Case report

Paradoxical embolism in a boy with cystic fibrosis and a stroke

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Abstract

An 11 year old boy with cystic fibrosis suffered a stroke, producing right sided weakness. Four years previously a totally implantable venous access device (Port-a-Cath) had been inserted. Magnetic resonance angiography revealed a filling defect in the left middle cerebral artery. Transoesophageal echocardiography demonstrated a thrombus attached to the tip of the Port-a-Cath and also the presence of a patent foramen ovale. After an initial period of anticoagulation the defect was closed using a septal occlusion device introduced via a cardiac catheter. The boy's neurological signs completely resolved and he remains free from further thromboembolic episodes. Whilst pulmonary embolism has been described before in relation to a totally implantable venous access device, this is believed to be the first description of a paradoxical embolism in relation to such a device.

Keywords: cystic fibrosis; paradoxical embolism; catheterisation

An 11 year old boy with cystic fibrosis was admitted to hospital with sudden onset of confusion and slurred speech. On examination he was found to have a right-sided hemiparesis, expressive and receptive dysphasia. He had originally presented at the age of two days with a meconium ileus and was subsequently found to be homozygous for the AF508 deletion. A sweat test performed at the age of four months confirmed the diagnosis of cystic fibrosis. Since the age of four he had required many hospital admissions for intravenous antibiotic therapy. In February 1992 a Port-a-Cath was inserted via the right internal jugular vein and secured to the anterior chest wall. His lung function was considerably compromised with a forced expiratory volume in one second (FEV1) of 0.63 l (35% predicted) and a forced vital capacity (FVC) of 0.98 l (49% predicted).

A computed tomographic (CT) brain scan performed on the day after admission revealed a poorly defined area of low attenuation in the left temporoparietal region which was suggestive of ischaemia in the territory of the left middle cerebral artery. Magnetic resonance angiography confirmed recent ischaemia in this region with evidence of an embolus in the left middle cerebral artery. A transthoracic echocardiogram was performed which showed an unusual Ebstein's-like deformity of the tricuspid valve; the proximal part of the septal leaflet of the tricuspid valve was displaced apically with a point of attachment in the mid body of the right ventricle. Mild tricuspid regurgitation was also seen but no other abnormalities were apparent.

Ebstein's anomaly is associated with abnormal intra-atrial connections and therefore a transoesophageal echocardiogram was arranged. This was performed under general anaesthesia and demonstrated a small patent foramen ovale, the anterior border abutting the posterior aspect of the ascending aorta. The Port-a-Cath was seen in the right atrium and was noted to impinge against the tricuspid valve during the cardiac cycle. In addition, a large thrombus was seen attached to the tip of the Port-a-Cath in the right atrium.

Despite using intravenous contrast, no right to left shunt was demonstrable during the procedure. Techniques to enhance any right to left shunt such as coughing and the Valsalva manoeuvre were not possible because of the general anaesthetic.

The patient was anticoagulated with warfarin and started on an anti-platelet dose of aspirin. One month later the defect was closed using a 9 mm atrial septal occlusion device introduced via a cardiac catheter (fig 1). By this time the neurological signs had completely resolved and aspirin was discontinued after three months. There have been no further episodes of thromboembolism.

Figure 1  Septal occlusion device clamped across the atrial septum.
Surgery and respiratory muscles

In their review of the effects of surgery on the respiratory muscles Siafakas and co-workers have cited my work incorrectly on two occasions.1 We reported a study of respiratory mechanics after abdominal surgery with measurements of the pressure-volume characteristics of the rib cage and abdomen.2 This report has been cited to support statements on the effects of surgery on gas exchange efficiency of the lung and of general anaesthesia on the thorax. On neither occasion is this citation appropriate. We found evidence that the abdominal muscles were active in patients after abdominal surgery; that this activity was variable, and that it could possibly explain the patterns of movement otherwise considered to represent “diaphragmatic dysfunction”.3 These observations, along with a short review of the published work on the subject, formed an editorial4 in which I argued that the concept of diaphragmatic dysfunction was outmoded. This work has been cited in support of the effects of laparoscopic cholecystectomy, which is incorrect. Indeed, there is remarkably little direct evidence that the intercostal inspiratory muscles become more active in the patient after surgery. There is also little direct evidence in humans that the diaphragm is the respiratory muscle most affected by surgery.

Many of the changes in the shape of the thorax caused by the induction of anaesthesia can be attributed to a loss of skeletal muscle tone, with a change in the shape of the vertebral column. If this is prevented, then the changes in thoracic dimensions during induction of anaesthesia are small, variable, and do not require the hypothesis of major movements of intravascular volume as indicated in fig 1 of their review.4 This is supported by direct measurements of intravascular volume, which do not show these shifts.5

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LETTERS TO THE EDITOR

Surgery and respiratory muscles

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Discussion

Paradoxical embolism was first described by Cohnheim in 1877 but until 1930 only post-mortem cases were reported in the literature. In recent years more advanced techniques for detection of a patent foramen ovale have allowed the accurate diagnosis of presumptive paradoxical embolism during life.

Thromboembolism has been described as a complication relating to the use of totally implantable venous access devices2 but we believe this is the first time that a paradoxical embolism has been described in relation to the use of such a device.

Paradoxical embolism can only be considered proven if a venous thrombus is detected lodged in an intracardiac septal defect. This degree of certainty is extremely rare, but has been demonstrated during life using both transsthoracic and transoesophageal echocardiography.3,4 More often we can assume paradoxical embolism if “Johnson’s triad” exists—that is, (1) venous thrombosis with or without pulmonary embolism, (2) an intracardiac defect with right to left shunting, and (3) arterial embolism without a corresponding source in the left heart or proximal arterial tree.5

The reported incidence of a patent foramen ovale varies from 5% to 30%. In younger adults with ischaemic stroke, where the cause may be undefined in up to 35% of cases, the incidence of a patent foramen ovale is significantly higher at around 40%.6 This suggests that paradoxical embolism occurs more frequently than was previously thought.

Paradoxical embolism is more likely in the setting of a chronic cough, as in cystic fibrosis. Coughing and the Valsalva manoeuvre are used during contrast echocardiography to promote right to left shunting across a patent foramen ovale, and indeed coughing is felt to be the most effective manoeuvre to demonstrate such shunting.7

Any child with an unexplained stroke requires a careful cardiological examination, particularly if there are risk factors such as an indwelling venous access device and a chronic cough. If transthoracic echocardiography shows no abnormality then more invasive investigations should be considered such as transoesophageal echocardiography.

Transcatheter techniques such as that used in our patient can offer significant advantages over open surgery in patients with cystic fibrosis. Postoperative recovery is quicker with less interruption to physiotherapy, and the avoidance of sternotomy may have important implications for any proposed heart-lung transplantation.

Postoperative air leaks

The study by Waller et al did not attempt to compare the clinical benefit, cost-effectiveness, or relative convenience of the two alternative chest drainage systems—a flutter valve drainage bag or the conventional underwater seal. Instead, it claims that the flutter valve offers a "physiologically more effective" alternative to the underwater system. However, a pneumothorax is a pathological rather than a physiological condition in which it is imperative to restore and maintain the negative intrapleural pressure, which is achieved by negative intrapleural pressure (MIP) being the pressure produced by the diaphragm. Thus, it is logical to suggest that, if MIP is not excessively reduced after surgery, this is primarily due to diaphragmatic dysfunction. We believe that the above differences may be due to the different experimental conditions (quiet breathing versus maximum static pressures).

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A further theoretical but serious consideration is that of re-expansion pulmonary oedema (REPE). This has been associated with excessively negative pleural pressures after removal of air or fluid from the pleural space.

The study concludes that an ideal postoperative drainage system will “allow the maintenance of a negative intrapleural pressure, even in the presence of an air leak”. In our view a negative pleural pressure in this situation would only serve to encourage the egress of more air from the damaged lung surface into the pleural cavity, thus worsening the situation.

Whilst accepting that the postoperative situation may differ somewhat from that which pertains in a spontaneous pneumothorax because of the presence of fluid/blood in the pleural cavity, we would expect the same physiological principles to apply, especially in the presence of an air leak. There is a risk that the conclusions from this paper might be extrapolated into general respiratory practice and the scenario of spontaneous pneumothorax. For all of the above reasons we would urge caution before abandoning the standard and well tried technique of drainage of the pleural cavity (underwater seal) in favour of the suggested alternative, at least before data from larger, controlled clinical trials become available.


AUTHORS’ REPLY We thank Dr Henry and colleagues for their comments regarding our study. We must first emphasise that we were specifically addressing the situation may differ somewhat from that which pertains in a spontaneous pneumothorax because of the presence of fluid/blood in the pleural cavity, we would expect the same physiological principles to apply, especially in the presence of an air leak. There is a risk that the conclusions from this paper might be extrapolated into general respiratory practice and the scenario of spontaneous pneumothorax. For all of the above reasons we would urge caution before abandoning the standard and well tried technique of drainage of the pleural cavity (underwater seal) in favour of the suggested alternative, at least before data from larger, controlled clinical trials become available.

We welcome the opportunity to discuss this common but seldom debated area of respiratory practice. The standard and well tried method of underwater seal drainage is a source of many misunderstandings and complications. The Heimlich flutter valve, whilst accepted as being effective by many, has been shown to be clinically effective by Graham et al and others and further data from a randomised clinical trial in prolonged air leakage will soon be forthcoming.


Rare diseases

We welcome the series of articles on rare pulmonary disorders which started in the March 1999 issue of Thorax. In the introduction, reference is made to the series Tattersfield and Du Bois describe the frustrations felt by patients unable to obtain information about their rare pulmonary condition from clinicians with little or no experience of that disorder. The isolation of such patients is emphasised when they are unable to share their experiences with others diagnosed with the same disorder. Whilst we appreciate that this is true for many patients, we would draw attention to the massive range of information on rare pulmonary disorders available to both patients and doctors via the Internet. There are over three million UK subscribers to the Internet currently and, with the advent of digital television, this number will rise exponentially over the next few years. The problem then facing the patient (and clinician) is too much information. For example, lymphangioleiomyomatosis, the subject of the first article in the series, has over 500 Internet sites accessible worldwide to patients. We hope to provide assistance to patients who may lack confidence in knowing where to turn for information relevant to their needs.
The North East Thames Training Programme for Specialist Registrars has now an Internet based educational programme for medical trainees for over two years. Using this experience, trainees and trainers are now opening a website for patients with rare pulmonary disorders. The group is evaluating existing websites for validity of medical information and the relevance of presentation and content for patient rather than medical needs. It is hoped that the resulting reference site will index all available Internet information and allow patients to access information that is both reliable and relevant. To achieve this goal we are working with the help of patient support groups based with the British Lung Foundation, Organising Medical Networked Information (OMNI), and the Oxford University and British Library health care information team.

This is an enormous project which we feel will have increasing importance with time. We have already received offers of help from registrars in Wales, Scotland, and Australia. The North East Thames registrars welcome offers of co-operation from other similar groups.

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AUTHORS’ REPLY We agree with Dr Roberts that the Internet raises special issues for patients with rare diseases and that the problem is often too much information rather than too little. With respect to lymphangiolojomyomatosis (LAM), our approach in Nottingham has been to produce a four page fact sheet for patients which we have given to patients in the LAM Trust and to some of the doctors looking after the patients. The fact sheet was piloted amongst a few patients with LAM and modified in the light of the feedback we received. Some patients have obtained the fact sheet from the LAM Foundation in the USA which goes into slightly more detail than our document, particularly with respect to prognosis; as might be expected from an organiser of LAM. We will give further information whilst others do not.

Whether specialist registrar trainees should be deciding what patients with a rare disease should be encouraged to read is more debatable since some will never have met a patient with the disease in question. It seems more appropriate to us for fact sheets and information to be provided by people with some knowledge and expertise of managing patients with the particular disease, in conjunction with the patients themselves. The British Thoracic Society is planning to develop an orphan disease register and to encourage research into rare disorders. One of their responses will be to consider what information is required and how it should be presented and piloted.

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The paper by Murayama et al contains the unwary statement that their study may have been the first to demonstrate the suppressive effects of Aspergillus products on antifungal host defences by both human alveolar macrophages and PMNs. A search for Aspergillus in the eThorax website would have saved both them and your referees from accepting this. In a series of papers published in the 1980s Maura Robertson and I showed this in animal and human cells, demonstrated the paradoxical effect of complement and, perhaps importantly, showed that the substance produced by the spores had similar effects on soil protozoa, thus explaining the biological paradox as to why an organism that gains nothing from colonising animal lungs should have developed such exquisite antiphagocytic properties. Some of this work was summarised in our paper published in the Lancet in 1989. These effects are discussed in at least one well known textbook of respiratory disease.1 It is to be hoped that the “wheel reinventing” tendency of authors who search the literature back only five years and the short memory or ignorance of referees may be alleviated by use of your new web site.

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NOTICE

The Dr H M (Bill) Foreman Memorial Fund

The Trustees of the Dr H M (Bill) Foreman Memorial Fund invite applications for grants relating to study in respiratory disease. Limited funds are available for registered medical practitioners to assist in travelling to countries other than the UK to study only respiratory disease, and also for support for clinical research abroad. Intending applicants should write for further details to Dr Brian H Davies, Lindoahouse Hospital, Penarth, Vale of Glamorgan CF64 2XX, UK.
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