Invasive pulmonary aspergillosis: a rare presentation of non-Hodgkin’s lymphoma

Miguel Garcia-Gonzalez, Antonio L. Sanroman, Rosario Arribas, Gustavo Torres, Carmen Cuesta and Victor F. Moreira

Gastroenterology Service and Pathology Department, Hospital Ramón y Cajal, Ctra de Colmenar Viejo, Km 9, 400, 28034-Madrid, Spain

Summary: We describe a patient with rapidly progressive pneumonia and a high level of serum lactate dehydrogenase, in whom postmortem study revealed the presence of a diffuse, small and large-cell multicentric non-Hodgkin’s lymphoma, together with an invasive pulmonary aspergillosis. Aspergillosis is rare as a presenting feature of a lymphoproliferative disease; only one previous case has been reported to the best of our knowledge. Invasive aspergillosis and lymphoma should be considered in patients presenting with pneumonia and high level of lactate dehydrogenase.

Introduction

Aspergillosis is a rare presenting feature in patients with lymphoproliferative disease, and only one case has been reported previously to our knowledge.1

We report an elderly male who presented with fever, jaundice and pneumonia. Postmortem study disclosed invasive pulmonary aspergillosis superimposed on a diffuse, small and large-cell multicentric non-Hodgkin’s lymphoma (NHL) (Group F of the Working Formulation2).

Case report

A 82 year old man was admitted because of fever and jaundice. He had been well until 15 days earlier, when fever and cough had begun and was treated with amoxycillin–clavulanate for 6 days, without any improvement. Nine days before admission, physical examination showed fever (38°C), scattered bronchial rhonchi, modest liver enlargement and tenderness in the right upper abdominal quadrant. Laboratory evaluation disclosed 3,100 leukocytes with 1,000 neutrophils/mm³. Chest X-ray showed a bilateral interstitial pattern. Erythromycin was prescribed. Fever persisted, and the patient began to experience progressive dyspnoea and jaundice. On admission the white cell count was 3,370 with a total neutrophil count of 2,510/mm³, haematocrit reached 33%, total bilirubin was 229.5 μmol/l (N<20.52), aspartate aminotransferase (AST) 3.72 μkat/l (N<0.668), alanine aminotransferase (ALT) 1.62 μkat/l (N<0.668) and lactate dehydrogenase (LDH) 86.35 μkat/l (N<7.6682). Arterial blood, drawn when the patient was breathing room air, revealed mild hypoxaemia. Ziehl–Neelsen stain of sputum was negative for acid-fast bacilli. Urinalysis showed the presence of bilirubin. Abdominal ultrasound was normal. Twenty-four hours later the patient developed progressive respiratory failure, and died on the third hospital day.

The necropsy revealed a diffuse multicentric small and large-cell non-Hodgkin’s lymphoma (Group F of the Working Formulation). Lung, pericardium, spleen, adrenal glands, bone marrow and mediastinal nodes were involved. The liver showed a strikingly dense portal infiltrate by atypical lymphocytes. Peripheral and abdominal nodes were free of lymphoma. The presence of septate hyaline hyphae of uniform diameter (4 μm) with dichotomous branching at 45° angles was observed in both lower lung lobules and in the middle right lobe, with vascular invasion (Figure 1). This finding was considered to be diagnostic of invasive pulmonary aspergillosis.

Discussion

Lungs are the classic site of invasive disease caused by Aspergillus species. This infection is air-borne, and occurs particularly in patients who remain neutropenic for a prolonged period of time. The duration of granulocytopenia seems to be crucial.1 Aspergillosis is not uncommon in immunosuppressed adults and children with lymphoproliferative...
Figure 1 Aspergillosis hyphae in a pulmonary vessel (H&E, × 40).

Invasive disease, but is infrequently a presenting feature. To our knowledge, invasive pulmonary aspergillosis as a primary manifestation of a malignant NHL has been reported only once.

Probably, the most common manifestation of invasive pulmonary aspergillosis is 'haemorrhagic infarction'. The very high rise of LDH level in our patient could be ascribed to pulmonary microinfracts, although 27% of NHL without pulmonary involvement have a LDH level higher than 250 U/L.

Invasive aspergillosis can be associated with haematological malignancy. Young et al. stated that lymphoma is second only to leukaemia as underlying malignancy with invasive aspergillosis. Boon et al. in their study, reported 10.4% of patients with haematological malignancy, either treated or untreated, developing invasive pulmonary aspergillosis. However, in another series, only 11 patients with LNHL (11%) died of pneumonia, and just two of them presented infections traditionally associated with decreased cellular immunity (disseminated cryptococcosis and candidiasis). The incidence of invasive aspergillosis in immunosuppressed 'high-risk' patients, reported by Boon et al., is surprisingly high, probably due to the fact that they included only postmortem diagnosis. The true clinical incidence of this complication is probably very low, as reported previously.

Although culture of aspergillus from respiratory secretions is generally thought to be insensitive and not specific, the monoclonal antibody EB-A1 stain on sputum could be useful in the diagnosis of aspergillosis, even in the absence of hyphae. Furthermore, diffuse infiltrative lesions of both lungs in patients with NHL are reported only in a few cases.

Finally, jaundice is occasionally reported in patients with NHL and hepatic involvement, and is usually ascribed to the neoplastic portal infiltration, as was seen in the present case.

In conclusion, a patient is described in whom a malignant lymphoma, with diffuse infiltrative lesions of both lungs and a very high level of LDH, diagnosed after death, presented with invasive pulmonary aspergillosis.

References

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