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*CASE STUDY*

# Cerebral air embolism complicating bilevel positive airway pressure therapy

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*Cerebral air embolism complicating bilevel positive airway pressure therapy. S-C. Hung, H-C. Hsu, S-C. Chang. ©ERS Journals Ltd 1998.*
**ABSTRACT: A 13 yr old male with acute lymphoblastic leukaemia who received bilevel positive airway pressure ventilation *via* a face mask for post-transplant pneumonitis developed subcutaneous emphysema, radiographic evidence of pulmonary interstitial emphysema, pneumomediastinum and 6 h later, right hemiparesis and focal livedo reticularis. This case illustrates that severe barotrauma may complicate noninvasive bilevel positive airway pressure ventilation.**
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Most forms of barotrauma including pulmonary interstitial emphysema, pneumomediastinum, pneumothorax, pneumoperitonium and subcutaneous emphysema commonly occur in both adult and paediatric patients placed on mechanical ventilation. However, barotrauma is considered to be rare in patients receiving noninvasive positive pressure ventilation (NPPV) as bilevel positive airway pressure (BiPAP) ventilation. In this report, an unusual case is presented of pulmonary barotrauma in a 13 yr old leukaemic patient with post-transplant pneumonitis who developed pulmonary barotrauma and possibly cerebral air embolism while being noninvasively ventilated with BiPAP.

## Case report

A previously well 13 yr old male was admitted to our hospital in February 1997 because of a one-month history of pallor, fatigue and febrile episodes. Physical examinations showed splenomegaly and purpura over the lower limbs. The blood biochemistries were within normal ranges. The complete blood count revealed a haematocrit of 16.0%, a white blood count of $21.9\times10^9$ cells·$L^{-1}$ with 74% lymphoblasts and a platelet count of $29\times10^9$ cells·$L^{-1}$. Haematological malignancies were highly suspected and a bone marrow aspiration was performed. Microscopic examination of the bone marrow aspirate revealed >90% of lymphoblasts. A diagnosis of acute lymphoblastic leukaemia was established.

Chemotherapy with vincristine, prednisolone, daunorubicin, and asparaginase was started. The patient's postchemotherapy course was complicated by acute pancreatitis and hyperglycaemia. Because complete remission was not achieved after induction chemotherapy, the regimen was switched to cytosine arabinoside for 7 days and daunorubicin for 3 days (A7D3) and additional cytosine arabinoside for 5 days and idarubicin for 2 days (A512). Repeated bone marrow examination, however, still showed excessive lymphoblasts. On April 15, cytosine arabinoside and novantrone were administered. High-dose methotrexate chemotherapy was performed on April 29 because of refractory leukaemia. On May 5, he began to receive buffy coat transfusion from his father, but the response was poor. He then agreed to have an allogeneic transplantation.

The patient underwent allogeneic peripheral blood stem cell transplantation (PBSCT) on May 22 following conditioning with cyclophosphamide and total body irradiation. On day 10 after transplantation, a grade III acute graft *versus* host disease developed but resolved after immunosuppressive therapy. He was treated with broad-spectrum antibiotics and frequent blood transfusions for his prolonged pancytopenia and fever. Prophylactic gancyclovir against cytomegalovirus (CMV) was also given. His condition stabilized. On July 20, 58 days post-transplant, progressive dyspnoea developed. A chest radiograph showed diffuse interstitial pulmonary infiltrates. Sputum cultures yielded normal mixed flora and multiple blood cultures grew no micro-organisms. Further invasive studies were not performed because of the patient's reluctance. Combinations of high-dose steroids, *i.v.* trimethoprim (TMP)/sulphamethoxazole (SMX) and gancyclovir were administered for the interstitial pneumonitis. In addition, BiPAP therapy *via* a nasal mask was applied with an inspiratory positive airway pressure (IPAP) of 16 $cmH_2O$, an expiratory positive airway pressure (EPAP) of 5 $cmH_2O$ and an oxygen flow of 12 L·$min^{-1}$ to maintain the arterial oxygen saturation ($S_{a,O_2}$) above 90%. The patient suffered from severe diarrhoea for the next week. The CMV immunoglobulin (Ig)M became positive at the same time. His clinical features were thought to be related to CMV pneumonitis and enteritis.

On August 3, after 2 weeks of BiPAP therapy, he was found to have subcutaneous emphysema over the right anterior chest accompanied by localized skin marbling. A chest radiograph was taken immediately and revealed pneumomediastinum (fig. 1). Six hours later, the patient

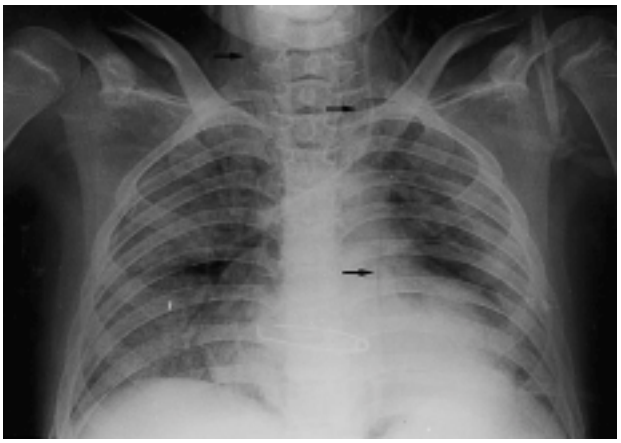

Fig. 1. – Anteroposterior chest radiograph revealing fine streaks of air (arrows) within mediastinum, extending upwards to the neck.

suddenly noticed weakness of his right side limbs. Physical examination revealed right hemiparalysis, but no heart murmur or carotid bruit suggestive of cardiogenic or thrombotic embolism. A noncontrast computed tomography (CT) scan of the brain showed a low attenuation over the posterior limb of internal capsule of the left cerebrum (fig. 2), a finding consistent with cerebral infarction. A diagnosis of cerebral arterial air emboli was considered. The inspired oxygen fraction was increased and the head-down position was adopted. However, his neurological deficit showed only little recovery. Over the next 5 days, the patient had worsening dyspnoea. The subcutaneous emphysema extended progressively down to his right forearm. Arterial blood gas analysis (IPAP 14 $cmH_2O$, EPAP 5 $cmH_2O$, $O_2$ 15 $L \cdot min^{-1}$, respiratory frequency 24 $breaths \cdot min^{-1}$) showed an arterial oxygen tension ($P_{a,O_2}$) of 5.5 kPa (41 mmHg), an arterial carbon dioxide tension ($P_{a,CO_2}$) of 4.0 kPa (29.5 mmHg) and a pH of 7.446. He was intubated and assisted with mechanical ventilation. However, the $S_{a,O_2}$ could not be elevated and the patient died of respiratory failure.

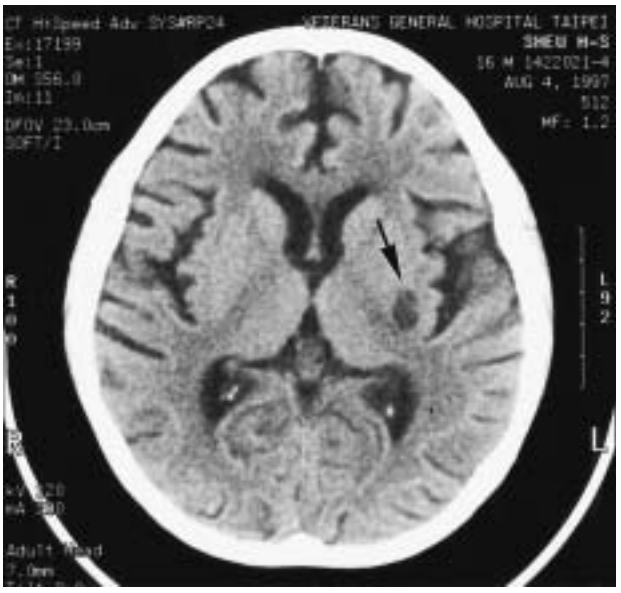


Fig. 2. – Computed tomography scan of the brain showing a low attenuation (arrow) over the posterior limb of the internal capsule of the left cerebrum.

## Discussion

BiPAP ventilation, a form of NPPV, has been widely used in both acute and chronic respiratory failure in the 1990's. In selected patients, NPPV can avoid the need for intubation and reduce the complication and mortality rate [1]. In general, NPPV is safe and well tolerated. Among the few side-effects, most are due to interface-related discomforts [2]. Pulmonary barotrauma, though an important complication of positive pressure ventilation, had seldom been reported in patients receiving NPPV. Pulmonary barotrauma is related primarily to both the airway pressure and the associated pulmonary pathology. It is considered to be a rare event in patients receiving NPPV because of a relatively low inspiratory pressure and stable pulmonary condition. With the increasing use of NPPV therapy in the current critical care, however, barotrauma can be expected to occur more frequently.

When the airway pressure is elevated by increasing the IPAP and EPAP, or the pulmonary tissue is destroyed by the inflammatory process, gas in the alveoli may follow the path of least resistance and rupture into the interstitium, producing the radiographic manifestations of interstitial emphysema. It then moves centrally within the bronchovascular sheath and dissects into the mediastinum, or travels along the fascial planes into the neck or trunk, resulting in pneumomediastinum and subcutaneous emphysema [3]. Previous studies have indicated that 40 $cmH_2O$ is a clinically important peak airway pressure level above which barotrauma is likely to occur. Other investigators believe that positive end-expiratory pressure (PEEP) is the most significant factor [4]. However, in those patients who have severe pre-existing lung disease, especially emphysema, necrotizing pneumonia and adult respiratory distress syndrome, even a low airway pressure may cause damage to the alveolar wall and air leakage.

It is possible for extra-alveolar air to enter the systemic circulation if there is bronchovenous communication and an adequate pressure gradient. Gas that has ruptured from alveoli into the bronchovascular sheath may preferentially enter the pulmonary venous system if the vascular structures have been disrupted by a necrotizing process [3]. We suspect that this was the case with our patient. Even if a small amount of gas enters the systemic circulation from the pulmonary vein, it can lead to catastrophic embolic events including stroke and acute myocardial infarction. Despite of its striking clinical presentations, the presence of gas in the systemic circulation is difficult to prove because a very small amount of intravascular gas is able to produce life-threatening symptoms but is cleared quickly. Furthermore, the direct demonstration of intravascular gas often requires computer-enhanced image studies or surgery, which are not always practical or safe for use in critically ill patients [5].

Our patient developed an abrupt onset of right hemiparalysis 2 months after the allogeneic PBSCT. Stroke is infrequent in patients receiving allogeneic bone marrow transplant. In a recent review of neurological complications in 425 patients who underwent bone marrow transplantation (310 allogeneic, 115 autologous) for leukaemia, the most common complications were central nervous system (CNS) haemorrhage (3.8%), metabolic encephalopathy (3%) and CNS infection (2%). Only two patients had ischaemic disorders [6]. In the other report examining

the clinical and autopsy findings in 78 patients who died after bone marrow transplantation, CNS infarct was found in three patients and was associated with endocarditis in all cases. Nonbacterial thrombotic endocarditis was found in five patients and was the cause of cerebral infarction in two. Acute bacterial endocarditis due to enterococcus occurred in one patient and was also the cause of a cerebral infarction [7]. Our patient did not have clinical evidence of bacterial endocarditis or a hypercoagulable state.

Although the possibility of nonbacterial thrombotic endocarditis, the most frequent cause of stroke in the transplant recipient cannot be completely excluded, without an echocardiographic document, the subsequent development of stroke after subcutaneous emphysema strongly supports a causal relation. Further evidence that makes the clinical diagnosis of cerebral air emboli beyond much doubt is the presence of localized skin marbling and focal livedo reticularis. This unusual dermal feature represents venodilation in response to arteriolar occlusion and is considered a definitive clinical sign of gas embolism [5, 8]. Cerebral air embolism may occur following diving accidents [9], neonatal respiratory distress syndrome [10], cardiovascular surgery, neurosurgery and central line placement [11]. To our knowledge, this is the first report of its association with BiPAP therapy.

Classically, a CT scan of brain may reveal intravascular air within the cranium if the image study is performed early enough after the occurrence of cerebral air embolization. Resolution of the air-density lesion with a residual area of low density consistent with infarction will be observed on the later scan, but the time needed for resolution varies with the individual. Our patient was noted to have a lacunar infarction, which usually develops in patients with long-term hypertension. A similar finding was reported in a 23 yr old male with end-stage renal disease who suffered from bilateral small infarcts around thalamic regions as an iatrogenic cerebral air embolism during the placement of an arteriovenous fistula [12]. Accordingly, cerebral air embolism might present as lacunar syndrome in previously normotensive patients.

After a careful review of the patient's chest film (fig. 3) 1 day before the development of cerebral air embolism, pulmonary interstitial emphysema, the earliest sign of alveolar rupture, was observed. This condition is identified radiographically as small parenchymal cysts, perivascular halos, linear streaks of air radiating toward the hilum, pneumatoceles or subpleural air [4]. Pulmonary interstitial emphysema is a space-occupying lesion which compresses the surrounding lung parenchyma. It may severely impair the patient's already compromised respiratory ability and is the forecast of impending severe barotrauma [4]. This case demonstrated the fact that the bilevel positive airway pressure therapy is not as safe as is generally assumed. Accordingly, clinicians should always be aware of the subtle radiographic changes in pulmonary barotrauma, even in patients receiving bilevel positive airway pressure therapy. Once pulmonary interstitial emphysema develops, respiratory therapeutic strategies or alternative ventilatory modes should be considered to ameliorate the airway pressure aggressively [5]. Preparations for the management of barotrauma should be made if the above efforts fail to resolve the condition.

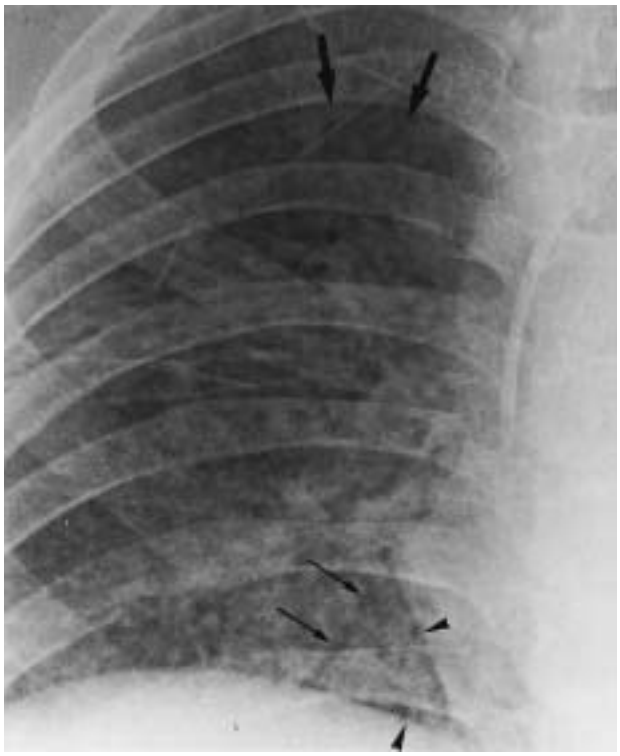

Fig. 3. – Anteroposterior chest radiograph showing perivascular halos (thick arrows) against a consolidated lung, and linear streaks of air (thin arrows) representing large vessels surrounded by circles of air within the perivascular sheath. Subpleural air (arrowheads) is also present.

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