Although translocation (15;17) and PML/RARα fusion are regarded as highly specific for acute promyelocytic leukemia (APL), they have been reported in rare cases of acute leukemias that were neither morphologically or immunophenotypically consistent with APL.[4-8] However, these cases showed therapeutic response to ATRA despite non-APL features. These observations showed that morphologic, cytogenetic and molecular features must all be considered for an accurate diagnosis of APL. Our case highlights the importance of this combined approach. While the t(15;17)(q22;q21) translocation seen in this patient was indistinguishable from that in APL, the clinical and hematologic features were not compatible with a diagnosis of APL. Detailed molecular analysis showed no evidence of PML/RARα rearrangement, which confirmed that the translocation breakpoints in this patient did not involve the PML and RARα gene. In fact a similar case of AML with t(15;17)(q24.3;q21.1) not associated with APL has previously been reported,[9] in which detailed molecular analysis did not reveal any involvement of PML and RARα genes. Interestingly, both cases showed AML-M2 morphology and expression of stem cell antigen CD34. In addition to CD34, the present case showed multi-lineage antigen expression, suggesting the involvement of an early hematopoietic progenitor cell.

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Lung toxicity following fludarabine, cytosine arabinoside and mitoxantrone (FLAN) treatment for acute leukemia

The clinical profile of pulmonary drug toxicity of fludarabine phosphate associated with other drugs, particularly cytarabine (ARA-c), is not well defined. We describe the pulmonary complications observed in two patients, treated with these drugs.

Case #1. A 31-year old man was diagnosed as having acute myeloid leukemia M2 in October 1998. A partial remission was obtained with a course of ICE and a second course of FLAN (fludarabine 60 mg/daily for 5 days; ARA-c 4,000 mg/daily for 5 days and mitoxantrone 12 mg/daily for 3 days was given. Seven days after therapy discontinuation, during severe neutropenia, the patient developed fever and dyspnea (pO_2 39 mmHg). The chest roentgenogram showed patchy alveolar shadows in the left hemi-thorax. An high resolution computed tomography (HRCT) showed bilateral pulmonary ground glass opacities (Figure 1) Empirical intravenous antibiotic therapy was administered, with 0.8-1 mg/kg prednisolone. Blood cultures were positive for *Staphylococcus simulans*. The cytospin preparations of bronchoalveolar lavage (BAL) fluid showed a pattern of alveolar haemorrhage. After 6 days clinical symptoms and blood gas abnormalities had resolved (pO_2 93.6). Transbronchial lung biopsies performed 20 days after the first BAL, showed a patchy interstitial mononuclear cell inflammation and intralveolar loose fibrotic buds. BAL fluid analysis showed: 540,000 cells/mm^3, macrophages with vacuolated cytoplasm 67%, neutrophils 1%, lymphocytes 32%. Flow cytometric analysis of lymphocytes showed: $CD3^+$ cells 95%, $CD4^+$ cells 24%, $CD8^+$ cells 47%, CD20 0%, CD 3/$CD25^+$ 2%, $CD3^+DR^+$ 66%, CD4 /CD8 ratio< 0.5%. Virus cultures and tests for acid-fast bacilli were negative.

Case #2. A 14-year old boy was treated in May 1997 for acute lymphoblastic leukemia (FAB L2) standard risk, $CALLA^+$. After 9 months of complete remission, he relapsed and was treated with FLAN. Twenty-four days after CHT, he developed acute respiratory distress syndrome, requiring mechanical ventilation

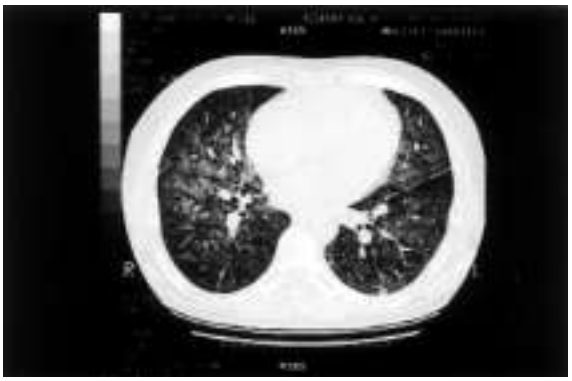

Figure 1. HCRT Bilateral pulmonary ground glass opacities.

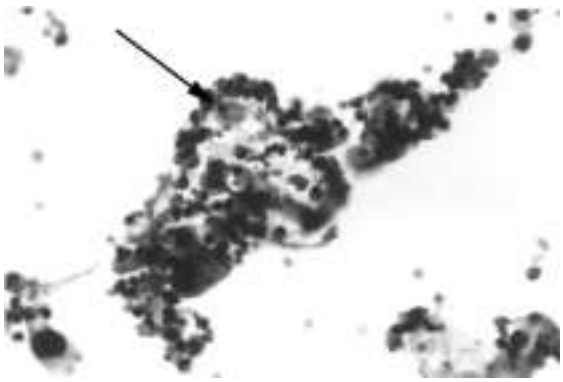

Figure 2. Bronchoalveolar lavage: macrophages, lymphocytes and atypical epithelial cells clustered around cyanophilic amorphous material (arrow).

(pO_2 20 mmHg; pCO_2 32.8; sat O_2 32.6; pH 7.37). Patchy alveolar shadows were present in the left lower lobe. HRCT showed areas of alveolar opacification in both lower lobes with an air bronchogram and patchy areas of ground glass appearance. BAL profile: 540,000 cells/mL, macrophages 9%, lymphocytes 3%, neutrophils 87%, eosinophils 1%. Atypical epithelial cells clustered around cyanophilic amorphous material were detected in a background of alveolar hemorrhage (Figure 2). BAL was negative for BK, CMV, adenovirus, synctial respiratory virus, Herpes simplex type I, influenza and parainfluenza viruses. The patient did not respond to intravenous trimethoprim-sulfadiazole, fluconazole, ceftazidime or teicoplanin; blood cultures remained negative. The patient rapidly improved only after initiation of prednisolone 60 mg/die.

Pulmonary toxicity of both ARA-C and fludarabine has been occasionally described in the past.[1-6] Based on our data, we want to highlight the occurrence of alveolar hemorrhage in both our patients, not frequently reported in the literature. In Case #1, fludarabine may have played a role in causing a subacute organizing pneumonia-like picture, as previously reported.[6] Steroid therapy ameliorates the lung damage probably by inactivating a cytokine network produced by drug-induced cell toxicity.[7]

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Difficulties in the diagnosis of primary cardiac lymphomas

Primary cardiac lymphoma (PCL) is defined as a non-Hodgkin lymphoma involving only the heart and pericardium. Clinical presentations are non-specific for variable involvement of cardiac structures. We describe a case of PCL presenting with left pleural effusion. A cardiac malignancy was suspected by magnetic resonance imaging but pathological diagnosis made only after thoracotomy.

Sir,

A 78-year-old woman was admitted to our hospital with the complaint of dyspnea. She had a well controlled hypertension and suffered from Herpes zoster affecting the gluteal region one month earlier.

Physical examination revealed dullness to percussion at the base of the left lung. There was no jugular