CASE REPORT

Recurrent metastatic breast cancer presenting with paraneoplastic scleroderma

Timothy David Reynolds, Sally Elizabeth Knights

Yeovil District Hospital, Yeovil, UK

Correspondence to
Dr Timothy David Reynolds,
reynoldstd@doctors.org.uk

Accepted 11 February 2014

SUMMARY

A 44-year-old woman presented to the rheumatology clinic with a 5-month history of stiffness and tightness of the skin of the distal fingers, together with pruritus and skin changes throughout the limbs and chest. She had also developed Raynaud's phenomenon (during the summer months), fatigue and abdominal discomfort with early satiety. She had a history of adenocarcinoma of the left breast and had undergone a wide local excision and axillary node clearance 11 years earlier with adjuvant chemotherapy and hormone therapy to which she had responded well. She was found to have sclerodactyly with skin thickening over the knees, upper arms, face and chest wall together with nodularity at the scar site and distortion of the left breast. Subsequent investigations revealed recurrent metastatic breast cancer with paraneoplastic scleroderma. We explore this interesting case and review our current understanding of paraneoplastic scleroderma.

BACKGROUND

We live in an ageing population and unfortunately new diagnoses of malignancies are a common part of 21st century medicine. It is important that we recognise that a significant proportion of newly diagnosed cancers present atypically.

There are a large number of different paraneoplastic phenomena that have been described within the medical literature that can mimic other conditions but often only improve on treatment of the underlying malignancy or any common aetiological factors.

Rheumatological manifestations of different malignancies are recognised (especially inflammatory myopathies) and can have a wide variety of different features. In addition to paraneoplastic myopathies, there are also reports of vasculitis, inflammatory arthritis, lupus and scleroderma-like syndromes associated with malignancy.

CASE PRESENTATION

A 44-year-old woman was referred to the rheumatology clinic with a 5-month history of stiffness and tightness of the skin of the fingers, particularly over the distal aspects. She had also noticed generalised tenderness and pruritus affecting the skin throughout the limbs and trunk.

She had experienced recurrent Raynaud's phenomenon (even during the summer months), coryzal symptoms and abdominal discomfort with early satiety. She had also developed considerable fatigue, making it very difficult for her to look after her two young children.

She had a history of a high grade infiltrating ductal carcinoma of her left breast (oestrogen receptor positive, progesterone receptor negative) that spread to three of 13 retrieved lymph nodes. This was diagnosed 11 years prior to her presentation to our clinic and she had been treated with a wide local excision and axillary node clearance alongside adjuvant Zoladex, tamoxifen and chemotherapy consisting of six cycles of 5-fluorouracil, epirubicin and cyclophosphamide (FEC regimen). She had responded well to her treatment and was undergoing two yearly follow-up mammography.

On further questioning, she had noticed some thickening of the skin, together with nodularity around the scar tissue at the site of her previous breast surgery.

On examination, there was sclerodactyly with fixed flexion of the proximal interphalangeal joints. There was also skin thickening over the knees, upper arms and face with a solitary telangiectasis on the face. Breast examination revealed nodularity at the scar site on the left breast with some distortion of the overlying skin together with sclerodermatous changes of the skin over the chest wall.

The liver edge was just palpable on abdominal examination but there was no obvious palpable lymphadenopathy.

INVESTIGATIONS

Her blood tests revealed a mild normocytic anaemia (haemoglobin 111 g/L) but an otherwise normal full blood count, thyroid function and haematinics. Renal and liver function tests were normal. Immunoglobulin levels, calcium and creatine phosphokinase levels were also unremarkable. Her erythrocyte sedimentation rate was elevated at 37 mm/h but C reactive protein level was normal (8 mg/L). Serology for antinuclear antibody and extractable nuclear antigens was negative. She was subsequently found to have an elevated carcinoma antigen 15-3 level of 69.8 units/mL but a normal carcinoma antigen 125 level (35 units/mL).

Plain film imaging of the hands revealed bone resorption of the terminal tufts of the distal phalanges (figure 1).

She underwent repeat mammography that demonstrated some irregular nodularity in the deep lateral and central left breast together with thickening of the skin secondary to scleroderma (figure 2).

CT of the chest, abdomen and pelvis revealed bilobar hepatic metastases (figure 3) with para-aortic and mesenteric deposits together with bone metastases in the right hemipelvis and a complex

CrossMark

To cite: Reynolds TD, Knights SE. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2014-203575

Figure 1 Plain film radiograph of the hands.

Figure 2 Mammography of the left breast.

Figure 3 CT scan of the abdomen.

right ovarian mass (likely to be a Krukenberg tumour that had spread from the breast).

She underwent a core biopsy of her left breast under ultrasound guidance that revealed a grade 2 invasive ductal carcinoma (oestrogen receptor positive, progesterone receptor negative).

DIFFERENTIAL DIAGNOSIS

The clinical features demonstrated by this patient were in keeping with a connective tissue disease such as systemic sclerosis. Nonetheless, in view of the rapid progression of symptoms together with the history of breast cancer, we felt that it was important to exclude paraneoplastic scleroderma.

TREATMENT

She was started on low-dose oral steroids (10 mg prednisolone daily) while her subsequent investigations took place. She was later started on docetaxel chemotherapy for recurrent metastatic breast cancer and until now has received two cycles.

OUTCOME AND FOLLOW-UP

Following the first cycle of chemotherapy, there was a noticeable improvement in skin thickening and no evidence of renal crisis or pulmonary disease/pulmonary arterial hypertension. An interval CT scan and repeat tumour markers are planned before the fourth cycle of chemotherapy.

DISCUSSION

There is a recognised association between malignancy and scleroderma. It has been noted that certain malignancies occur more commonly among patients with systemic sclerosis. For example, longstanding oesophageal dysmotility and reflux oesophagitis predispose the patient to oesophageal carcinoma. Longstanding interstitial lung disease (that can be a feature of systemic sclerosis) is likely to increase the likelihood of developing bronchial carcinomas. Furthermore, the use of immunosuppressive treatments in patients with scleroderma may also increase the likelihood of subsequent development of certain malignancies.

However, in addition to patients with an existing diagnosis of scleroderma who later develop malignancies, there are reports of scleroderma occurring as a discrete entity that arises secondary to (or alongside) an underlying malignancy. There are reports of paraneoplastic scleroderma developing in association

with T-cell lymphoma,¹ gastric carcinoma,² malignant melanoma as well as several other primary sites that have been described in the literature.^{3 4}

Another consideration is that some medical treatments and interventions can be associated with skin thickening and fibrosis. This may have been particularly relevant in our patient if she had been treated with bleomycin when she was diagnosed with breast cancer in the past (however, this was not part of her chemotherapy regimen).⁵ It is also not uncommon to see localised skin thickening following radiotherapy (but she did not undergo radiotherapy as part of her treatment regimen either).

Interestingly, there are case reports of patients developing scleroderma-like skin changes following treatment with docetaxel.⁶ These reports describe increasing subcutaneous oedema and skin tightness, particularly of the lower limbs with normal autoantibody levels and capillaroscopy findings but biopsy results in keeping with scleroderma. These changes arose during treatment with docetaxel but then resolved on discontinuation, without progression to overt fibrosis of the skin.⁶ Nonetheless, the patient described in this article has continued to improve on docetaxel treatment until now.

The management of paraneoplastic scleroderma should evidently centre on the treatment of the underlying malignancy. Other symptomatic measures such as emollients, anti-inflammatories and antihistamines (if there is significant pruritus) can be useful.

Steroid use should be approached with caution due to the increased risk of precipitating renal crisis (so chemotherapy regimens containing significant doses of steroids need to take this into account).

The body of literature regarding how to differentiate paraneoplastic scleroderma from the more common forms of scleroderma/systemic sclerosis is somewhat limited. It would appear that the levels of conventional markers such as antinuclear antibody, anticentromere and antitopoisomerase I (anti-Scl70) are often not significantly elevated among patients with paraneoplastic scleroderma.⁴

There does, however, appear to be a correlation between rapidly progressive scleroderma, the new onset of malignancy and the presence of RNA polymerase III autoantibodies.⁷ The exact role of these antibodies in the pathogenesis of disease is not yet clear; however, Shah *et al* highlighted a case series of six patients, all of whom were diagnosed in close temporal proximity with scleroderma and a new malignancy (lung cancer, ovarian cancer, non-Hodgkins lymphoma and 3 patients with breast cancer) within the period of 1–2 years who all had elevated levels of RNA polymerase III antibodies. They went on to find RNA polymerase III staining patterns in four of five cancer pathology specimens removed from the patients within this group. They hypothesised that the RNA polymerase III antigen may develop in the malignant cells and provoke an immune

reaction that subsequently leads to the development of scleroderma.⁷

Nonetheless, in any patient with a rapid onset of scleroderma-like features, especially if they extend into the neck and trunk (beyond the distal manifestations that would typically be present in limited cutaneous systemic sclerosis) that are associated with contractures, we should be suspicious of an underlying malignancy. This is particularly relevant in those over 50 years of age, with constitutional symptoms (night sweats, fevers and weight loss) or significant risk factors for malignancy.

Learning points

- ▶ We live in an ageing population and the diagnosis of cancer is becoming an all too frequent part of our lives making it essential that we can recognise atypical presentations.
- ▶ There is a recognised association between scleroderma and malignancy, so it is important not to delay investigation for an underlying malignancy in high-risk patients.
- ▶ Consider paraneoplastic scleroderma in
 - Patients with rapidly progressive scleroderma-like features (especially if this extends beyond the distal extremities).
 - Patients with constitutional symptoms/risk factors for malignancy.
 - Those with RNA polymerase III autoantibodies (although how extensively we should screen this subgroup of patients for malignancies is not yet clear).

Contributors TDR followed up the case and was involved in writing the case report. SEK reviewed the manuscript and made changes.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Hasegawa M, Sato S, Sakai H, *et al*. Systemic sclerosis revealing T-cell lymphoma. *Dermatology* 1999;198:75–8.
- 2 Matsuta M, Chiba C, Akasaka T, *et al*. A case of systemic sclerosis associated with gastric cancer. *J Dermatol* 1999;26:611–14.
- 3 Thoenke A, Schmid HP, Figl R, *et al*. Jo-1 positive paraneoplastic systemic sclerosis in a patient with metastatic melanoma. *Eur J Dermatol* 2006;16:428–30.
- 4 Racanelli V, Prete M, Minoia C, *et al*. Rheumatic disorders as paraneoplastic syndromes. *Autoimmun Rev* 2008;7:352–8.
- 5 Finch WR, Rodnan GP, Buckingham RB, *et al*. Bleomycin-induced scleroderma. *J Rheumatol* 1980;7:651–9.
- 6 Battafarano DF, Zimmerman GC, Older SA, *et al*. Docetaxel (Taxotere) associated scleroderma-like changes of the lower extremities. A report of three cases. *Cancer* 1995;76:110–15.
- 7 Shah AA, Rosen A, Hummers L, *et al*. Close temporal relationship between onset of cancer and scleroderma in patients with RNA polymerase I/III antibodies. *Arthritis Rheum* 2010;62:2787–95.

Copyright 2014 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow