Cancer Chemother Pharmacol (1990) 27: 168–169

Cancer Chemotherapy and Pharmacology

Short communication

Hydroxyurea-induced acute alveolitis in a Patient with chronic myeloid leukaemia

Graham H. Jackson, Jonathon Wallis, Joanne Ledingham, Anne Lennard, and Stephen J. Proctor

Department of Haematology, Royal Victoria Infirmary, Queen Victoria Road, Newcastle upon Tyne, NE1 4LP, UK

Received 2 February 1990/Accepted 15 August 1990

Summary. A number of cytotoxic agents have been implicated in the production of widespread pulmonary alveolar damage. We present a case of life-threatening alveolitis in a patient on hydroxyurea for chronic myeloid leukaemia. The clinical course suggests that the alveolitis was induced by the hydroxyurea. This is the first reported case of hydroxyurea-induced pulmonary alveolitis.

Introduction

Various pulmonary disorders have arisen from the deleterious effects of drugs on the lung. Certain cytotoxic agents have been implicated in the production of widespread alveolar damage [1, 2], including bleomycin, busulphan, melphalan and chlorambucil. Hyroxyurea rather than busulphan is being increasingly used to control myeloproliferative disorders, in part because of its relative lack of side effects. We report a case of life-threatening alveolitis that occurred in a patient who had recently started a course of hydroxyurea therapy. The clinical course and relapse during a second course of therapy suggests that the alveolitis was induced by the hydroxyurea.

Case report

A 66-year-old previously healthy man presented with chronic myeloid leukaemia. He received 500 mg hydroxyurea twice daily and was on no other medication. Three weeks later he presented as an emergency with sweating, lethargy, weakness and shortness of breath on exertion. He was febrile, with coarse crepitations being heard posteriorly at both lung bases. Chest X-ray showed bilateral basal consolidation; sputum and blood were sterile. Hydroxyurea therapy had produced a moderate fall in the white cell count, but there was no change in the percentage of eosinophils seen on the blood film. Viral, legionella and mycoplasma serology were negative.

Offprint requests to: G. H. Jackson

Hydroxyurea therapy was stopped and the patient was given Timentin, gentamycin and erythromycin. He improved over the next 7 days and was restarted on hydroxyurea. Within 24 h he developed an increasing cough, resulting in copious sputum and dyspnoea, and again became pyrexial, with extensive coarse crepitations being detectable throughout both lung fields. Chest X-ray showed extensive pulmonary consolidation, with slight right-sided pleural effusion. Numerous sputum samples were sent for microscopy and culture, and a non-encapsulated *Klebsiella* species was grown from only one of these. Bronchoscopy and broncoalveolar lavage were considered on admission but were not felt to be justified in view of the copious sputum production and the patient's clinical state. No acid fast bacilli, yeasts, hyphae or pneumocysts were seen on any of the sputum samples obtained. Blood cultures were sterile. Viral, legionella and atypical pneumonia serology remained negative.

The patient was given Timentin, gentamycin and high-dose Septrin, to which the *Klebsiella* isolate was sensitive. Over the next 10 days there was a progressive deterioration in his clinical condition, chest X-ray appearances (Fig. 1) and blood gasses, with his pO_2 on air falling to 3.5 kPa. Hydroxyurea therapy was stopped and treatment with 40 mg prednisolone was introduced. Within 24 h there was a dramatic improvement in his clinical condition and his blood gasses, with his pO_2 on air

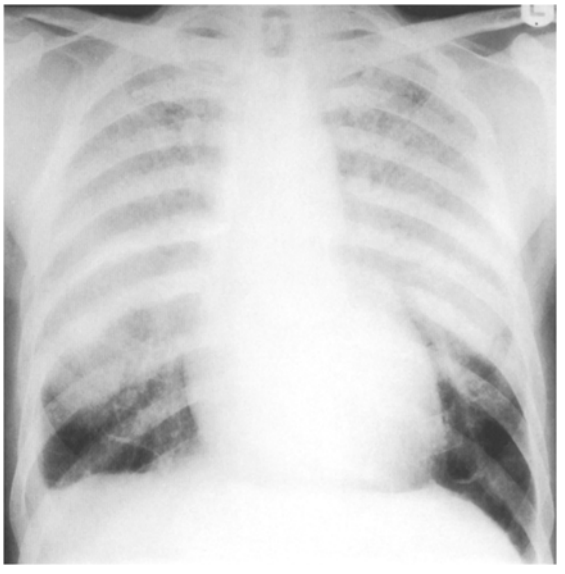

Fig. 1. Chest X-ray taken 10 days after the patient's second admission and before steroid therapy

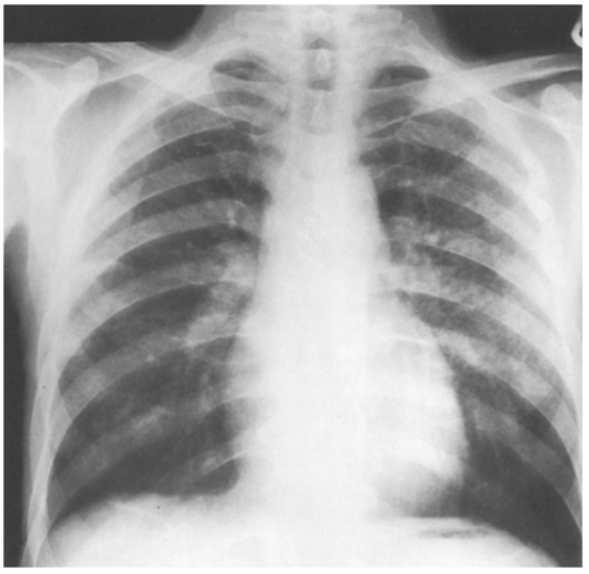

Fig. 2. Chest X-ray taken 48 h after the initiation of steroid therapy

rising to 8.3 kPa. This improvement in the patient's clinical condition continued throughout steroid therapy, and his X-ray (Fig. 2) appearances also improved. Antibiotics were stopped and the patient was continued on steroids until his discharge 4 weeks after admission. At that stage he was feeling completely fit and well and did not experience any dyspnoea on exertion. The chest X-ray appearances and blood gasses had returned to normal. Subsequent therapy for chronic myeloid leukaemia using oral thioguanine has been uneventful.

Discussion

This 66-year-old patient with chronic myeloid leukaemia developed life-threatening alveolitis whilst on hydroxyurea therapy. We believe that the alveolitis was due to hydroxyurea rather than being a coincidental infectious process. The one isolate of a non-encapsulated *Klebsiella* that was cultured from only one of many sputum samples was almost certainly irrelevant, as the clinical course and chest X-rays were not indicative of *Klebsiella* pneumonia and there was no response to optimal antibiotic therapy. The response to steroids suggested a non-infective aetiology for the alveolitis. Hydroxyurea-induced pulmonary alveolitis has neither been previously described nor reported to the Committee on the Safety of Medicines. We believe that the importance of this case lies in the near-fatal outcome of this reaction, which mimicked an opportunistic infection, and its rapid response to steroid treatment.

References

1. Gibson GJ (1987) Drug induced lung disease. In: Weatherall DJ, Ledingham JGG, Warrell DA (eds) Oxford textbook of medicine. Oxford University Press, Oxford, pp 15 141–15 144
2. Rosenow EC III (1980) Chemotherapeutic drug-induced pulmonary disease. Semin Respir Med 2 (2): 88–96