Clinical and Experimental Rheumatology 2015; 33: 731-733.

Low prevalence of malignancy in patients with idiopathic inflammatory myopathies in Jordan

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Received on January 7, 2015; accepted in revised form on May 4, 2015.

Key words: malignancy, cancer, inflammatory myopathies, polymyositis, dermatomyositis, Jordan, Arabs

Competing interests: none declared.

ABSTRACT

Objective. *To estimate the frequency of malignancy among patients with idiopathic inflammatory myopathies (IIM) in Jordan.*

Methods. *This was a retrospective review of case records of patients with IIM in Jordan.*

Results. *We identified 94 cases of IIM, (47 polymyositis (PM) and 47 dermatomyositis (DM)). Sixty-seven (71%) were females and 27 (29%) were males. The mean age at diagnosis was 39.7± 15.7 years (range 17–72), median 40 years and the mean follow-up was 5.05±4.03 years (0.2–19). Malignancy was diagnosed in only 4 patients (4.25%) with IIM. Among patients with DM, malignancy was found in three patients (6.4%).The age-standardised rate was 2.7% (95% confidence interval: 0. 6% to 7.1%). The standardised incidence ratio was 0.998. Diagnosis of associated malignancy was made close to the time of IIM diagnosis. Two male patients had nasopharyngeal carcinoma at the ages of 51 and 59 years, while the other two were female with breast and ovarian cancer at the ages of 40 and 45 years, respectively.*

Conclusion. *Malignancy in association with IIM was found to be low in our cohort in comparison to reports from other countries. The observed number of cancer cases in this group of patients is similar to the expected number of cases that would occur in general population of Jordan. This could be related to younger age of disease onset. The benefits of long-term screening for malignancy in our population are not clear.*

Introduction

Idiopathic inflammatory myopathies (IIM) are immune mediated diseases, characterised by chronic inflammation of skeletal muscles and the skin, resulting in muscle weakness. IIM may be primary or secondary to other connective tissue diseases or it may be a paraneoplastic manifestation of malignancies. The overall risk of malignancy has been shown to be stronger with DM, ranging between 11 and 45%, than with PM ranging between 4.4 and 27% (1-10). However several reports documented lower cancer risk in patients with IIM between 1–9% (2, 4, 5, 11-14).

The link between malignancy and IIM has been confirmed in different populations. However, the variability in the strength of such association has been observed across different reports from different parts of the world. Such variability could be due to genetic factors, age differences among the different reports, selection bias or geographical factors. However, published data reported in Arabs is scarce. The available reported data are insufficient to evaluate the prevalence or types of malignancies in Arab patients. Therefore, we sought to determine the prevalence and the types of the malignancies in our patients with IIM attending the rheumatology services at the three major tertiary care centres; Jordan University Hospital (JUH) between 1996 and 2014, the Royal Medical services, and King Abdullah University Hospital

Methods

This was a retrospective review of case records of all patients with IIM attending the rheumatology services between 1996 and April 2014 at three tertiary care hospitals; Jordan University Hospital (JUH) (50 patients) the Royal Medical Services (22 patients), and the King Abdullah University Hospital in northern Jordan (22 patients). All patients were of Arab descent and all fulfilled the Bohan and Peter's criteria for a definite diagnosis of PM or DM (15). Diagnosis was made by a qualified rheumatologist at each centre. Only cases with histologically confirmed cancer made at either centres diagnosed 1–2 years before and up to 2–3 years after the diagnosis of myositis were included as cancer-associated myositis (16). Data collection at JUH started in August 2009, so all patients included after that time were followed in a prospective manner, while data on patients diagnosed prior to that at JUH and all patients from Royal Medical Services and at King Abdullah University Hospital were retrospective. Demographic and clinical data extracted from medical records including sex, age at disease onset and follow up period were

obtained. Investigation for malignancy included careful history and complete physical examination that included breast examinations. Chest radiographs were obtained in all patients. In female patients mammography was done as part of the routine testing. Ultrasound, computerised tomography (CT), and magnetic resonance imaging were done when felt appropriate. CT of the chest was done in 51% of patients as part of assessment for pulmonary involvement in patients with abnormal pulmonary function tests. Ultrasound of the pelvis screening for ovarian mass was carried out in all women over the age 30 years. Abdominal CT was performed on selected patients, while upper gastrointestinal endoscopy was done in all patients with dysphagia. Anti-P155 / 140 antibodies were not routinely tested in our patients. Data were described using means and percentages.

Results

Ninety-four patients with IIM were identified (67(71%) females and 27 (29%) males). A total 47 had DM and 47 had PM. All patients had the onset of their disease after the age of 17 years. The mean age at diagnosis of IIM was 39.7±15.7 years (median 40, range: 17–72 years). Twenty five patients (27%) were 50 years of age or older at the time of the diagnosis of myositis. The mean age for DM patients was 36.54±15.61 (range: 17–72), and for PM patients was 40±9.2 (range: 17-71). The mean follow-up was 5.05±4.03 years (range: 0.2–19). Sixty nine patients (74%) were followed up for at least 2 years following the onset of the manifestations of myositis. Muscle biopsy revealed inflammatory myositis in 70 patients, unremarkable in 8 patients, and biopsy was not done on the remaining 16 patients. Among the 94 cases of IIM, malignancy was identified in 4 patients (4.25%) at the time of the diagnosis of muscle disease. In the 4 cases, the diagnosis of the malignant tumour was made simultaneously at the time of diagnosis of myositis. The age-standardised rate was 2.7% (95% confidence interval: 0.6%–7.1%). The standardised incidence ratio (SIR) was 0.998 (95% confidence interval: 0.3–2.6) indicating that the observed number of cancer cases in this group of patients is similar to the expected number of cases that would occur in general population of Jordan. Excluding those with IIM not histologically confirmed, cancer was seen in 5.7% of patients. Nasopharyngeal carcinoma was found in 2 male patients; both had DM at the age of 59 and 51 years. Two females were diagnosed with malignancy at the time of IIM diagnosis. The first patient with PM was 45 years old when she was diagnosed with breast cancer, and the second patient with DM was 40 years old when she was diagnosed with ovarian cancer.

Table I. Comparison between current and previous studies of cancer cases in patients with IIM.

References	Number of patients		Number of CAM %		SIR	SIR	SIR
	DM	PM	DM	PM	DM/PM (IIM)	DM	PM
Current study	47	47	3 (6.4)	1 (2.0)	0.998	-	-
Hill (17)	618	914	198 (32)	137 (15)	-	3	1.3
Stockton (6)	286	419	77 (27)	71 (17)	-	7.7	2.1
So MW (2)	98	53	23 (23.)	2 (3.8)	-	14.2	1.4
Azuma K (3)	70	51	17 (24)	15 (6)	13.8		
Buchbinder (1)	85	321	36 (42)	58 (18)	2.6	6.2	2
Airio A (9)	71	175	-	-	2.1	6.5	1.0
Chen YJ (12)	1,012	643	95 (9.4)	33 (4.4)	-	5.11	2.15
Chow (24)	203	336	31 (15)	26 (7.7)	-	3.8	1.7

CAM: cancer associated myositis; DM: dermatomyositis; PM: polymyositis; SIR: standardised incidence ratio.

Discussion

Very little is known about the prevalence of malignancy in patients with IIM among the Arab population. To our knowledge this is the first report from the eastern side of the Arab world about this prevalence.

The well documented concomitant concurrence of cancer and DM/PM at the same time or within short period of diagnosis cannot be overlooked. However, the remarkable wide range of frequencies between different populations raises questions about this association. This could be due to ethnic variation, geographic factors, reporting biases due to differences between studies' methodology, patient population studied, or utilisation of extensive screening investigations for malignancies.

In this observational study we found very low occurrence of malignancy in patients with IIM, in contradistinction to the majority of previous reports from other populations (1, 4, 6, 17). Similar observation has been reported in several studies where cancer was seen in less than 10% of patients with IIM (5, 11-14). The finding of lower cancer risk in younger patients with IIM was reported in two studies (11, 18). In these studies the mean age at diagnosis of IIM were 35 and 37 years respectively; however 34% and 24% of the patients had IIM associated with other connective tissue diseases in Porkodi *et al*. and Ramirez *et al*. reports respectively. In our study the mean age at diagnosis was 39.7±15.7 years, and only two patients had associated other CTD. In a recent study from Tunisia with similar number of patients and mean age at diagnosis, malignant disease was found in 12.8% of the patients (mainly gynaecological and nasopharyngeal cancer) (19). In most studies, there was increased prevalence of cancer in patients with IIM above the age of 45 years ((3, 6, 8, 9). However because the incidence of malignant diseases increases with age in the general population, the difference in incidence between elderly patients with IIM and elderly persons in the general population may be not-significant (20). The age-standardised rate of 2.7% (95% confidence interval: 0.6% to 7.1%) and an SIR of about 1 indicates that the observed number of cancer cases in patients with IIM in Jordan is similar to the expected number of cases that would occur in general population of Jordan. This was much lower than that found in a recent report from Korea where the SIR for malignancy in patients with DM was 14.2 (95% CI

9.0–21.3) and from Japan where the SIR of malignancies in patients with IIM was 13.8 (range 9.0–21.1), while SIR between 3 and 7.7 for malignancy in patients with DM has been reported from several countries (1-3, 6, 9, 12) (Table I).

Significant excesses for ovarian cancer observed in IIM was seen in several reports (3, 5, 6, 9, 10, 21), while an increased risk of nasopharyngeal carcinoma was observed in Southeast Asian patients (7, 10, 12, 14, 22, 23). The type and site of malignancy in patients with IIM probably parallels the expected probability of that cancer in each ethnic or regional population (2). In the four patients who had cancer with IIM in this study, two had nasopharyngeal carcinoma while the other two had ovarian and breast cancer, respectively.

The temporal relationship between the occurrence of cancer and IIM has been demonstrated to be within two to three years of the diagnosis of IIM (1, 5, 6, 20). In this study malignancy was observed near the onset of IIM is consistent with such reports.

Conclusion

The previously described strong association between IIM and cancer was not confirmed in our data. Such an extremely weak association could be due to younger age group of this cohort; however inter-populations variability of disease spectrum could be a likely one. Questions still need to be answered regarding the clinical implications of such association. Based on our results and previous observations of the low occurrence of cancer in IIM, investigations aimed at early cancer detection in younger patients with IIM need further evaluation by larger studies. In patients with IIM, evaluation for cancer especially in older age group, and within few years from the time of first diagnosis, are still advisable. On the other hand, long term screening for cancer other than that, which is recommended in the general population with increasing age, cannot be addressed by this study population.

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