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Case report

Malignancy in patients with sarcoidosis

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ABSTRACT

The relationship between sarcoidosis and malignancy is not clear yet. We retrospectively evaluated 131 sarcoidosis patients followed-up at the single Rheumatology center. The incidence of malignancies was investigated in this cohort. A total of 6 (4.6%) patients with malignancy were identified in our cohort of 131 patients with sarcoidosis. Hodgkin lymphoma (HL) was detected in three patients, followed by one patient with breast cancer, one patient with thyroid cancer and one patient with testicular cancer. All patients had chronic sarcoidosis with pulmonary involvement, and only 1 patient had acute sarcoidosis with Löfgren's syndrome. HL developed concomitantly with sarcoidosis in one patient while other two patients developed disease before and after sarcoidosis diagnosis. Two patients with solid tumors developed malignancy years before sarcoidosis diagnosis, while one patient developed thyroid cancer during sarcoidosis follow-up. All 6 sarcoidosis–malignancy patients survived after six year years follow up. We found low incidence of malignancy in patients with sarcoidosis in our small cohort. The sarcoidosis–malignancy relationship can only be a coincidence and/or can be explained by a common pathogenesis. New prospective studies involving large patients series are needed in this regard.

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Malignidad en pacientes con sarcoidosis

RESUMEN

La relación entre sarcoidosis y malignidad no está clara todavía. Evaluamos retrospectivamente 131 pacientes con sarcoidosis seguidos por un centro de reumatología. En esta cohorte se investigó la incidencia de neoplasias malignas. Se identificó un total de 6 (4,6%) pacientes con neoplasia maligna en esta cohorte. El linfoma de Hodgkin (LH) se detectó en 3 pacientes, seguido de un paciente con cáncer de mama, un paciente con cáncer de tiroides y un paciente con cáncer testicular. El LH se desarrolló concomitantemente con sarcoidosis en un paciente, mientras que los otros 2 desarrollaron la enfermedad antes y después del diagnóstico de sarcoidosis. Dos pacientes con tumores sólidos desarrollaron malignidad años antes del diagnóstico de sarcoidosis, mientras que el paciente con cáncer de tiroides lo presentó durante el seguimiento. Los 6 pacientes con sarcoidosis y malignidad sobrevivieron durante 6 años de seguimiento. Encontramos baja incidencia de malignidad en pacientes con sarcoidosis en nuestra cohorte. La relación sarcoidosis–malignidad puede ser coincidental y/o puede explicarse por una patogénesis común.

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Introduction

Sarcoidosis is a systemic disorder of unknown etiology, which is characterized by non-caseating granuloma reaction.¹ There are contradictory data in the literature regarding the relationship

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Table 1
Characteristics of patients with sarcoidosis–malignancy in our cohort.

Features	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Age/sex	52/F	32/M	44/F	33/F	40/F	73/M
Malignancy type	Thyroid cancer	Testicular cancer	Breast cancer	HL	HL	HL
Disease duration (year)	12	3	2	2	3	1
Occurrence of malignancy	During sarcoidosis follow-up	5 years before sarcoidosis	1 year before S.	1 year before S.	3 years after S.	Concomitantly
Stage of sarcoidosis	1	2	1	2	1	2
Uveitis	No	No	No	No	Yes	No
Myositis	No	No	No	No	No	No
Arthritis	Ankle joint	Ankle joint	Knee	Ankle	Knee	No
NCG on bx	Yes	Yes	Yes	Yes	Yes	Yes
Smoking	No	Yes	No	Yes	Yes	No
Elevated ACE	Yes	No	No	No	Yes	Yes
Elevated CRP	Yes	Yes	Yes	Yes	Yes	Yes
Elevated ESR	Yes	Yes	Yes	Yes	Yes	Yes
Current treatment	HQ	CS	HQ	CS	CS	CS

Abbreviations: NCG: non-caseating granuloma; HL: Hodgkin lymphoma; ACE: angiotensin converting enzyme; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; CS: corticosteroids; HQ: hydroxychloroquine.

between sarcoidosis and malignancy.² The reasons of those controversial results may be explained with biases in patients selection and different classification method used. Herein we reported the incidence of malignancy in a small cohort sarcoidosis patients.

Clinical observation

Our study is a retrospective analysis of 131 patients diagnosed with sarcoidosis at the single Rheumatology center. Sarcoidosis diagnosis was made through clinical, laboratory, radiologic and histopathological investigations. The incidence of malignancies was investigated in this cohort. Malignant diseases were diagnosed by histopathology. The clinical data of patients with sarcoidosis and malignant diseases were further analyzed. Six (4.6%) patients with malignant diseases were identified in our cohort. Hodgkin lymphoma (HL) was detected in 3 patients, followed by one patient with breast, thyroid and testicular cancer. Five patients had chronic sarcoidosis with pulmonary involvement, and one patient presented as Löfgren's syndrome. HL developed concomitantly with sarcoidosis in one patient while other two patients developed disease before and after sarcoidosis diagnosis. Sarcoidosis presented prior to the malignancy in 2 of 6 patients (Table 1). Among 6 sarcoidosis–malignancy patients 4 were female and 2 were male, the mean age was 45.6 years and mean disease duration was 3.8 years (1–12 years). All 6 patients had pulmonary involvement, 5 patients had arthritis, and one patient had uveitis. On laboratory tests, all 6 patients had elevated acute phase reactants, while 3 patients had elevated serum ACE levels. In terms of current drug usage, 4 patients received low-dose corticosteroids, and two patients received hydroxychloroquine. All 6 sarcoidosis–malignancy patients were survived during six year follow-up.

Discussion

Our study showed no significant association between sarcoidosis and malignancy. Only 6 (4.6%) patients with malignant diseases were identified in our cohort of 131 patients with sarcoidosis. Our results were with concordance with previously reported data. There are conflicting results in the literature regarding the relationship between sarcoidosis and malignancy.³ Yamaguchi et al. evaluate the excess mortality in a cohort of 1411 cases of sarcoidosis for a period of 3 years using the standardized mortality ratio (SMR).⁴ They reported that lung cancer, leukemia and uterine cancer showed a statistically significant SMR. Kataoka et al. observed a

significantly greater than expected incidence of thyroid and laryngeal cancer and leukemia in sarcoidosis patients.⁵ Boffetta et al. reported the increased incidence of colon and kidney cancer in sarcoidosis patients in USA.⁶ Moderate association between sarcoidosis and malignancy was showed in a meta-analysis study.⁷ The authors reported two-fold higher risk of developing skin and hematopoietic cancers while there was not a significant increase in risk of lung cancer. The low prevalence of smoking in sarcoidosis patients may be a reason for the lack of an association between lung cancer and sarcoidosis. Ungprasert et al. investigated the incidence of malignancy in patients with sarcoidosis and not found any significant association.⁸ The exact mechanism which may explained the association between sarcoidosis and malignancy is not fully understood. Immune dysregulation and chronic inflammation seen in sarcoidosis may be a risk factor for malignancy development.⁹ Activation of Th1/Th17 cells, released of some proinflammatory cytokines, impaired CD4 T-cells and decreased regulatory T cells, may promote angiogenesis, cells proliferation, stromal growth, and tissue remodelling.¹⁰

Conclusion

We found low incidence of malignancy in patients with sarcoidosis in our small cohort. On the basis of the available data, the association between sarcoidosis and malignancy is still under debate. More prospective studies are needed in this regard.

Conflict of interests

The authors declare no conflict of interests.

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