BRITISH JOURNAL OF HOSPITAL MEDICINE

CASE REPORT

A case of rapidly progressive diffuse scleroderma following treated cervical cancer

Liyang Pan[1]

Valeriya Kopanitsa[2]

Elliott Lever[1]

Jessica Manson[1]

Author details can be found at the end of this article

Correspondence to:
Jessica Manson;
Jessica.Manson@nhs.net

How to cite this article:
Pan L, Kopanitsa V, Lever E, Manson J. A case of rapidly progressive diffuse scleroderma following treated cervical cancer. Br J Hosp Med. 2021. https://doi.org/10.12968/hmed.2021.0221

Introduction

A 46-year-old woman presented to the acute medical take with rectal bleeding and was noted to have features in keeping with systemic sclerosis. The patient had recently been treated for cervical cancer with radiotherapy and chemotherapy and had noticed changes in her appearance over a 3-month period. There is limited literature associating cervical

Case report

A 46-year-old woman presented with rectal bleeding to the emergency department. On questioning, she described a 4-month history of progressive swelling and tightness of her fingers, face, abdomen and limbs. For several months there had been ulceration of the right index and middle fingers, as well as Raynaud's phenomenon for the past 2 years (Figure 1). She reported no weight loss, dysphagia, abdominal pain, breathlessness, or coughing.

Past medical history was significant for squamous cell carcinoma of the cervix (FIGO stage IIb) diagnosed 2 years ago and treated with radical chemoradiotherapy (cisplatin and brachytherapy) with curative intent. She had been in remission for 2 years; a magnetic resonance imaging scan of the cervix 2 months before this presentation showed no residual disease but showed features of radiation proctitis.

There was no family history of systemic sclerosis or rheumatic conditions in the family. She worked in the laundry department of a hotel.

On examination, she had diffuse subcutaneous oedema of the limbs, especially in the upper abdomen, and ascites. Telangiectasia were noticeable on her face and her mouth opening was reduced to two finger breadths. Skin on the elbows was notably 'waxy' in appearance (Figure 2). Calcinosis was not evident. Observations were within normal limits.

Her haemoglobin level was 66 g/litre on admission (from 104 g/litre 2 months earlier). Flexible sigmoidoscopy showed radiation proctopathy. Oesophagogastroduodenoscopy did not show any oesophageal dysmotility.

Blood tests showed antinuclear antibodies positive 1:1280 speckled, Ro52 and RNAP III weakly positive (1:155).

Her lung function tests were normal: forced expiratory volume in the first second (FEV_1) was 75% of predicted, and FEV_1/forced vital capacity ratio was 78%. Carbon monoxide transfer coefficient was 83% predicted. A high-resolution computed tomography showed small bilateral pleural effusions with some subsegmental collapse and ground glass opacification in the adjacent lower lobes. There was a small pericardial effusion, a dilated lower thoracic oesophagus, and large volume ascites.

Echocardiogram demonstrated a mild pericardial effusion (<1 cm). Her N-terminal-pro hormone brain natriuretic peptide level was moderately elevated at 594 ng/litre, her troponin T level was mildly raised at 36 ng/litre (reference range 0–14 ng/litre) and her creatine kinase level was 154 IU/litre.

An ascitic tap was performed which had a serum:ascites albumin gradient of 6. Cytology showed inflammatory cells. No malignant cells were seen. A positron emission tomography computed tomography was performed which did not identify any fluorodeoxyglucose avid recurrence or metastasis.

She was diagnosed with rapidly progressive scleroderma. She responded well to 5 days of continuous intravenous iloprost infusion, and was started on mycophenolate mofetil 2000 mg/day.

She died at home 2 months later with a certified cause of death of COVID-19.

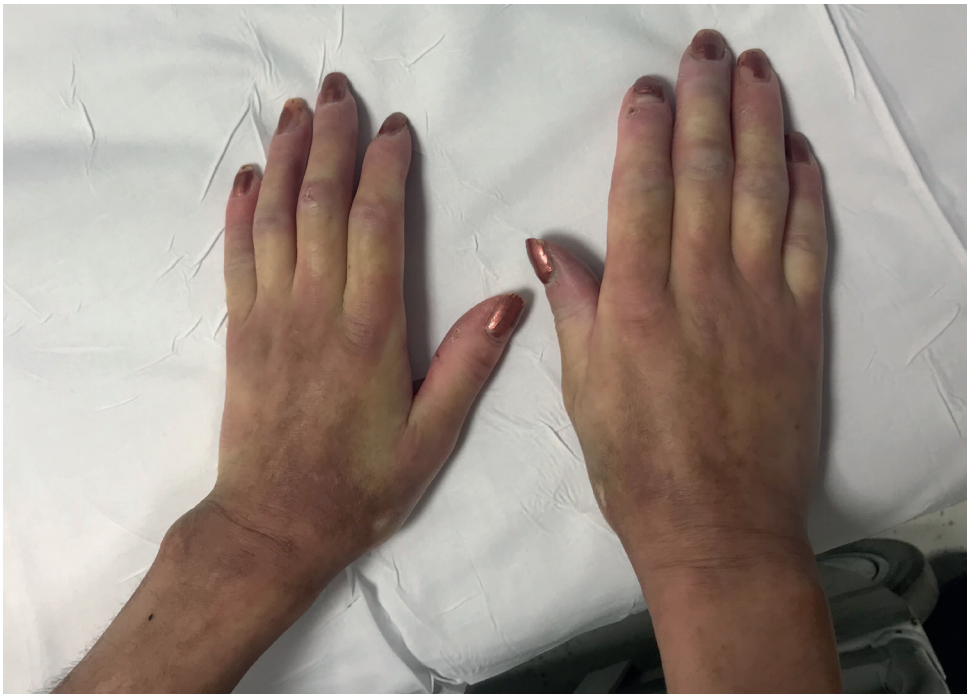

Figure 1. Photograph of the hands showing ulceration of left third digit and right index finger, with bluish discolouration of the skin and sclerodactyly.

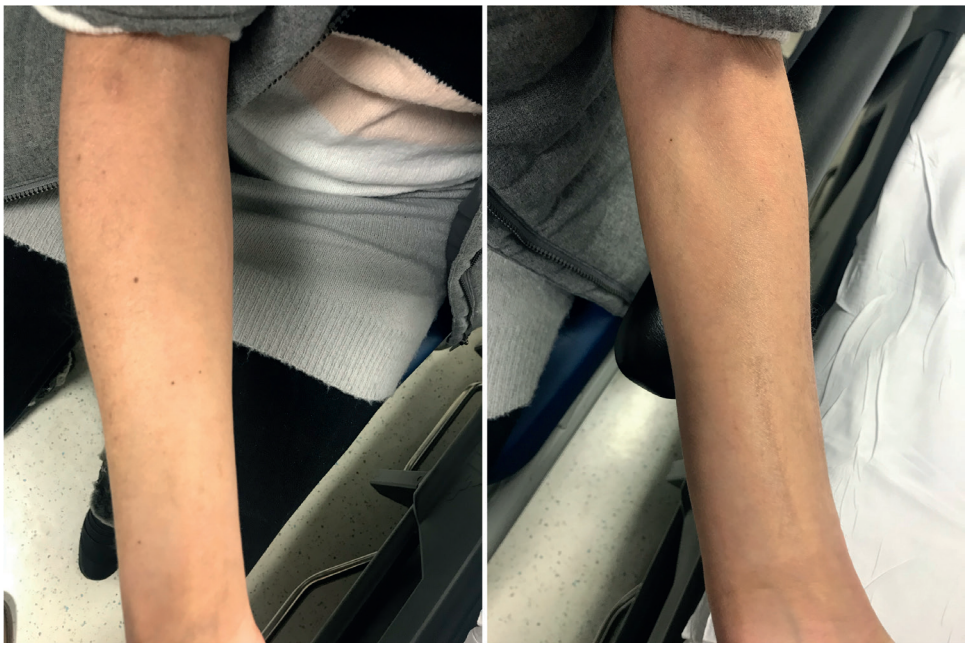

Figure 2. Patient's right and left arms, showing waxiness of the skin.

cancer and cisplatin chemotherapy before scleroderma developing. Whether this is a paraneoplastic phenomenon or a chemotherapy-related event remains unclear.

Discussion

The diagnosis of systemic sclerosis seems to be temporally associated with a diagnosis of malignancy (Olesen et al, 2010). This is associated with positive antibodies to RNAPIII, RNPC3 (Shah et al, 2017), as well as antinuclear antibodies positivity with negative anti-topoisomerase I (Topo), and positive anti-centromere (CENP) and anti-RNAPIII antibodies (Shah et al, 2015). RNAP III has the strongest link with developing cancer in systemic

Learning points

- There is a relationship between scleroderma and cervical cancer risk.
- RNAP III has the strongest link with cancer.
- Chemotherapy has been implicated in the development of scleroderma but the evidence is limited.

sclerosis patients, with a 5-fold increase in cancer diagnosis within 2 years of scleroderma onset (Shah et al, 2015). There are no studies that have investigated the development of scleroderma in RNAPIII positive cancer patients.

There are various possible pathophysiological explanations for the association of systemic sclerosis and cancer, such as chronic inflammation, fibrosis, epigenetic changes, aberrant signal transduction pathways, as well as chemotherapy for cancer triggering autoimmunity (Maria et al, 2019).

Scleroderma does seem to be associated with cervical cancer (Nevskaya et al, 2013). Patients with systemic sclerosis seem to have greater incidences of cervical dysplasia (Bernatsky et al, 2008) and high-risk and multi-genotype herpes papillomavirus infection (Martin et al, 2014), although herpes papillomavirus prevalence itself was not different.

There are only a small number of reports of chemotherapy-related systemic sclerosis. Scleroderma is often seen as a paraneoplastic disease in this patient subgroup. It is postulated that chemotherapy could have a direct effect on body tissues. There are fewer than twenty cases of systemic sclerosis-like conditions in patients treated with cisplatin or paclitaxel and taxols may affect tumour necrosis factor alpha (TNFα) and IL-6 at the tissue level. Other drugs implicated in the development of scleroderma include polyvinyl chloride, bleomycin, valproate and cocaine. The strongest association with scleroderma is with breast and lung cancer. Lung cancer is also increased in patients who are anticentromere positive.

The differential for skin thickening is important including sclerodema, scleromyxoedema, morphoea and nephrogenic systemic fibrosis.

In this case the progression was rapid and should highlight to the reader to the important connection between scleroderma and cancer.

Author details

[1]Rheumatology Department, University College London Hospital, London, UK

[2]University College London Medical School, London, UK

References

Bernatsky S, Hudson M, Pope J et al. Reports of abnormal cervical cancer screening tests in systemic sclerosis. Rheumatology. 2008;48(2):149–151. https://doi.org/10.1093/rheumatology/ken442

Maria ATJ, Partouche L, Goulabchand R et al. Intriguing relationships between cancer and systemic sclerosis: role of the immune system and other contributors. Front Immunol. 2019. https://doi.org/10.3389/fimmu.2018.03112

Martin M, Mougin C, Prétet J-L et al. Screening of human papillomavirus infection in women with systemic sclerosis. Clin Exp Rheumatol. 2014;32(6 Suppl 86)

Nevskaya T, Chandran S, Roos AM et al. Epidemiology of cancer in systemic sclerosis—systematic review and meta-analysis of cancer incidence, predictors and mortality. Open J Rheumatol Autoimmune Dis. 2013;3(4):231–245. https://doi.org/10.4236/ojra.2013.34037

Olesen AB, Svaerke C, Farkas DK et al. Systemic sclerosis and the risk of cancer: a nationwide population-based cohort study. Brit J Dermatol. 2010;163(4):800–806. https://doi.org/10.1111/j.1365-2133.2010.09861.x

Shah AA, Hummers LK, Casciola-Rosen L et al. Examination of autoantibody status and clinical features associated with cancer risk and cancer-associated scleroderma. Arthritis Rheumatol. 2015;67(4):1053–1061. https://doi.org/10.1002/art.39022

Shah AA, Xu G, Rosen A et al. Brief report: anti–RNPC-3 antibodies as a marker of cancer-associated scleroderma. Arthritis Rheumatol. 2017;69(6):1306–1312. https://doi.org/10.1002/art.40065