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Nasopharyngeal carcinoma in dermatomyositis patients: A 10-year retrospective review in Hospital Selayang, Malaysia

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ABSTRACT

Aim: The objective of our review is to investigate the association between dermatomyositis patients and nasopharyngeal carcinoma (NPC) together with the clinical presentation of the patients and their management in otorhinolaryngology.

Background: NPC is a malignant disease with good prognosis on early diagnosis. However, the relationship between the dermatomyositis and NPC and its management is not well defined.

Materials and methods: A 10-year retrospective review of case records of 21 dermatomyositis patients seen in Otorhinolaryngology Department of Hospital Selayang from January 2000 to November 2010.

Results: These patients ranged from 19 to 74 years old and a total of 8 (38%) out of 21 adults with dermatomyositis were detected to have malignancy. Five out of 8 patients had NPC (62.5%). The mean age of patients with NPC and dermatomyositis was 48 years. NPC is diagnosed in 4 out of 5 patients (80%) in the first year of diagnosis of dermatomyositis. The clinical findings of the examination of nasopharynx ranged from hyperemia to exophytic nasopharyngeal mass. Histologically, it is only related to NPC of WHO types II and III.

Conclusions: There is a strong relationship between dermatomyositis and malignancy, especially NPC. Clinicians should have a high index of suspicion for malignancy in all

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dermatomyositis patients. Rigid nasoendoscopies and biopsies, serum Epstein–Barr viral capsid IgA antibody and imaging studies are helpful in detecting NPC in dermatomyositis patients.

1. Background

Dermatomyositis is defined as an idiopathic inflammatory myopathy with clinically distinctive cutaneous manifestations.[1] However, when the symptoms are associated with malignancies, the condition is known as paraneoplastic syndrome which represents the clinical manifestation of the remote and indirect effects produced by tumor metabolites or other products.[2]

Dermatomyositis is highly associated with various types of malignancies, namely carcinoma of nasopharynx, breast, lung, colorectal, uterus and non-Hodgkin lymphoma.[3] 10–47% of dermatomyositis patients have an underlying malignancy.[4–6] Out of these, nasopharyngeal carcinoma (NPC) had been reported as the most common type of cancer related to dermatomyositis in Asia[3,4,7] where NPC is found in more than 40% of the total cases of malignancies in dermatomyositis patients.[3,4,7,8] The onset of NPC in dermatomyositis patients is usually within the first 5 years from the diagnosis of dermatomyositis.[5]

2. Aim

The objective of our review is to investigate the association between dermatomyositis patients and nasopharyngeal carcinoma (NPC) together with the clinical presentation of the patients and their management in otorhinolaryngology.

3. Materials and methods

In this 10-year retrospective study, the case records of 21 patients who were diagnosed with dermatomyositis from January 2000 until November 2010 were reviewed using the hospital's electronic medical records. All of the patients were confirmed to have dermatomyositis by physicians based on the clinical features and investigations including muscle biopsy.

The criteria for diagnosis of dermatomyositis were based on Tanimoto's classification and diagnostic criteria for polymyositis and dermatomyositis.[9] Skin lesions include heliotrope rash, Gottron's sign and erythema or purpura on extensor surfaces of the extremity joints.[9] The items included in the criteria were proximal muscle weakness, muscle grasping and spontaneous pain, non-destructive arthritis or arthralgia, elevated creatinine kinase or adolase, presence of systemic inflammatory signs, myogenic changes on electromyography, positive anti Jo-1 antibody and pathologic findings compatible with inflammatory myositis.[9] Dermatomyositis were diagnosed if patients had at least one out of three skin lesions and four out of eight other criteria items.[9]

Patients diagnosed to have dermatomyositis were referred to the otorhinolaryngology department for head and neck examination and diagnostic work up to detect head and neck malignancy.

The diagnostic work out includes thorough history taking, general examination of the ear, nose and throat followed by flexible nasopharyngolaryngoscopy and biopsy of the post nasal space of any suspicious lesion supplemented by fine needle aspiration of any cervical lymph node.

All patients who had no detectable head and neck malignancy were reviewed again by the otorhinolaryngologist particularly if the work up for any malignancy was negative and the dermatomyositis symptoms frequently relapsed, or for those who showed no improvement despite being on immunosuppressive treatment.

4. Results

A total of 21 dermatomyositis patients were reviewed from January 2001 until November 2010. There were 10 male (48%) patients and 11 female (52%) patients. The youngest patient was 19 years old and the oldest patient was 74 years old. The mean age of presentation was 43.8 years old. Eight of the dermatomyositis patients were below 40 years old (38%) and the remaining 13 were above 40 years old (62%).

Eight out of 21 patients (38%) were detected to have malignancies (breast, nasopharynx and lymphoma) and 5 out of the 8 (62.5%) had NPC. Among those who were diagnosed to have NPC, the male to female ratio was 4:1.

The mean age of the NPC patients with dermatomyositis was 55.2 years (range 39–74 years). The maximum age incidence was in the fifth decade. In our center, 8 dermatomyositis patients were below 40 years old (3 males and 5 females) and only 1 (12.5%) was related to malignancy (NPC).

Meanwhile, 7 out of 13 patients (54%) aged 40 years and above had a malignancy. There were 7 males and 6 females in this group. Out of these 7 who had a malignancy, 4 patients (31%) had NPC (1 female and 3 males), 2 patients had breast carcinoma and 1 had lymphoma (Fig. 1).

There were a total of 5 patients with nasopharyngeal carcinoma. Three were detected concurrently with the diagnosis of dermatomyositis while the other 2 patients were diagnosed during subsequent follow ups which ranged from 2 months to 38 months. Thus, the diagnosis of NPC was made in as many as 80% of the patients within the first year of the diagnosis of dermatomyositis (3 concurrently and 1 after 2 months during follow up). The fifth patient was diagnosed 4 years from onset of dermatomyositis. One of them presented with epistaxis and otitis media and another with a submandibular mass. It is

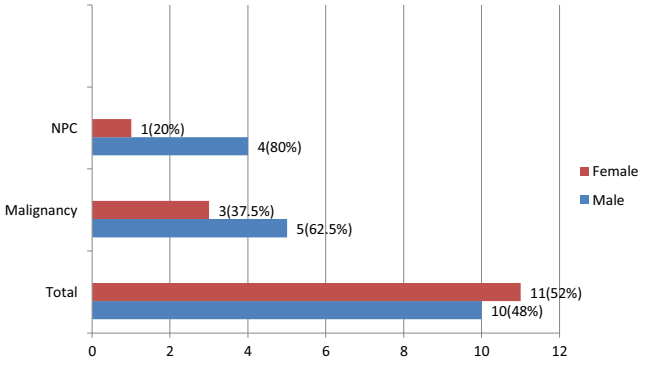

Fig. 1 – This bar graft shows the number of dermatomyositis patients with malignancies, dermatomyositis patients with nasopharyngeal carcinoma and the total number of dermatomyositis patients according to gender.

important to note that the rest of patients did not show any clinical symptoms related to NPC during their first presentation.

All patients with suspicious lesions, even without prominent masses (hyperemic area, fullness, hypertrophy, asymmetry of nasopharyngeal wall), were biopsied and three out of five biopsies were noted to be positive for malignancy. The nasopharyngeal masses of 3 patients were biopsied and two were squamous cell carcinoma, while the third one showed normal lymphoid tissue (adenoid).

One of the patients who were diagnosed concurrently with dermatomyositis had a stage T4 NPC (involving cavernous sinus). It was confirmed after a biopsy was done as the nasoendoscopy examinations showed only hyperemia of the fossa of Rosenmuller. Two patients had normal nasopharynx during their first visit but subsequently fullness of the fossa of Rosenmuller was noted in one of them, while the other developed a mass. The fourth patient had a mass at the nasopharynx during the first visit and the fifth presented with a slight fullness but no mass over the fossa of Rosenmuller. A total of 3 patients were diagnosed at stage 1 (all 3 were T1N0), one at stage 2 (T2N2) and another at stage 4(T4N0).

Three out of the 5 (60%) dermatomyositis patients with NPC had non-keratinizing differentiated squamous cell carcinoma of the nasopharynx (WHO type II). The remaining 40% (2 out of 5 patients) had non-keratinizing undifferentiated squamous cell carcinoma of the nasopharynx (WHO type III).

5. Discussion

Dermatomyositis is a paraneoplastic syndrome and it is strongly associated with different types of malignancy. The association between the myopathy with malignancy was first reported by Stertz[10] in 1916 and many centers have since reported the association of dermatomyositis and malignancy. In Malaysia, Tang and Thevarajah[3] reported in 2010 that 47.4% of dermatomyositis patients had underlying malignancy. Chan[7] reviewed the records of Singaporean dermatomyositis patients and noted that 41% of dermatomyositis patients had cancer. While in Taiwan, a cohort study done in 2010 reported that 9.4% of dermatomyositis patients had cancer.[5] In our study, 38% of the dermatomyositis patients in the present series had cancer, and this shows that the incidence of cancer in dermatomyositis patients in the South East Asia region is high.

Dermatomyositis is not cancer specific. Instead, it is associated with different types of cancer in different populations. In Asia, it is strongly associated with NPC. A study done in Singapore showed that NPC was the most common cancer associated with dermatomyositis (46.7%).[7,11] In Malaysia, a previous study done in 2010 showed similar figures (61.1%)[3] as in our study (62.5%). A study done in Guandong, China, also showed that NPC was the main type of cancer associated with dermatomyositis (51.3%).[4] However, the risk of developing a specific type of cancer associated with dermatomyositis is unequal in different populations. Hill et al.[12] reported on specific cancer types in dermatomyositis in Sweden, Denmark and Finland, where ovarian, lung and pancreatic cancers were reported as the three main types of cancers associated with dermatomyositis.[12] In Scotland, lung cancer was the most common cancer related to dermatomyositis,[6] while in Tunisia it was breast cancer.[13]

The risk of malignancy is higher in patients with aged 40 and above. In our center, only 13.0% of those below 40 years old suffered from NPC, while 31% of our patients aged 40 years and above had NPC. Zhang et al.[4] also reported that the risk of dermatomyositis patients developing cancer was higher in the older age group (7.4% in patients below 40 years old and 24.4% in patients aged 40 years and above). Stockton et al.[6] also reported a higher risk of malignancy seen in dermatomyositis patients aged between 45 and 75 years.

Male patients had stronger malignancy association compared to female patients in our population. Forty percent of males and 9.1% of females were diagnosed to have NPC. It was also shown in a study in China where men were more likely to have malignancy[4] than women (35.0% versus 17.0%), while in Singapore, it was noted that the female to male ratio of dermatomyositis (without malignancy) was 2.53:1 but the ratio was reversed when malignancy was associated with the female to male ratio which was 1:3.[11] However, reports from other centers showed inconsistent results with regards to gender predilection. In the United States,[1] Tunisia[13] and Europe[14] where NPC is less common, women are more likely to have cancer than men.

The risk of NPC is the highest during the first year from the diagnosis of dermatomyositis and remains high for the next 4 years. In our study, 4 patients with NPC were diagnosed within the first year from diagnosis of dermatomyositis. These patients accounted for 80% of the total NPC cases in dermatomyositis patients. Twenty percent of them (1 patient) was diagnosed in the fourth year. While in Singapore, Liu et al.[11] reported 7 NPC with dermatomyositis cases. Five out of 7 patients were diagnosed with malignancy within 1 year from diagnosis of dermatomyositis (71.4%) while 1 was diagnosed in the second year and another within the third year from diagnosis of dermatomyositis (14.3% each).

The onset of NPC is equivalent to the onset of other cancers, as reported by Zhang et al.[4] They reported that cancer

(all types including nasopharyngeal carcinoma) was detected in the first year after dermatomyositis was diagnosed in 83.5% of patients, 13.9% in the second year and 2.5% in the third year. Chow et al.[14] and Chen et al.[5] reported that the risk is higher in the first year and declined in subsequent years. Although the risk of malignancy in dermatomyositis patients is higher during the first 5 years, it remains elevated compared to the general population.[5] Hence, the search for malignancy should be continued lifelong for patients with dermatomyositis.

In our center, biopsies were taken from nasopharynxes which appeared suspicious (hyperemia, fullness of fossa of Rosenmuller, asymmetry or bulging of nasopharynx) even though there were no obvious or exophytic masses and definitely in patients with a mass in the nasopharynx. Sixty percent of our biopsies from nasopharynxes without prominent masses showed positive results, while 66% of our biopsies of nasopharynx masses showed malignancy. One of the patients was diagnosed with stage T4 of NPC without prominent mass in the nasopharynx. It was reported in Malaysia that blind biopsies which had been taken in 10 patients without obvious masses and one with a mass resulted in 7 out of 11 found to have NPC.[3] Therefore, biopsy should be considered in all dermatomyositis patients even though there is no lesion seen.

Team approach in managing dermatomyositis can lead to an early detection of malignancy. In this study, 3 out of 5 patients (60%) were diagnosed with T1, one patient (20%) with T2 and another with T4 stage. Four patients (80%) did not have any lymph nodes at diagnosis and one patient had N1 during the diagnosis of NPC. In Tunisia, nasopharyngeal carcinoma was detected at stage T3–4 in 7 cases (87.5%) and stage N2–3 in 5 patients (62.5%).[13]

From this study, undifferentiated and non-keratinizing squamous cell carcinoma showed a strong relationship with dermatomyositis compared to keratinizing well differentiated squamous cell carcinoma. Histopathological reports of dermatomyositis patients with NPC showed 2 patients with WHO type III (40%) and 3 patients with WHO type II (60%). None of the patients had WHO type I squamous cell carcinoma. These 2 types of carcinoma are related to the Epstein–Barr virus[15] and in China it was reported that serum Epstein–Barr viral capsid antigen (VCA) IgA antibody was positive in all 59 patients with NPC, ranging from 1:20 to 1:320.[4]

The limitations of this study include a relatively small sample size and data collection limited to case records, as it was done retrospectively. The investigation and the follow-up of the patients were also not standardized. Serum Epstein–Barr viral capsid IgA antibody was not measured during the screening for malignancies in our patients.

We recommend that all dermatomyositis patients be seen early by an otorhinolaryngologist and have regular follow up within the first five years. Serum Epstein–Barr viral capsid IgA antibody screening might be helpful in early detection of malignancy but rigid nasoendoscopy and biopsy is recommended in all patients. The screening of dermatomyositis patients for malignancy could be done using a PET scan when it is more affordable and readily available. Future research on using PET scan as a diagnostic tool for malignancy in dermatomyositis may be considered then.

6. Conclusions

There is a strong relationship between dermatomyositis and malignancy. NPC is more common in Asia. Therefore, dermatomyositis is more commonly related to nasopharyngeal carcinoma in Asia. Clinicians should have a high index of suspicion for malignancy in all dermatomyositis patients. Rigid nasoendoscopies and biopsies, serum Epstein–Barr viral capsid IgA antibody and imaging studies have been proven to be helpful in detecting NPC in dermatomyositis patients. Subsequent follow up should be done monthly for the first 3 months, then every 3 months for the first two years and every six months for five years.

Conflict of interest

None declared.

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None declared.

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