that seen in asthma. It is tempting to speculate that some individuals are genetically predisposed to over-express HLA-G in response to specific signals. Once secreted, HLA-G could promote a cascade of events that result in worsening inflammation. Several polymorphisms in the promoter region of *HLA-G* coincide with transcription factor binding sites could account for inter-individual differences in expression of HLA-G [10]. We previously identified a polymorphism in the 3′ untranslated region of *HLA-G* which disrupts a microRNA target site and demonstrated allele-specific expression of HLA-G in the presence of microRNAs that bind to that target [5]. Therefore, either lack of suppression or over-expression of HLA-G could explain the association we report here with asthma. We note that the small numbers of subjects in this study precludes more detailed analysis of relationships between genetic variation and HLA-G expression. Futuremore, larger studies are required to clarify the potential modulating role of HLA-G on the clinical manifestations of asthma and the role of genetic variation on expression levels.

In conclusion, sHLA-G is present in greater concentrations in BAL in mild asthma. We suggest that the overexpression or lack of suppression of HLA-G contributes to the disease process and that sHLA-G represents a novel pathway of asthma pathogenesis.

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Pneumocystis pneumonia in an HIV-negative patient with no overt risk factors on presentation

To the Editors:

Pneumocystis pneumonia (PCP) is a potentially life-threatening opportunistic infection that can occur in HIV-positive and HIV-negative individuals. The most significant risk factor for PCP in HIV-negative patients is chemotherapy, with a median time from cancer diagnosis to the first episode of PCP of 2 yrs. We report here a case of PCP in an adult male who had no identifiable risk factors on presentation. 3 weeks after the first signs and symptoms of PCP, he manifested blast crisis of acute myeloid leukaemia. This would be the first case demonstrating PCP as the sole presentation of an underlying occult leukaemia.

Our patient was a 55-yr-old homosexual male nonsmoker who presented with a 7-day history of progressive dyspnoea, dry cough, fever and chills. On examination, the patient's blood pressure was 130/70 mmHg, heart rate was 95 beats·min^{-1}, respiratory rate 25 breaths·min^{-1}, oxygen saturation 95% (3 L nasal oxygen), and temperature 37.9°C (100.2° F). The remainder

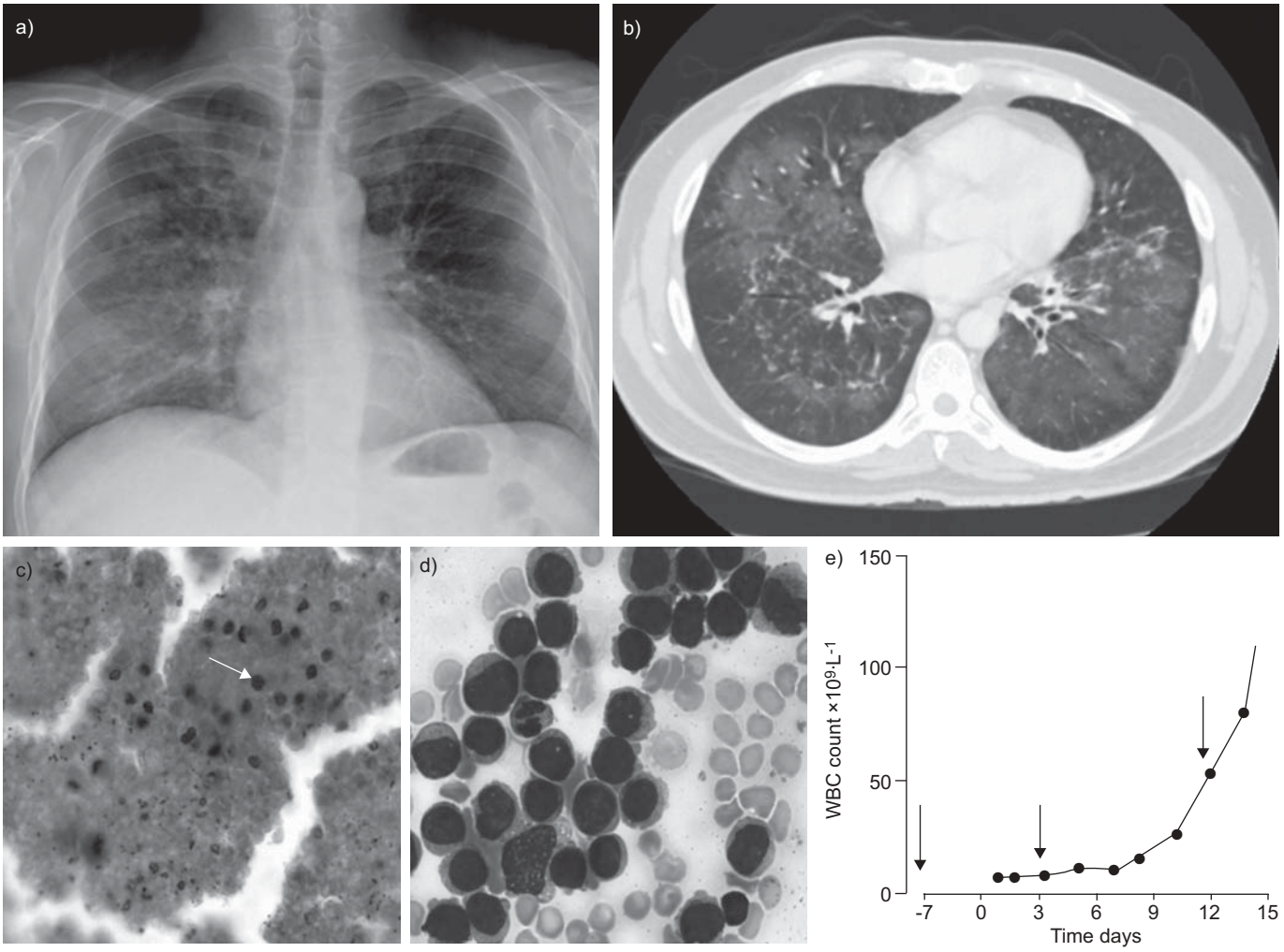

FIGURE 1. a) Chest radiograph on presentation: bilateral reticular markings with no pleural effusions. b) Computed tomography scan of chest (third day): diffuse bilateral ground glass opacities consistent with *Pneumocystis* pneumonia (PCP). c) *Pneumocystis jirovecii* (arrow) with Gömöri methenamine silver (shown in greyscale here) stain on bronchoalveolar lavage fluid (third day). d) Bone marrow analysis (ninth day): marked megakaryocytic hypoplasia. Increased monocytes and atypical lymphocytes. Flow cytometery interpretation revealed non-M3 acute myeloid leukaemia (AML) with monocytic differentiation, most consistent with M5. Final diagnosis (12th day): acute myeloid leukaemia, monoblastic type (FAB M5a). e) Graph depicting the chronology of events, with white blood cell count ($\times 10^9$ L^{-1}) (normal 4–10×10^9 L^{-1}) plotted against the time in days. From left to right, the first arrow (not to scale: 1 week before hospital admission) marks the onset of signs and symptoms of PCP. The second arrow (third hospital day) marks the diagnosis of PCP. The third arrow marks the final diagnosis of AML (12th hospital day).

of the physical examination was unremarkable. Chest radiograph (CXR) showed bilateral reticular markings with no pleural effusions (fig. 1a). Pertinent laboratory results (normal values in parentheses) included a white blood cell (WBC) count of 8.1×10^9 L^{-1} (4–10×10^9 L^{-1}) with a differential of 45% neutrophils, 23% lymphocytes and 2.1% monocytes. No blasts or atypical cells were noted on the peripheral smear. Haemoglobin was 12.7 g·dL^{-1} (12.0–18.0 g·dL^{-1}) and platelet count was 220×10^9 L^{-1} (140–440×10^9 L^{-1}). Rapid HIV screen was negative. Influenza (nasal swab) and *Legionella* (urine) antigen were not detected. The patient was started on ceftriaxone and azithromycin, but demonstrated no clinical improvement over the following 2 days. Computed tomography (CT) scan of the chest on the third day showed diffuse bilateral ground glass opacities, without adenopathy or pleural effusions (fig. 1b). Serum lactate dehydrogenase (LDH) was 1,560 U·L^{-1} (313–618 U·L^{-1}) and HIV polymerase chain reaction was negative. CD4 count was 807 μL^{-1} (393–1,771 μL^{-1}). Bronchoalveolar lavage (BAL) yielded fluid that was diagnostic for *Pneumocystis jirovecii* by Gömöri methenamine silver stain (fig. 1c). No viral cytopathic inclusions were seen. His treatment was thus changed to intravenous trimethoprim-sulphamethaoxasole and methylprednisone on the third day.

The patient demonstrated significant clinical improvement over the following 3 days, coinciding with the resolution of reticular markings on his CXR. However on the eighth hospital day, his WBC count increased to 15.1×10^9 L^{-1} (fig. 1e). The monocyte differential was 22% (2.1% on presentation) and atypical lymphocytes were noted on the peripheral smear. Viral, fungal and bacterial cultures were negative, both from the blood and BAL fluid. In view of higher than expected (in a patients with PCP) LDH level, and doubling of the WBC counts the next day; a bone marrow biopsy was performed (ninth hospital day). It revealed acute myeloid leukaemia

(AML) (fig. 1d). The patient was referred to oncology where he was treated for the blast crisis of AML. A repeat BAL fluid analysis after 14 days of treatment for PCP was negative for *P. jirovecii*.

HIV-positive patients with a CD4 count $<200\ \mu L^{-1}$ are considered at risk for PCP [1]. HIV-negative patients with PCP are predominantly those on immunosuppression or chemotherapy for an underlying disease process [2]. Irrespective of the underlying cause, the predisposition to PCP in the ''at risk'' patients is primarily due to a decrease in their cell-mediated immunity [3]. Additionally, in patients on glucocorticoids for >12 weeks, suppression of lung surfactant may be an additional factor [4]. Though haematological malignancies constitute 30% of all the malignancies associated with PCP, the median time from cancer diagnosis to the first episode of PCP is usually 2 yrs [2]. Moreover, PCP as the sole presenting feature of an underlying occult haematological malignancy has not been reported previously.

On presentation, our patient had no evidence of leukaemia. In retrospect, PCP was thus the first clinical manifestation of his occult malignancy. Though the blast crisis manifested 3 weeks after the first signs and symptoms of PCP, a bone marrow analysis would have revealed AML even on presentation. This would in turn explain the decreased immunity and, therefore, his predisposition to PCP. The infiltrates on CT scan of the chest could not be attributed to leukaemia because the WBC count was normal at that time. Serum LDH generally ranges from 361 $IU{\cdot}L^{-1}$ to 1,217 $IU{\cdot}L^{-1}$ in patients with PCP [5]. The higher than expected LDH served as an additional clue towards an underlying haematological malignancy in our patient.

In conclusion, PCP can thus be the sole atypical presentation of leukaemia. Since the transformation time from occult to overt leukaemia can be variable (weeks to months), bone marrow analysis should be considered in HIV-negative patients with no identifiable risk factors for PCP on presentation.

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Unusual treatment of patent foramen ovale after pneumonectomy

To the Editors:

As has often been said by Dr Harold C. Urschel Jr, pneumonectomy is ''a disease'' in itself. It is a major procedure with frequent perioperative complications such as empyema, fistula, cardiac problems or respiratory insufficiency. Besides frequent post-operative cardiac and respiratory complications, long-term sequelae are also seen.

After pneumonectomy, anatomical adaptations occur with repositioning of intrathoracic structures. Common changes are elevation of the hemidiaphragm (especially after phrenic nerve damage), mediastinal shift, diminished intercostal space and filling of the postpneumonectomy space with fluid. Infrequently, these adaptations may lead to invalidating complications. The most frequent complication is the so-called post-pneumonectomy syndrome caused by compression of the remaining bronchus against the vertebral column or aorta. Since positioning of the organs may take years, symptoms may occur even after 5–10 yrs.

In this letter, we will focus on a rare complication, shunting through a patent foramen ovale (PFO), as a long-term complication of right-sided pneumonectomy or bilobectomy. Only a few cases have been published, although this complication might be under-reported since the diagnosis of PFO is difficult, especially after pneumonectomy. This letter describes three patients who were diagnosed with shunting through a PFO following lung resection. In these patients, right ventricular compression by the elevated right hemidiaphragm was the main cause of PFO and surgical plication of the right hemidiaphragm was sufficient to close the PFO.

CASE SERIES

Patient A

A 67-yr-old male underwent a right-sided pneumonectomy 14 yrs earlier because of a bronchial carcinoid. Partial resection of the pericardium with transection of the phrenic nerve were needed for complete resection He developed progressive