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. (Thorax 1999;54:1139–1140)

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 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.
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 devices 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 intrahemid septal defect. This degree of certainty is extremely rare, but has been demonstrated during life using both transthoracic and transoesophageal echocardiography. 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. The reported incidence of a patent foramen ovale varies from 5% to 30%. In younger adults with an ischemic 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%. 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.

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.

2 Nimmo AF, Drummond GB. Respiratory mechanics after abdominal surgery with emphasis on changes in chest wall compartment volumes on induction of anaesthesia with etomidate, propofol, and thiopentone. Br J Anaesth 1996;76:536–73.

LETTERS TO THE EDITOR

Surgery and respiratory muscles

In their review of the effects of surgery on the respiratory muscles Siakas and co-workers have cited my work incorrectly on two occasions. We reported a study of respiratory mechanics after abdominal surgery with measurements of the pressure-volume characteristics of the rib cage and abdomen. 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”. These observations, along with a short review of the published work on the subject, formed an editorial 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. This is supported by direct measurements of intravascular volume, which do not show these shifts.

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AUTHORS’ SUPPLY
We wish to thank Dr Drummond for pointing out the incorrect citation of his work in our recent review. We apologise for this, especially for quoting his editorial for the effects of laparoscopic cholecystectomy on the respiratory muscles. However, we have extensively discussed the semantics of the term “diaphragmatic dysfunction” in the methodological part of our review, sharing some of Dr Drummond’s views. Furthermore, we have cited the work of Dr Drummond and colleagues in the general discussion of the function of respiratory muscles during surgery, arguing that respiratory muscle dysfunction, in the general sense of the term, could influence functional residual capacity. We believe that this is in agreement with Dr Drummond’s findings that upper abdominal surgery alters the relative activity of respiratory muscles (including the abdominal muscles) leading to changes in the rib cage abdominal configuration (fig 1, Nimmo and Drummond).

Similarly, we have cited his work to support the argument that general anaesthesia causes volume displacement between the thoracic and abdominal cavities. Dr Drummond

4 Spons HJ, Drummond GB, Wrath PK. Changes in chest wall compartment volumes on induction of anaesthesia with etomidate, propofol, and thiopentone. Br J Anaesth 1996;76:536–73
The study by Waller et al. do not attempted 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 reexpand the pleural cavity. In this situation the pleural pressures will be higher than in the normal physiological state and, indeed, air will only exit the pleural cavity via a chest drain when the pleural pressure exceeds atmospheric pressure. Flutter valves are a double blind study. Thorax 1993:48:693–7.


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 worldwide. We hope to provide assistance to patients who may lack confidence in knowing where to turn for information relevant to their needs.

Postoperative air leaks

The study by Waller et al. argues that this could be due to the loss of skeletal muscles. We have no objection to this since the respiratory muscles are skeletal muscles too. Furthermore, the changes seen in the pattern of breathing after upper abdominal surgery and the relative contributions of the rib cage and abdomen during quiet breathing have been attributed by most investigators to dysfunction of the diaphragm. However, Dr Drummond’s experiments offer another explanation, pointing out the role of the abdominal muscles (the major expiratory muscles). Our own experiments have shown that upper abdominal surgery impairs the global strength of the inspiratory and expiratory muscles to produce maximum pressures. It is well known that the major contributor to the maximum inspiratory pressure (MIP) is the pressure produced by the diaphragm. Thus, it is logical to suggest that, if MIP is 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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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. 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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AUTHORS’ REPLY
We thank the editors for the opportunity to respond to the concerns raised by Professor Seaton. His group1,2 and Drs Mullbacher, Eicher et al in Australia3 are pioneers in studies of the antiphagocytic activity of Aspergillus culture products and they have done some excellent work. We cited some of their original articles in our previous paper. Professor Seaton et al have shown that spores and spore diffusates of A fumigatus suppress the production of superoxide anion and hydrogen peroxide by rodent phagocytic cells4 and that diffusates of A fumigatus spores inhibit phagocytosis of antibody coated radiolabelled sheep red blood cells by mouse peritoneal exudate cells. They have also performed experiments using human cells and have shown that spore diffusates of A fumigatus reduce the migration of human polymorphonuclear leukocytes and decrease the capacity of mouse peritoneal exudate cells to spread on glass. They have measured the ability of human pulmonary macrophages to bind and kill A fumigatus spores and have examined the effects on killing of heat labile serum components. However, they have not presented data on the suppressive effects of Aspergillus derived products on polymorphonuclear leucocyte mediated damage to A fumigatus. It has been considered that selective protection against Aspergillus spores by mononuclear phagocytes and against hyphae of Aspergillus by polymorphonuclear phagocytes are critical host defences in humans. Since Aspergillus spores enter mainly through the respiratory tract and proliferate in mycelial form in human tissues, our study has focused on interactions between Aspergillus spores and human alveolar macrophages, and also between Aspergillus hyphae and human polymorphonuclear leukocytes. In our study5 we showed that A fumigatus culture filtrate inhibited not only human polymorphonuclear leucocyte mediated A fumigatus hyphal damage but also inhibition of spore germination of A fumigatus by human alveolar macrophages, and suggested that A fumigatus derived products may suppress antifungal (anti-A fumigatus) activity of human alveolar macrophages and polymorphonuclear leucocytes.

To our knowledge, our study is the first to demonstrate the suppressive effects of Aspergillus derived products on human polymorphonuclear leucocyte mediated hyphal damage of Aspergillus and also on inhibition of spore germination by human alveolar macrophages.

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8 Schütz produces a variety of substances, not only respiratory disease, and also for support for clinical research abroad. Intending applicants should write for further details to Dr Brian H Davies, Landlough Hospital, Penarth, Vale of Glamorgan CF64 2XX, UK.

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 United Kingdom to study in respiratory disease, and also for support for clinical research abroad. Intending applicants should write for further details to Dr Brian H Davies, Landlough Hospital, Penarth, Vale of Glamorgan CF64 2XX, UK.