Malignancy associated with dermatomyositis – a retrospective single-center study with 33 patients

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ABSTRACT

Background: Dermatomyositis (DM) is a multisystemic inflammatory disease that has been associated with neoplastic disease.
Objectives: To assess the clinical/laboratory data in a series of patients with DM and identify association with malignancy.
Material and Methods: Retrospective study of DM inpatient files between 1965 and 2011. All patients with DM diagnosis, admitted to our department were only included if they fulfilled at least four of the five *Bohan and Peter* diagnostic criteria. Malignancy was considered associated with DM only if its diagnosis had preceded or followed the DM diagnosis by up to three years. Data were analyzed with a significance level of 5%.
Results: 33 patients fulfilled the inclusion criteria for DM, with a median age of 56 years old (s= 14.329) and female to male ratio of 1.36:1. Neoplastic disease was associated with DM in 30%, predominantly colorectal and prostatic cancer (each one representing 30% of the malignancies) and the majority of these patients were men (p=0.042 in Fisher s exact test). In the group of DM associated with malignancy, the patients tended to be older than in the group not associated with malignancy. In 70% of these patients, malignancy was diagnosed simultaneously or in the first year after DM diagnosis.
Conclusions: This study emphasizes the association between malignant disease and DM within a short period of time around the diagnosis.

Keywords: Dermatomyositis; Malignancy; Prognosis; Retrospective study.

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INTRODUCTION

Dermatomyositis (DM) is a multisystemic inflammatory disease and its association with neoplastic disease has long been recognized[1-3]. Associated risk of malignancy in DM varies widely (between 6 and 60%), probably due to the small series from different countries and the selected nature of patients studied in referral centers[1], in a relatively rare disease. Malignancies are found associated with DM especially in older patients[4-6] and age has recently been shown to be a predictive factor of malignancy particularly in newly-diagnosed DM[5].

Prevalence of neoplasms may vary according to several factors, such as gender, age, geographic location and ethnic diversity[3,4]. In our country, no study has ever been published whose primary endpoint was the association between malignancy and DM in adults.

The objective of the present study is to assess the clinical/laboratory data in a series of patients with DM and identify significant factors associated with malignancy.

MATERIAL AND METHODS

This was a retrospective study of the inpatients admitted to our department between 1965 and 2011 with the diagnosis of DM, using clinical data from the patients' files.

Our hospital is a referral center for Lisbon and southern Portugal and all patients included in this study were admitted to our department with the main diagnosis of DM. Patients admitted after 1975 fulfilled at least four of the five *Bohan and Peter* diagnostic criteria[7,8]. For patients admitted before 1975, DM diagnosis was made based on clinicopathological features, because at that time there were no established DM criteria. *Bohan and Peter* criteria were applied in those patients retrospectively, based on clinical and laboratory data obtained in the clinical process, and patients were only included if they fulfilled at least four of the five

criteria (Table I). Patients were included in the study if they were more than 18 years old at the time of diagnosis and had been admitted to our ward for DM (at least once). Juvenile DM patients were excluded.

Malignancy was considered as being associated with DM only if its diagnosis had preceded or followed the DM diagnosis by up to three years (according to the modified *Bohan and Peter* criteria)[9].

The demographic and clinical data recorded were: sex, age at the time of diagnosis, length of inpatient stay, time between first symptoms and DM diagnosis, temporal relation between cancer and DM diagnoses, treatments and mortality during admission. The following laboratory analyses were included: complete blood count, erythrocyte sedimentation rate, albumin, lactate dehydrogenase (LDH), aspartate aminotransferase (AST) and alanine aminotransferase (ALT). These laboratory parameters were chosen because they were uniformly recorded in the clinical files, in contrast to autoantibodies, C-reactive protein, and tumor markers, which were not performed during the inpatient stay in the older clinical files.

TABLE I. PATIENTS DIAGNOSED WITH DERMATOMYOSITIS BEFORE 1975

Patients	Age	Gender	Year of diagnosis	Dermatomyositis manifestations
1	56	M	1965	Gottron papules, heliotrope, photodistributed erythematous macules; proximal muscle weakness; muscle biopsy and EMG suggestive of myositis; aldolase and LDH elevation.
2	57	M	1966	Gottron papules, photodistributed erythematous macules; proximal muscle weakness; muscle biopsy suggestive of myositis; aldolase and LDH elevation.
3	74	F	1966	Heliotrope, photodistributed erythematous macules; proximal muscle weakness; muscle biopsy and EMG suggestive of myositis; aldolase and AST elevation.
4	53	M	1966	Photodistributed erythematous macules; proximal muscle weakness; muscle biopsy and EMG suggestive of myositis and aldolase elevation.
5	70	F	1967	Gottron papules, heliotrope, photodistributed erythematous macules; proximal muscle weakness; muscle biopsy and EMG suggestive of myositis; LDH elevation.
6	18	M	1967	Gottron papules, heliotrope, photodistributed erythematous macules; proximal muscle weakness; muscle biopsy and EMG suggestive of myositis; aldolase, ALT, AST and LDH elevation.
7	52	F	1968	Heliotrope, photodistributed erythematous macules; proximal muscle weakness; muscle biopsy and EMG suggestive of myositis; aldolase and LDH elevation.
8	28	M	1970	Gottron papules; proximal muscle weakness; EMG suggestive of myositis; CPK and LDH elevation.
9	49	F	1970	Gottron papules, heliotrope, photodistributed erythematous macules; proximal muscle weakness; EMG suggestive of myositis; aldolase and LDH elevation.
10	61	F	1972	Gottron papules, heliotrope, photodistributed erythematous macules; proximal muscle weakness; muscle biopsy and EMG suggestive of myositis; AST and LDH elevation.
11	63	F	1973	Heliotrope, photodistributed erythematous macules; proximal muscle weakness; muscle biopsy and EMG suggestive of myositis; LDH elevation.

Legend: creatine phosphokinase (CPK); lactate dehydrogenase (LDH); aspartate aminotransferase (AST); alanine aminotransferase (ALT); electromyogram (EMG).

Serum creatine phosphokinase (CPK) or aldolase levels were determined in all patients. However, as at least one of these two parameters of muscle injury was not evaluated systematically in all individuals, statistical analysis was not applicable.

All laboratory data used were the highest values recorded during the acute phase. Finally, electromyogram, skin and muscle biopsy were also recorded.

All the patients with DM diagnosis were screened for neoplasia with routine examination: assessment of gastrointestinal and genitourinary tract (including gynecological exam in women), lungs and hematological system. Complementary exams (i.e.: imaging exams, such as axial tomography scan) were performed according to clinical findings and neoplasia diagnosis based on anatomopathological analysis.

Bivariate analysis of qualitative variables was done with Pearson's c^2 (or the alternative Fisher exact test, when there were expected frequencies less than 5). If a significant association was found, the V-Cramer (V) measures were also applied. Differences in terms of quantitative variables were investigated by Mann-Whitney non-parametric test, after checking the assumptions of the parametric t-test. Statistical tests were performed at a significance level of 5%.

RESULTS

A total of 33 patients fulfilled the inclusion criteria, between 1965 and 2011. Seven patients were excluded: three patients with juvenile DM (diagnosis made at 6, 9 and 12 years of age) and the remaining lacked clinical criteria (n=3) and laboratory data (n=1).

The patients included in the study had a mean age

TABLE II. BIVARIATE ANALYSIS OF ASSOCIATION BETWEEN SELECTED VARIABLES AND MALIGNANCY ASSOCIATED WITH DERMATOMYOSITIS (DM)

Studied variables	Patients with malignancy associated with DM (n=10)	Patients with DM, not associated with malignancy (n=23)	Total of patients with DM (n=33)	
Female: male ratio	0.43:1*	2.29:1	1.36:1	*p=0.042 in Fisher's exact test
Mean age	61	53	56*	*s= 14.329
First symptoms cutaneous (instead of muscular weakness)	70% (7/10)	70% (16/23)	70% (23/33)	Ns
Mean time between first symptoms and DM diagnosis (months)	9	14	12	Ns
Mean inpatient stay (days)	44	71	63	Ns
Mean leukocyte count	8x10⁹/L	6.7x10⁹/L	7.1 x10⁹/L	Ns
Mean lymphocyte count	1.5x10⁹/L	1.6x10⁹/L	1.5x10⁹/L	Ns
Mean serum albumin (g/L)	32	34	33	Ns
Mean ESR (mm/h)				
(Female)	33 (30)	49 (55)	44 (54)*	* p=0.009
Mean LDH (U/L)	1338	698	892	Ns
Mean ALT (U/L)	106	45	65	Ns
Mean AST (U/L)	110	70	83	Ns
Mortality during admission	2	2	4	Ns

A nonparametric test (Mann-Whitney) was chosen for the quantitative variables. Non-significant associations are displayed as ns and (*) statistical significance. Legends: erythrocyte sedimentation rate (ESR); lactate dehydrogenase (LDH); aspartate aminotransferase (AST); alanine aminotransferase (ALT).

of 56 years (s= 14.329) at admission and were predominantly female (female: male ratio of 1.36:1). The majority of patients presented the classic DM type (97%), while only one patient showed the hypomyopathic variant. The median ward stay was 12 days.

Demographic, clinical and laboratory variables analyzed in both DM groups (associated and not associated with malignancy) are presented in Table II.

Neoplastic disease was associated with DM in 10 patients (30%) and patients tended to be older (median age: 61 years), compared to the group of DM not associated with malignancy (median age: 56 years), but the differences did not reach statistical significance.

There was a predominance of male patients in the group of DM associated with neoplastic disease (70%), statistically significant (p=0.042, on Fisher s exact test).

The malignancies associated with DM were (Table III):

- prostatic cancer, non-Hodgkin's lymphoma (NHL) and metastatic cervical adenopathy from squamous cell carcinoma (in male patients);
- endometrial cancer and melanoma (in female patients);
- colorectal cancer (in both sexes).

Colorectal cancer and prostatic cancer were the most frequent malignancies found, each corresponding to 30% of the cases of neoplastic disease associated with DM in this series.

Only one case was found in accordance with the paraneoplastic syndrome definition, which requires that its manifestations have a parallel course with systemic neoplasm and that remission accompanies the neoplasm cure. A 55-year-old male diagnosed simultaneously for DM and NHL presented complete remission of DM after undergoing chemotherapy (rituximab + cyclophosphamide + doxorubicin + vincristine) for the NHL, without any other therapy of DM (namely, systemic corticosteroids). Of course, since the treatment of choice for NHL is chemotherapy (instead of surgery), the possibility that DM remission was due to its immunosuppressive effect cannot be excluded.

In 70% of these patients, malignancy was diagnosed simultaneously or in the first year after DM diagnosis (60% simultaneously and 10% in the first year after DM diagnosis).

Furthermore, four patients died during hospitalization: one of stroke, another of congestive heart failure and two of unknown causes. Of those, three were women (75%) and the proportion of patients with DM with or without associated malignancy was the same (50%).

DISCUSSION

Dermatomyositis is the most common inflammatory myopathy in all age groups, and although it is well known for its association with cancer[10], studies of large series of malignancy associated with DM are rare in the literature. The largest studies are Scandinavian[1, 4].

Our study represents a small series of DM from a single center and it is composed by patients diagnosed either before or after the diagnostic criteria for DM proposed by Bohan and Peter (1974). All patients included in our study before 1974, fulfilled the referred criteria. However they were not necessarily treated with the presumptive diagnosis of DM. This is the first study in Portugal whose primary purpose was to evaluate the association between malignancy and DM in adults. Two retrospective Portuguese DM series were published in

TABLE III. DM ASSOCIATED WITH MALIGNANCY: TYPE OF CANCER AND TEMPORAL RELATION BETWEEN DIAGNOSES

	Type of cancer						Temporal relation with malignancy		
	Colorectal cancer	Prostatic cancer	Endometrial cancer	NHL	Melanoma	Metastatic adenopathy ±	Previous	Simultaneous	Posterior
Female	1	–	1	–	1	–	1	2	–
Male	2	3	–	1	–	1	2	4	1
Total	3	3	1	1	1	1	3	6	1
(%)	(30%)	(30%)	(10%)	(10%)	(10%)	(10%)	(30%)	(60%)	(10%)

Legend: dermatomyositis (DM); non-Hodgkin's lymphoma (NHL). ± Metastatic adenopathy from a squamous cell carcinoma.
Note: Malignancy was only considered to be associated with DM if the diagnosis was made within three years before or after DM diagnosis (according to the modified *Bohan and Peter* criteria)[8]. Cancer was diagnosed after DM in only one case (seven months after DM diagnosis).

1980[11] and 1993[12], but the association of malignancies with DM was not the primary endpoint of either study.

The majority of patients were women, as reported in the majority of the series[2-3,5,9,11-13]. The median age at disease onset was 56 years (the same as found in the larger DM series[4]) and above 45 years old, in conformity with the remaining studies[2,3]. The mean age in the group of patients with DM associated with malignancy was slightly higher (61 years), as has also been reported in the literature[2,3,5,6,14].

Malignancy was found to be associated with DM in 30%, in conformity with literature (frequencies reported within 6-60%)[1,11,12]. The diagnosis of malignancy associated with DM was more frequent in men, as also seen in Asian series[3,14] but in contrast to the female predominance reported in Western series[1,5,11,15].

Concerning the type of cancer associated with DM, the most prevalent in our series were prostatic and colorectal cancer. The latter is one of the cancers more strongly associated with DM according to literature[4], but both are also frequently found in the general population. Reports show that NHL is associated with DM, especially in the first year after DM diagnosis[4], which was true in our case. Cases of melanoma[16] and metastasis (as we found in this series) have also been reported as being associated with DM[5,17]. Compared to the previous Portuguese series, we found similar distribution of malignancies, except for breast cancer, found in about 1/3 of the cases in those series[11,12] and absent in ours. However, distinct from our study in the referred series, the time between the DM and neoplastic diagnosis was not clearly defined.

Besides, the malignancies found in our series did not differ much from the general population of the same age group in terms of the target organs.

We found that the large majority of malignancies were diagnosed simultaneously with DM, and when diagnosed later it was within the following year, again as found in the literature[4,5]. In fact, cancer associated with DM may be diagnosed before, simultaneously, or after onset of DM, with the higher risk of cancer persisting during the first year and then declining[3,4,18].

Nevertheless, this was a retrospective single-center study, with the inherent limitations, such as the small sample size, the lack of some clinical and laboratory data over the years. It should also be noted that possible sensitivity and specificity variations in laboratory data over the years could have happened, although not affecting the final results of this study.

CONCLUSIONS

This study emphasizes the association between malignant disease and DM within a short period of time around diagnosis.

According to our study, screening for malignant disease should be routinely performed in the first year after diagnosis.

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