CASE REPORT

Recurrent spontaneous subcutaneous emphysema in a patient with rheumatoid arthritis

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SUMMARY

Pulmonary air leak syndromes are extremely rare complications of systemic autoimmune connective tissue diseases and the occurrence of spontaneous subcutaneous emphysema (SSE) from pulmonary leak in the absence of pneumothorax or pneumomediastinum is even rarer. We report a case of recurrent SSE in a patient with rheumatoid arthritis and interstitial lung disease. The SSE was managed conservatively each time and it resorbed over several days. There has been no previous documented report of SSE in the absence of pneumomediastinum, pneumothorax or pulmonary nodules in a patient with RA.

BACKGROUND

Pulmonary air leak syndromes include pulmonary interstitial emphysema, pneumothorax (PT), pneumomediastinum (PM), pneumopericardium, pneumoperitoneum, subcutaneous emphysema (SE) and systemic air embolism. Spontaneous subcutaneous emphysema (SSE) results from trapping of air within tissues beneath the skin, without a history of a penetrating injury or procedure. It has been reported as a rare association with various connective tissue diseases such as systemic lupus erythematosus,¹ systemic sclerosis² and dermatomyositis.³ When it is so reported, SSE from a pulmonary leak usually co-exists with PM and runs a benign course.⁴ There have, however, been few cases of pulmonary air leak syndromes reported in association with rheumatoid arthritis (RA).^{5–7} Isolated SSE in the absence of a PM or PT has, however, not been reported. The better-known pulmonary manifestations of RA are interstitial lung disease (ILD), rheumatoid nodules and pleural effusions. Less common manifestations include bronchiolitis obliterans and cryoarytenoid arthritis.⁸ We report a case of recurrent symptomatic subcutaneous emphysema extending from the face, through the neck, to the chest, in a patient with ILD secondary to RA presenting to the Rheumatology Unit of Lagos State University Teaching Hospital.

CASE PRESENTATION

A 38-year-old man presented with symmetrical inflammatory polyarthritis affecting the wrists, proximal interphalangeal and metacarpophalangeal joints as well as the shoulders, knees and feet. He had significant early morning joint stiffness but there were no subcutaneous nodules. Laboratory tests showed elevated Erythrocyte sedimentation rate (ESR) and C reactive protein, while

rheumatoid factor was positive and anticyclic citrullinated peptide and antinuclear antibodies were negative. He was diagnosed with RA and was started on methotrexate tablets, 10 mg weekly with folic acid supplement. He was also placed on prednisolone tablets, 15 mg daily, to be tapered off eventually. He, however, defaulted from follow-up until 2 months thereafter, when he presented acutely ill with a fever of 38.7°C and marked dyspnoea. He was still on prednisolone and methotrexate on the day of presentation. Chest examination showed widespread crepitations in the lung fields. Chest radiograph and high resolution CT (HRCT) showed extensive fibrosis of the lung fields with honeycombing and some ground glass opacities. Work ups for opportunistic bacterial and fungal infections were negative. The patient was admitted and treated as a case of acute pneumonia with a background pulmonary fibrosis and placed on intravenous pulse methylprednisolone, 500 mg daily for 3 days, with which he improved. He was also placed on broad spectrum antibiotics while the septic work up was being awaited. We discontinued methotrexate and started leflunomide tablets, 20 mg daily and prednisolone tablets 15 mg daily after completing the 3-day course of pulse glucocorticoid. By the third day on current treatment, the articular symptoms had improved with the tender joint count now reduced to 10 from an initial count of 24, and the fever had resolved. The patient, however, woke up to notice a small swelling in the right supraclavicular fossa. This swelling was fluctuant, non tender with palpable and auscultated crepitations over it. Over the following 24 h, it increased in size to involve the contralateral supraclavicular fossa and the neck. The patient had moderate pain in the neck and upper back. Radiographs of the chest and neck showed subcutaneous emphysematous changes extending from both supraclavicular areas into the neck (figure 1). There was no associated PM or PT and no pulmonary nodules were seen. The patient also had new onset dysphagia and odynophagia to both solid and liquid meals. Liver function test showed elevated aminotransferases for the first time after 4 days on leflunomide, and the leflunomide was stopped. The subcutaneous emphysema was managed conservatively and it resorbed completely over 5 days.

Two weeks later, there was a new onset of SSE rapidly expanding from the supraclavicular fossae up through the neck and into the face. It also extended down over the chest with associated pain

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Figure 1 X-ray showing subcutaneous emphysematous changes in the neck and the suprascapular areas.

in the upper trunk and neck. A third event occurred a month after the second episode, with a pattern of involvement similar to that of the second episode. However, there was less pain and no dysphagia. Each time, the air leak resorbed with conservative management. HRCT showed features of ILD and subcutaneous emphysema (figures 2 and 3). The patient had to be placed on continuous oxygen therapy on account of dyspnoea and frequent desaturation in room air.

INVESTIGATIONS

Chest X-ray (posteroanterior view) and neck X-ray revealed diffuse subcutaneous emphysema without apparent airway abnormality. There was no associated pneumothorax or pneumomediastinum. Patchy opacities consistent with fibrotic changes were seen involving bilateral lower lung zones. Rheumatoid factor was 160 IU/ML, while anti cyclic citrullinated peptides and antinuclear antibodies were negative. Aspartate aminotransferase was 1491 U/L (reference: <40) and alanine aminotransferase was 176 IU/L (reference: 15–40). ESR was 55 mm in 1 h and full blood count was normal. C reactive protein was 8.8 mg/L (reference: <5.0) while sputum

Figure 2 High resolution CT showing honeycomb lung with anterior and lateral chest wall subcutaneous emphysema.

Figure 3 High resolution CT showing chest wall, axillary and neck subcutaneous emphysema with features consistent with interstitial lung disease.

microscopy and culture were negative for bacterial or fungal pathogens. Sputum smear and culture for acid-fast bacilli, Mantoux and QuantiFERON TB Gold tests were negative. Spirometry result was as follows: the forced expiratory volume in 1 s (FEV1) 59% and FEV1/FVC (forced vital capacity) 77%.

DIFFERENTIAL DIAGNOSIS

Supraclavicular abscess is a differential diagnosis that was readily ruled out by the X-rays; TB was also excluded, by negative Mantoux and QuantiFERON TB Gold tests as well as negative sputum AFB smear and culture. Various opportunistic pulmonary fungal and bacterial infections were considered, and sputum microscopy and culture for these were negative. Viral studies could not be carried out in our setting. Community-acquired pneumonia was excluded by a negative sputum microscopy and culture while pulmonary infarction was excluded by the absence of pleuritic chest pain, pleural effusion, negative d-DIMER test and non supportive features on chest HRCT.

TREATMENT

The subcutaneous emphysema was managed conservatively each time and it gradually regressed over several days. The patient was placed on azathioprine tablets 50 mg twice daily and the prednisolone tablets were step-wise reduced to 5 mg daily. He had intravenous co-amoxiclav 1.2 g twice daily for 5 days and azithromycin tablets 500 mg daily for 3 days. He also had diclofenac 75 mg daily and tramadol 100 mg daily for his pain, on an intermittent basis. Rituximab infusions were later started and he has now had two courses.

OUTCOME AND FOLLOW-UP

In all, the patient has had three episodes of SSE and had to be admitted on two occasions. Each time, complete resolution of the air leak was achieved without intervention. The arthritis improved with no swollen or tender joints. He is now off oxygen therapy.

DISCUSSION

SSE and PM occur frequently in critically ill patients in association with blunt or penetrating trauma, soft-tissue infections, or any condition that creates a gradient between intra-alveolar and perivascular interstitial pressures.⁹ However, pulmonary air leak syndromes are extremely rare in patients with RA.¹⁰ To the best of our knowledge, our case is the first report of SSE in the absence of pneumomediastinum, PT or pulmonary nodules in a patient with RA.

The risk factors for SSE and other air leak syndromes in systemic connective tissue diseases include ILD,^{11 12} cutaneous vasculopathy,¹³ rheumatoid nodules⁵ and steroid treatment.^{12 13} Our patient manifested with rapidly progressing swelling around the neck extending into the face and anterior chest with only minimal added discomfort ascribable to the SE. This is typical of SE, which may even be entirely pain-free. Possible risk factors for the SSE in our patient included the existing ILD and the fact that he had been on prolonged prednisolone use. The pulse methylprednisolone given may have added to the risk due to the glucocorticoid. Rheumatoid nodules were not found in any of his chest images and he had no evidence of cutaneous vasculopathy. Despite the size and rapidity of accumulation of the subcutaneous emphysema, conservative management was enough each time as there was no associated life-threatening effect of the air leak.

In a patient who has been on immunosuppressive medications continuously for 2 months, opportunistic infections are possible. Sputum microscopy and cultures were checked for bacteria, mycobacteria and fungi. Bronchoalveolar lavage or lung biopsy samples may have increased the chances of detection of infective pathology but bronchoscopy or CT-guided transthoracic needle aspiration could not be carried out in our case. Multiple sputum samples were, however, stained for *Pneumocystis jirovecii*, aspergillosis and other fungi. All of these were negative. Blood or urine antigen testing for legionella or other atypical bacteria could not be undertaken, but these were covered for with antibiotics. Facilities for cytomegalovirus, herpes and influenza serology or culture are not available in our centre. Methotrexate was changed to leflunomide because we considered the possibility that the patient may be experiencing methotrexate-induced pneumonitis. This is known to be a hypersensitivity disorder to methotrexate and the improvement experienced by our patient with its withdrawal and intensified immunosuppression also supported this possibility. However, a concurrently treated atypical bacterial infection could not be fully excluded.

Also, the fact that leflunomide has been associated with pharyngitis, stomatitis and liver failure¹⁴ later compelled its stoppage as our patient developed odynophagia and rising levels of aminotransferases on three occasions. Liver enzymes were within normal ranges at presentation but were elevated within 4 days of starting leflunomide and normalised after a few days of discontinuation of the drug. Serious leflunomide-induced hepatotoxicity is found in only 0.02% of treated patients, but isolated fatalities from liver failure have been documented.¹⁵ Oxidative stress is believed to be responsible for this hepatotoxicity.¹⁶ We could not find any documented links between SSE and liver dysfunction in the literature. Moreover, liver function tests were consistently normal during the last two episodes of SSE when our patient had been off leflunomide.

This patient was subsequently placed on azathioprine due to the drug's documented safety in RA patients with ILD as compared to methotrexate, leflunomide or the tumor necrosis factor α inhibitors.¹⁷ He was offered an off-label treatment with

rituximab but he declined due to financial incapacity. The option of lung transplant was discussed with him on account of his deteriorating lung function. This, however, cannot be performed in Nigeria at present. The patient later got a sponsorship to India for further care but could not be placed on the Indian transplant list. He returned to Nigeria and accepted the treatment with rituximab and has since made remarkable improvement. He is now able to maintain oxygen saturation in room air and has been off continuous oxygen.

This case report seeks to bring to the fore SSE as a possible, albeit, extremely rare complication of RA.

Learning points

- ▶ Pulmonary air leak syndrome can occur in rheumatoid arthritis (RA), although it is extremely rare.
- ▶ Spontaneous subcutaneous emphysema (SSE) is associated with interstitial lung disease and corticosteroid use.
- ▶ Conservative management is often sufficient to manage SSE in RA

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