Unusual presentation of more common disease/injury

Dermatomyositis and chest radiography leading to the diagnosis of lung cancer and subsequent confusions in staging due to the presence of tuberculosis

Swaroop Revannasiddaiah,¹ Manoj Kumar Gupta,¹ Madhup Rastogi,¹ Avinash Arjun Rao Kesari,² Rajeev Kumar Seam,¹ Manish Gupta,¹ Suneel Chauhan,³ Irappa Madabhavi⁴

¹Radiation Therapy and Oncology Department, Regional Cancer Center, Indira Gandhi Medical College, Shimla, India;

²Radiodiagnosis Department, King Edward Memorial Hospital, GSMC, Mumbai, India;

³Nuclear Medicine Department, Regional Cancer Centre, Indira Gandhi Medical College, Shimla, India;

⁴Internal Medicine Department, Indira Gandhi Medical College, Shimla, India

Correspondence to Dr Swaroop Revannasiddaiah, swarooptheone@gmail.com

Summary

This clinical scenario describes dermatomyositis as a presenting feature of carcinoma of the lung. However, the coincident existence of tuberculosis in the opposite lung gave rise to a false impression of contralateral lung metastasis and hence confusions with regard to staging ensued, which were clarified after further investigation confirmed a unilateral lung adenocarcinoma and contralateral tuberculosis. The patient was initiated on oral antiepidermal growth factor receptor therapy with erlotinib, as well as on multi-drug therapy for tuberculosis. This report intends to illustrate that paraneoplastic syndromes such as dermatomyositis can be the presenting feature of lung cancer, and also that the co-incident presence of carcinoma and tuberculosis can cause confusions with regard to staging and management.

BACKGROUND

Dermatomyositis could be a heralding feature of underlying malignancy, more so in the case of the older. The presence of co-existing lung carcinoma and tuberculosis is not an uncommon occurrence, especially in areas with a high prevalence of tuberculosis. This clinical scenario, where in the described patient harboured a right-sided bronchial adenocarcinoma, was provisionally staged-IV in view of suspected contralateral pulmonary involvement. However, in the course of the investigation, it was realised that the contralateral space-occupying lesion was indeed due to tuberculosis, and the patient was then staged-IIA. Since patient management largely depends upon the stage of the malignancy, factors confounding the process of staging can indeed confound the process of decision making.

CASE PRESENTATION

An older gentleman aged 74 years presented with erythematous patches over the dorsal aspects of the hands (figure 1), bilateral weakness in the limbs lasting 2 weeks, dry cough and low-grade fever lasting for about a year.

The patient would experience dyspnoea after few min of walking even on level ground (grade 3 as per the MRC Breathlessness Scale).¹ The history was negative for any previously diagnosed cardio-pulmonary disorders, chronic infectious diseases or neurological disorders. The patient denied history of ever smoking.

Patches of erythema over the dorsal aspect of the hands were noted to be co-existing (and coalescing) with reddish, keratotic macules (Gottron's sign) over the extensor surface of the finger joints (figure 2).

A symmetric proximal muscular weakness was noted to be involving the limbs and the trunk. In addition, there was tenderness on palpation over the deltoids, the trapezius and the thigh muscles.

INVESTIGATIONS

The measured temperature at presentation was 99.2°F (axillary). The complete blood counts and differential counts were unremarkable; however the erythrocyte sedimentation rate was elevated-28 mm in the 1st h, by the Westergren method. Electromyography demonstrated activity in the form of spontaneous fibrillations, positive sharp waves and complex repetitive discharges. Serum creatine-kinase levels were elevated at 1224 U/l (normal upper limit: <400 U/l) and serum aldolase levels were elevated at 15.6 U/l (normal upper limit: <7.6 U/l).

With the above findings, the patient fulfilled the Tanimoto criteria for dermatomyositis.² Even as further evaluation to rule out an underlying malignant process was being planned, a chest-radiograph which was in fact obtained as part of evaluation of chronic cough demonstrated the presence of mass lesions in both the lungs (figure 2). A fibre-optic bronchoscopy revealed an external indentation over the right middle bronchus. There was a fleshy growth in the left main bronchus and histopathology yielded an adenocarcinoma which was positive for the epidermal growth factor receptor mutation (EGFR) mutation.

Given the presence of bilateral pulmonary mass lesions, the patient was provisionally staged-IV due to a presumed 'M_{1a}' status (since the presence of separate 'tumour nodule' in the contralateral lung is classified as M_{1a} as per the seventh edition of the AJCC-TNM staging system).³

Figure 1 Confluent erythematous patches over the dorsum of the hand, continuous with, and extending beyond the Gottron's patches (arrows).

Figure 2 Chest radiograph showing intrapulmonary space occupying lesions bilaterally.

However, a CT scan revealed differences in the characteristics of the lesions in the two lungs. While the lesion in the left lung appeared to be solid and heterogeneously enhancing on contrast (figure 3A), the lesion in the right lung appeared to be cystic (figure 3B). While CT-guided needle aspiration cytology from the left-sided lung mass was positive for adenocarcinoma, the aspirate from the right-sided lung lesion was clear, straw coloured and negative

for malignancy on cytology. A PCR test performed on the fluid aspirate from the right-sided lung lesion was positive for *Mycobacterium tuberculosis*.

The patient was hence finally assigned the diagnosis as 'stage T_{2b}N₀M₀ (stage IIA) adenocarcinoma of the left lung with right pulmonary tuberculosis'.

TREATMENT

The patient's advanced age, myopathy, co-existing tuberculosis and a poor performance status of 50% (as per the Karnofsky Performance Status Scale) precluded any surgical intervention. Given that the patient's tumour was EGFR mutated, the patient was initiated on oral anti-EGFR therapy in the form of erlotinib at a dose of 200 mg once a day. A pulmonology consultation was obtained for the initiation of a multi-drug regimen for tuberculosis. The initiated multi-drug regimen consisted of isoniazid, rifampicin, pyrazinamide and ethambutol administered as per protocols of the Revised National Tuberculosis Control Programme of India.^{4 5}

OUTCOME AND FOLLOW-UP

As on the date of this writing, the patient has tolerated 10 weeks of concurrent administration of erlotinib and a multi-drug antitubercular regimen. The patient reported mild pruritus and self-limiting rashes, which being known adverse effects of anti-EGFR therapies such as erlotinib have been symptomatically managed with antihistaminics.^{6 7}

The patient has enjoyed a better quality of life and the dyspnoea has improved to MRC grade-II. There has been an improvement in performance status, largely owing to an improvement in the proximal myopathy. The dermatological manifestations however, have not demonstrated any major change, which could be possibly reasoned to

Figure 3 CT image reconstruction (lung window) showing the nature of the right lung lesion to be cystic (A); and left lung lesion measuring around 5.2×3.3 cm as solid and contrast-enhancing on soft-tissue window (B).

the known potential for erlotinib by itself to promote dermatitis.

DISCUSSION

Dermatomyositis is an immune-mediated microangiopathy affecting the capillary endothelium of muscle and skin tissue. Depositions of membrane-attack-complexes in the capillary endothelium are postulated to be the cause of findings such as perifascicular atrophy in the skeletal muscles, and basal cell vacuolar degeneration in the epidermis.⁸

In the case of the patient described in this article, the diagnosis of dermatomyositis was rather straightforward since the patient qualified two of three skin lesion criteria and four other criteria of the criteria by Tanimoto *et al.*² The Tanimoto criteria were formulated in 1995 and are currently widely accepted. These criteria for establishing a diagnosis of dermatomyositis incorporate three skin lesions (Gottron's sign, erythema over the extensor surface of joints and the heliotrope) of which at least one must be fulfilled; and eight non-skin factors (proximal muscle weakness, elevated serum creatine-kinase or aldolase level, muscular pain on grasping or spontaneous pain, electromyography suggestive of inflammatory myopathy, positive anti-Jo-1 antibody test, non-destructive arthritis or arthralgia, systemic signs of inflammation and pathological findings of inflammatory myositis) of which at least four must be fulfilled. This system has a sensitivity of 94.1% and a specificity of 95.2%, when the minimal numbers of criteria are fulfilled. The sensitivity and specificity may increase if greater numbers of criteria are fulfilled.²

The earlier set of criteria (which were in use before the adoption of the Tanimoto criteria) were formulated by Bohan and Peter in 1975.^{9–10} The Bohan and Peter system included five criteria (progressive proximal symmetrical weakness, elevated muscle enzyme levels, electromyogram abnormalities, abnormal muscle biopsy and the presence of cutaneous lesions). As per this system, the diagnosis of dermatomyositis is 'definite', 'probable' and 'possible' when the presence of skin lesions are associated with three, two and one, of the other remaining criteria. Though the Bohan and Peter system was highly sensitive,

it had a high false-positivity rate too.¹¹ For the record, the patient under discussion would also fulfil the older Bohan and Peter system as a 'definite' case of dermatomyositis.

The presence of dermatomyositis is associated with an increased likelihood of the presence of an underlying malignancy, a likelihood of which increases with advancing age at presentation. The co-existing malignancy can often be detected at the time of diagnosis of dermatomyositis. However, even if no malignancy is detected at the time of presentation, there is a possibility of manifestation of a detectable malignancy even as late as 5 years after the diagnosis of dermatomyositis.¹²

The most common malignancies associated with dermatomyositis are ovarian carcinoma, lung carcinoma, gastro-intestinal malignancies, nasopharyngeal carcinoma (more so in Asian patients), haematological malignancies, etc.^{13–16} Dermatomyositis associated with an underlying malignancy confers a much worse prognosis when compared with dermatomyositis which is idiopathic (with no underlying malignancy). This is attributable to an increased mortality risk from the underlying malignancy. Treatment of the underlying malignancy is of utmost importance in improving the cancer associated prognosis. In addition, treatment directed at the underlying malignancy can be expected to alleviate the dermatomyositis too.¹⁷

An exhaustive 'search' for an underlying malignancy is crucial in every patient after a diagnosis of dermatomyositis. A thorough examination (clinical and radiological) can more often than not detect an underlying malignancy when present. Tumour markers (such as CA-125, CEA, etc.) may also provide important diagnostic clues. The use of positron emission tomography (PET) scan with the 18F-fluorodeoxyglucose (FDG-PET), or a fusion FDG-PET/CT scan can be expected to have a high sensitivity and a high negative predictive value in evaluating for malignancies of unknown origin.^{18–20}

In the patient under discussion, the search for an underlying malignancy was not difficult, since a chest-radiograph had demonstrated pulmonary malignancy. However, the presence of bilateral lung shadows had caused confusions in the staging of the left bronchial adenocarcinoma. Since

further investigation had proven the contralateral mass to be cystic and tubercular in nature, the patient had to be initiated on antitubercular treatment, for which the patient was referred to the pulmonology department, who initiated multi-drug therapy as per the guidelines of the revised national tuberculosis control programme, which is the national standard for management of tuberculosis in India.^{4 5}

The co-existence of tuberculosis and lung cancer is not uncommon. Tuberculosis is an independent predictor for lung cancer risk. Both tuberculosis and lung cancer can be silent and innocuous in the early stages and hence, pulmonary lesions from either of these diseases may progress to a considerable size before becoming clinically apparent.^{21–24}

Studies have shown that the association between tuberculosis and lung cancer as only significant with adenocarcinomas, and not squamous or small cell histologies.²⁵ This has been attributed to the gene remodelling effects of *Mycobacterium* since studies have shown that pulmonary adenocarcinoma associated with tuberculosis possess a higher probability of having EGFR mutations, especially the exon-19 deletions.²⁶

In the patient under discussion, though the stage of the left lung adenocarcinoma was amenable for surgical resection, the poor performance status had casted doubts about tolerability of surgery. Since recent data support the use of anti-EGFR oral therapy with erlotinib in patients with EGFR mutated adenocarcinomas, he was initiated on oral erlotinib, which is easily more convenient and tolerable compared with conventional intravenous chemotherapy.^{27 28}

The patient tolerated single agent therapy with oral erlotinib with little and easily manageable adverse effects. The intended end points with regard to an intended improvement in quality of life, respiratory status and functional status have been achieved at the time of this writing.

Due considerations should also be given to the potential benefit the patient may have had from the antitubercular multi-drug regimen which too, was initiated concurrently with erlotinib. This report also documents the first ever case of published literature which demonstrated the safety and tolerability of the concurrent administration of an anti-EGFR therapy (erlotinib) together with a multi-drug antitubercular regimen (with isoniazid, pyrazinamide, ethambutol and rifampicin).

Learning points

- ▶ The diagnosis of dermatomyositis warrants a search for an underlying malignancy, especially in the older.
- ▶ The presence of tuberculosis coincident with pulmonary carcinoma can cause confusions with regard to staging, and also may complicate decision-making with regard to treatment.
- ▶ Oral erlotinib appears to be safe when given concurrently with an antitubercular multi-drug regimen consisting of isoniazid, pyrazinamide, rifampicin and ethambutol.

Competing interests None.

Patient consent Obtained.

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