no recurrence of cancer during the follow up time duration. In this group, the mean age of cancer development and sarcoidosis diagnosis were also high, although both patients with breast cancer were diagnosed before 50 years of age.

Incidence of cancer in our sarcoidosis cohort is above 10% with the most common cancers found being those also more common in general population. Age seems to be the main factor for cancer development over time.

We could not draw any association of incidence of specific malignancy with sarcoidosis. Here the sample size is too small for postulating any hypothesis which demands large scale research in this field.

Authors' contributions

Both authors design the project and identify the patients. First author has done the data collection, literature review, writing the paper and references. Second author has done the literature review, data and paper review and editing of the final draft as well as the clinical follow up of this cohort.

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Conflict of interest

There is no conflict of interest.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.opresp.2022.100157.

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