CASE REPORT

The development of pulmonary aspergillosis and pneumothorax in a patient with neutropenic systemic lupus erythematosus and successful treatment of the first case

Omer Nuri Pamuk,¹ Gulsum Emel Pamuk,² Ebru Barutcu,³ Aygul Dogan Celik⁴

¹Department of Rheumatology, Trakya University Medical Faculty, Edirne, Turkey

²Department of Hematology, Trakya University Medical Faculty, Edirne, Turkey

³Department of Internal Medicine, Trakya University Medical Faculty, Edirne, Turkey

⁴Department of Infectious Diseases, Trakya University Medical Faculty, Edirne, Turkey

Correspondence to
Professor Gulsum Emel Pamuk,
gepamuk@yahoo.com

Accepted 3 May 2014

SUMMARY

There are reports on patients with systemic lupus erythematosus (SLE) with aspergillosis; however, aspergillosis-related pneumothorax has not been reported in SLE. We present a female patient with active SLE who was administered high-dose steroids, developed an opportunistic bacterial infection and had a cavitory pulmonary lesion. Sputum cultures yielded *Aspergillus fumigatus*. She was administered voriconazole. She developed dyspnoea and chest X-ray showed pneumothorax. She was placed with an underwater drainage chest tube; the pneumothorax and the pulmonary lesion regressed.

aminotransferase (AST) 69 U/L, lactate dehydrogenase 600 U/L (N<192), total protein 6 g/dL albumin 2.4 g/dL. Urinalysis was normal; she had no proteinuria. Complement C3 and C4 levels were normal. Anticytomegalovirus IgM, anti-Epstein-Barr virus IgM, HBsAg, antihepatitis B core IgM, antihepatitis C virus and anti-HIV were negative. Antinuclear antibody was homogeneously positive at a titre of 1/2560, anti-dsDNA was positive at titre 1/1000 and ANCA were negative. Chest X-ray and ECG were normal. There was no microbial growth in blood and urine cultures.

TREATMENT

The patient was diagnosed with SLE and administered prednisolone 30 mg/day and hydroxychloroquine 400 mg/day. In spite of regression of arthritides, morning stiffness and fever were persistent. Therefore, azathioprine 150 mg/day was added and the dose of prednisolone increased to 60 mg/day.

OUTCOME AND FOLLOW-UP

Meanwhile the patient developed dysphagia and oral lesions. Oral examination showed a hyperaemic pharynx and painful white candidal plaque lesions over her tongue and buccal mucosa. Esophagoscopy revealed numerous candidal ulcerative ulcers extending from the upper end of the oesophagus down to the lower end which easily bled on touch. Taking into account the endoscopic findings, candida oesophagitis was considered; oral nystatin and flucanazole 400 mg/day intravenously were administered. We tried to taper the dose of steroids, but because of the development of fever, leucopaenia and arthritis, we continued at the former dose. Antifungal therapy was discontinued after 14 days and the patient had no symptoms of oesophagitis. A chest X-ray performed because of fever and dry cough was normal and C reactive protein was 18 mg/dL. The haemocultures yielded methicillin-sensitive *Staphylococcus aureus*, and the patient was administered piperacillin-tazobactam with a presumptive diagnosis of nosocomial pneumonia. A thorax CT on the fifth day of antibiotherapy revealed a cavitory lesion in the middle zone of the right lung (figure 1). There was response to antibiotics and the patient's fever and CRP regressed; therefore, we continued with the same therapy.

BACKGROUND

Treatment-related complications are important causes of mortality and morbidity in patients with systemic lupus erythematosus (SLE).¹ Infections secondary to usage of, especially, corticosteroids and other immunosuppressive drugs pose serious problems in the therapy of SLE.² Aspergillosis is an opportunistic infection which may develop in patients using immunosuppressive drugs. Pneumothorax is an infrequently reported complication of SLE and carries a grave prognosis.³ We present a patient with SLE who was using steroids and azathioprine, and who in the meanwhile developed an aspergillosis-related cavitory pulmonary lesion and secondary pneumothorax.

CASE PRESENTATION

A 21-year-old woman was hospitalised in our rheumatology department in January 2008 having fever for the past 1 month and with widespread arthralgia and morning stiffness. She had been asymptomatic 1 month prior to admission and her medical history was non-significant. She denied smoking, drinking alcohol or taking any other drug.

INVESTIGATIONS

On physical examination, the temperature was 39°C, the liver was palpable 2 cm and there was symmetric polyarthritis of the small hand joints. Laboratory investigations showed haemoglobin 8.7 g/dL, leucocytes 2600/mm³, neutrophils 1100/mm³, lymphocytes 1000/mm³, platelets 92000/mm³, erythrocyte sedimentation rate 110 mm/h, C reactive protein 2 mg/dL, creatinine 0.8 mg/dL, alanine aminotransferase (ALT) 45 U/L, aspartate

CrossMark

To cite: Pamuk ON, Pamuk GE, Barutcu E, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-200818

Figure 1 The thorax CT showing a cavity in the middle zone of the right lung.

On the 10th day of therapy the patient had profuse mucopurulent sputum, right-sided pain and dyspnoea. On auscultation, breath sounds over the right lung area could not be heard. On chest X-ray the cavitory lesion was persistent and there was pneumothorax of the right lung (figure 2).

The thorax CT showed that, in addition to the cavitory lesion and pneumothorax, there was mediastinal emphysema. The patient was placed a chest tube with underwater drainage. Direct microscopic examination of the sputum revealed many septate hyphae with conidiophores suggesting *Aspergillus* infection. There was growth of *Aspergillus fumigatus* in the sputum culture. In addition, total serum IgE and *A. fumigatus*-specific IgE levels were elevated (1120 IU/mL and 4.2 IU/mL, respectively). Therefore, she was given voriconazole 4 mg/kg/day after a loading dose; piperacillin–tazobactam was discontinued after 3 weeks. In addition, she was given non-steroidal anti-inflammatory drugs and the dose of steroids was tapered quickly. Nevertheless, the patient could not tolerate this change in treatment regimen and developed arthritis and neutropenia. We planned plasmapheresis but her general condition did not permit the procedure. During follow-up there was resorption of her pneumothorax; CRP level became lower; her general condition and dyspnoea improved. We started to taper the dose of steroids. Voriconazole was administered for 12 weeks and then

Figure 2 The chest X-ray showing a cavitory lesion and pneumothorax of the right lung.

discontinued. In July 2010 the patient developed bilateral osteonecrosis of the hip joints. Currently, 5 years after admission, the patient is using 2 mg methylprednisolone/day, 100 mg/day azathioprine and 200 mg/day hydroxychloroquine and she has no problems.

DISCUSSION

Pleuropulmonary manifestations have been reported in approximately 50–70% of adult patients with SLE.^{4,5} Some of the pulmonary complications reported in patients with SLE include pleuritis, pneumonitis, infectious pneumonia, pulmonary haemorrhage and pulmonary hypertension.⁶ Although pleuropulmonary involvement is frequent, pneumothorax is rare in patients with SLE.⁷ It was reported that pneumothorax could occur in SLE with high disease activity.⁷ Our patient with SLE developed invasive aspergillosis-related pneumothorax. We present our patient which is the first case in the literature.

Infections are the leading cause of death in patients with SLE; therefore, all pulmonary infiltrates in SLE should be considered infectious in origin until proven otherwise.⁶ Infectious pulmonary infiltrations in patients with immunosuppressive SLE are caused by viruses, bacteria, fungi and protozoa.^{4,8} In the literature, there are about 40 cases of invasive aspergillosis in SLE.^{6,9} In most of these cases the diagnosis was delayed, cases were mortal and the diagnosis could be reached only in the post-mortem period.⁹ Although the development of pneumothorax in aspergillosis has been reported before, ours is the first reported case of patient with SLE who had this association. The diagnosis was reached relatively early in our patient and this was the main factor which prevented mortality. Risk factors for acquiring aspergillosis in patients with SLE were reported as high-grade disease activity, neutropenia, usage of steroids and other immunosuppressive drugs, and the presence of bacterial infection.^{6,9} Our patient was taking immunosuppressive drugs, was neutropenic and had a concomitant bacterial infection.

Learning points

- ▶ Patients with active systemic lupus erythematosus (SLE) using immunosuppressive drugs are under serious risk for the development of opportunistic infections.
- ▶ All kinds of opportunistic infections including invasive aspergillosis should be considered in patients with SLE.
- ▶ Invasive aspergillosis-related pneumothorax might be encountered as a rare complication in patients with immunosuppressive, neutropenic, active SLE.
- ▶ Whenever there is suspicion of infection in patients with SLE, pulmonary findings should be evaluated carefully and treated immediately without losing time.

Contributors ONP was responsible for literature search, wrote the manuscript and gave consent for the final form of the paper. GEP and EB read the manuscript, made suggestions and wrote some parts of paper, and gave consent for the final form of the manuscript. DCA commented on the patient's infectious findings, read the manuscript, made suggestions and wrote some parts of paper, and gave consent for the final form of the manuscript.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Nossent J, Cikes N, Kiss E, *et al*. Current causes of death in systemic lupus erythematosus in Europe, 2000–2004: relation to disease activity and damage accrual. *Lupus* 2007;16:309–17.
- 2 Falagas ME, Manta KG, Betsi GI, *et al*. Infection-related morbidity and mortality in patients with connective tissue diseases: a systematic review. *Clin Rheumatol* 2007;26:663–70.
- 3 Wilhelm M, Van Why SK. Pneumothoraces complicating systemic lupus erythematosus with nephritis. *Pediatr Nephrol* 2002;17:261–3.
- 4 Haupt HM, Moore GW, Hutchins GM. The lung in systemic lupus erythematosus. Analysis of the pathologic changes in 120 patients. *Am J Med* 1981;71:791–8.
- 5 Hunninghake GW, Fauci AS. Pulmonary involvement in collagen vascular diseases. *Am Rev Resp Dis* 1979;119:471–503.
- 6 Ciftci E, Yalcinkaya F, Ince E, *et al*. Pulmonary involvement in childhood-onset systemic lupus erythematosus: a report of five cases. *Rheumatology* 2004;43:587–91.
- 7 Yen JH, Tsai WC, Ou TT, *et al*. Systemic lupus erythematosus complicated by recurrent spontaneous pneumothorax—a case report. *Kaohsiung J Med Sci* 2001;17:540–4.
- 8 Segal AM, Calabrese LH, Ahmad M, *et al*. The pulmonary manifestations of systemic lupus erythematosus. *Semin Arthritis Rheum* 1985;14:202–24.
- 9 Katz A, Ehrenfeld M, Livneh A, *et al*. Aspergillosis in systemic lupus erythematosus. *Semin Arthritis Rheum* 1996;26:635–40.

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