apoptosis and ischaemic neuronal death, whereas an increase in the pro-apoptotic protein Bax has been shown to promote cell death by caspase activation. Our observation that mild hypothermia increases the Bcl-2/Bax ratio following DHCA is consistent with cerebral protection via decreased apoptotic cell death.

Dr Sakurai is thinking ahead—given that there is protection, what cell types would be affected? In the experiments reported, we did not attempt to determine whether neurons were the primary site of brain injury but focussed on whether hypothermia can decrease the injury [2]. The extensive literature on this subject shows that cardiopulmonary bypass and deep hypothermic circulatory arrest induce neuronal injury. In our publication, we discussed neuronal injury; however, our data did not distinguish among the different cell types.

In an identical experimental protocol, we used the terminal DUTP nick-end labelling to detect apoptotic cells (TUNEL) stain on the perfused piglet brain following 6 h of post-bypass recovery (unpublished data). We observed that there were increased numbers of TUNEL-positive cells following DHCA but, because of the short recovery period, the numbers were too low to allow testing for an effect of hypothermia. While TUNEL cannot distinguish apoptosis from necrosis, it is a valuable marker of neuronal cell damage. Experiments using 12-h recovery periods, where the number of TUNEL-staining cells is substantially higher, are in progress. TUNEL measurements are being combined in our long-term experiments (12-h recovery) with haematoxylin and eosin (H&E) staining to analyse the morphological characteristics of cell death and with immunochemical staining for caspase-3. The preliminary results indicate that there is an increase of caspase-3 immunostaining cells in different regions of the brain, and this effect is diminished by mild hypothermia, particularly in the striatum.

We are aware that it is possible to observe the distribution of Bax, Bcl-2 or other proteins involved in cell injury or protection in tissue slices as well as through other measurements suggested by Dr Sakurai. We have used in situ hybridisation and autoradiograms to show that hypoxia induces expression of the 72-kDa heat-shock protein (hsp72) mRNA in different regions of the newborn piglets’ brain and that this was significantly diminished, particularly in striatum, by the depletion of dopamine prior to hypoxia [3]. In another model of hypoxia—repetitive apnoea—we have shown that striatum of apnoeic pigs has a larger number of fluoro-Jade-positive neurons than that of sham-operated animals [4]. Such studies can identify the type of cells affected and the regional specificity of the injury, but at the expense of quantification.

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References


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We appreciate and read with great interest the article by Winearl et al. reporting a rare case where the diagnosis of Enterococcus faecalis endocarditis was established after intra-abdominal bleeding due to rupture of the spleen [1].

We recently experienced a case of a sudden, fatal, massive intra-abdominal bleeding from splenic artery rupture due to a mycotic aneurysm. A 52-year-old man presented with high-grade fever and malaise. Clinical examination revealed a generalised abdominal tenderness and a long systolic cardiac murmur. A trans-thoracic echocardiogram confirmed severe mitral valve regurgitation with vegetation on the posterior mitral valve leaflet (1.3 cm × 1.1 cm). Blood cultures on admission were positive for Staphylococcus aureus, and therefore intravenous antibiotic treatment was commenced. An abdominal computed tomography (CT) scan revealed multiple, small, acute infarcts in the liver and spleen, consistent with septic emboli, as well as an intramural haematoma in the stomach. At the same time, the patient became unstable and inotropic support was needed. Thus the decision for an emergency operation was made, and an urgent mitral valve replacement was performed using a 31-mm Carbomedics (SORIN BIOMEDICA CARDIO S.r.l., Sallugia, Italy) mechanical valve. Following surgery, the patient recovered and was discharged from the intensive care unit on the
third postoperative day. He became mobile on the fourth postoperative day, and no abdominal complaints were noted. The treatment plan was to have the patient complete a full course of intravenous antibiotic treatment specific for infective endocarditis complicated by visceral septic embolisation.

On postoperative day 13, the patient suddenly collapsed. Resuscitation efforts proved unsuccessful for more than 20 min. Significant abdominal distension was noted during resuscitation. As a desperate effort, the patient was taken to the operating room and an emergency laparotomy was performed, which revealed massive intra-abdominal bleeding with the presence of 4 l of fresh blood and rupture of a splenic artery mycotic aneurysm. Unfortunately, the patient died in the operating room despite resuscitative efforts.

Special attention should be paid to patients with infective endocarditis and multiple emboli following surgical treatment of the endocarditis. The postoperative period can be complicated by the consequences of septic embolisation, one of which could be infective aneurysm formation. The peripheral vessels affected by septic emboli can develop aneurysmal changes; the natural history of which is rapid growth and rupture, if not excised [3]. Of the six cases of infected splenic artery aneurysm that are reviewed in the literature, rupture had occurred in three [2]. Visceral emboli should be carefully monitored during the postoperative period until the patient’s complete recovery and healing of any embolic foci. The risk of extracranial mycotic aneurysm formation, despite its reported low incidence, should be considered as it requires early recognition and prompt treatment [3].

References


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Reply to the Letter to the Editor

Reply to Charokopos et al.

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We thank Charokopos et al. [1] for their reply, and for presenting their interesting case describing fatal intra-abdominal haemorrhage secondary to a splenic artery mycotic aneurysm rupture in the setting of Staphylococcus aureus mitral valve infective endocarditis (IE).

It is clear that the embolic complications of IE are well recognised and can be associated with significant morbidity and mortality. Splenic rupture and mycotic aneurysm rupture secondary to embolic phenomenon, although rare, are two of the potentially catastrophic complications associated with visceral embolism and IE.

We postulate there may be a role for routine screening to exclude systemic embolism in patients with proven IE, in an attempt to reduce the risk of these catastrophic complications. This would result in heightened awareness of embolic complications and would help guide further therapeutic interventions.

At present, however, there are no standardised recommendations for the routine screening for embolic complications following the diagnosis of IE. This is particularly important as it is very difficult to predict those patients at risk of systemic embolism. A number of risk factors have been identified, which are associated with a high risk of embolism, including the valve involved, the size of the vegetation and the causative micro-organism [2]. These factors, however, only serve as a clinical guide.

A variety of modalities could be used in the screening for embolic complications, such as ultrasound scan (US), computed tomography (CT), magnetic resonance imaging (MRI), labelled white cell scan and positron emission tomography (PET), each having its own pros and cons including diagnostic efficacy and radiation dose involved for the patient.

Small studies have concluded that scanning with labelled leucocyte scintigraphy (using either technetium [3] or indium labels [4]) is inadequately sensitive in either the diagnosis of IE or its embolic complications.

At present, CT and MRI are the two most widely used modalities for the diagnosis of embolic complications of IE. Their use is guided by the clinical index of suspicion of embolism, but clearly, as neither investigation is without risk, their use as a screening tool must be balanced against factors including radiation dose, accessibility and cost.

The expanding role of PET as a diagnostic investigation for IE shows some promise, as studied by Yen et al., in six patients [5]. There are clear possibilities for the utilisation of PET in the pursuit of septic embolism — although there is currently