Prediction of neurological outcome after cardiopulmonary resuscitation by serial determination of serum neuron-specific enolase

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Aims Data on the diagnostic accuracy of neuron-specific enolase (NSE) as marker of hypoxic brain damage are conflicting. The purpose of this prospective observational cohort study was to explore the prognostic value of serum NSE after cardiopulmonary resuscitation (CPR) and to define the most sensitive cutoff value with a specificity of 100% for the prediction of persistent coma.

Methods and results Serum NSE concentrations were serially determined in 227 consecutive unconscious patients after CPR who were classified according to the best Glasgow–Pittsburgh cerebral performance categories (CPC, 1–4) achieved within 6 months follow-up. Sixteen patients were excluded due to incomplete NSE data and 34 due to death under analgesia sedation. The prevalence of poor neurological outcome (persistent coma, CPC 4) in our 177 analysed patients was 33%. At a specificity of 100%, a peak NSE concentration above 80 ng/mL predicted persistent coma with a sensitivity of 63%, a positive predictive value of 100%, a negative predictive value of 84%, and a predictive accuracy of 88%.

Conclusion A peak serum NSE concentration exceeding 80 ng/mL is a highly specific but only moderately sensitive marker for a poor neurological outcome after CPR.

KEYWORDS Cardiopulmonary resuscitation; Neuron-specific enolase; Neurological outcome

Introduction Severe hypoxic brain damage is the most serious adverse outcome after initial successful resuscitation from cardiac arrest. Accurate assessment of neurological prognosis in the early period after cardiopulmonary resuscitation (CPR) is needed to identify those who might benefit from intensive care and to avoid unnecessary prolongation of intense medical therapy for those who most probably would not want to exist if there is no possibility of meaningful recovery. Various methods have been evaluated for assessing the neurological prognosis of unconscious cardiac arrest victims, including clinical algorithms, electrophysiological tests, neuroimaging techniques, and biochemical markers. Neuron-specific enolase (NSE) was first found in extracts of brain tissue and later in neuroendocrine cells and neuroendocrine tumours including small-cell lung cancer. NSE is assumed not to be secreted to the extracellular fluid by the intact cell, but rather to be set free by destruction of cells with neuronal (or neuroendocrine) differentiation and its concentration in the blood may be proportional to the extent of hypoxic brain injury after cardiac arrest.

Numerous investigations have already examined the value of serum NSE for the prediction of an unfavourable neurological outcome after CPR. However, these studies are hampered by small sample sizes or selection bias and yielded conflicting results regarding the cutoff value of NSE above which no patient in the respective series ever regained consciousness.

When assessing the neurological prognosis of patients after CPR, the diagnostic test must show a specificity of essentially 100% for poor neurological outcome (i.e. persistent coma), because a procedure used to support non-treatment decisions should ideally have no false-positive results. Therefore, the aim of this prospective observational study was to explore the prognostic value of serum NSE after CPR in a large cohort of consecutive patients and to define a cutoff value for NSE with a specificity of 100% for the prediction of persistent coma while preserving the maximal possible sensitivity of the test.

Methods Study design and patients We examined prospectively all consecutive patients who returned to spontaneous circulation after non-traumatic, out-of-hospital, or
in-hospital cardiac arrest, but were unconscious and mechanically ventilated on admission to the intensive care unit of our hospital. The recruitment period extended from July 1998 to August 2004. All pertinent data were collected from the ambulance reports or hospital charts, respectively. Cardiac arrest was defined as cessation of cardiac mechanical activity, confirmed by the absence of a palpable arterial pulse in the absence of ongoing chest compressions, and apnea. Basic and advanced life support was provided by the local ambulance service or the in-hospital cardiac arrest team. The estimated time interval between initial collapse and return of spontaneous circulation (ROSC), defined as evidence of any palpable pulse in the absence of ongoing chest compressions, was recorded. Ventricular fibrillation and pulseless ventricular tachycardia were categorized as shockable rhythms, asystole and pulseless electrical activity as non-shockable. Patients were admitted to the intensive care unit, where standard medical management including invasive monitoring, haemodynamic support, mechanical ventilation, and analgesia sedation were provided. In selected patients with cardio-genic shock, an intra-aortic balloon pump (IABP) was inserted, and in patients with acute renal failure continuous venovenous haemofiltration (CVVH) was performed. Additionally, starting in February 2003 patients with an estimated time to ROSC of more than 5 min underwent immediate therapeutic hypothermia at the discretion of the attending physician using an intravascular cooling device (CoolGard 3000, Alsius Corp., Irvine, CA, USA) with a target temperature of 33°C for 24 h.

Serum NSE concentrations (Cobas Core NSE EIA/EIA II; Roche Diagnostics, Mannheim, Germany; normal range 0–15 ng/mL) were serially determined on admission (day 0) and on the following 4 days in the intensive care routine. The maximum of this series was labelled as the peak NSE concentration of each individual patient. Samples that showed visible haemolysis were strictly discarded to avoid any falsely elevated values for serum NSE due to the relatively high content of NSE in red blood cells and platelets.

Although the treating physicians were not blinded for the biochemical test results, appropriate therapy including full intensive care was given to all patients irrespective of NSE values. During the entire study period, we complied with the established local policy regarding withdrawal of intensive care, which was performed if either irreversible post-resuscitation multi-organ failure or brain death due to massive post-anoxic cerebral edema occurred.

Patients were transferred to a step-down unit (intermediate care unit or general cardiology ward) if they were successfully weaned from mechanical ventilation and haemodynamically stable. This policy was also applied to patients with persistent coma. However, once transferred, they were never returned to the intensive care unit in case of deterioration (e.g. respiratory complications) and further attempts of CPR were withheld.

The neurological outcome was evaluated according to the Glasgow-Pittsburgh cerebral performance categories (CPC, 1–5) of the Utstein recommendations, defined as follows: CPC 1, conscious and alert with normal neurological function or only slight cerebral disability; CPC 2, conscious and alert with moderate cerebral disability; CPC 3, conscious with severe cerebral disability precluding independent existence; CPC 4, comatose or in a persistent vegetative state; and CPC 5, brain dead. Awakening from coma was defined as reproducible obedience to simple verbal commands and/or presence of orienting eye movements. The best CPC achieved within 6 months after CPR was used to analyse the diagnostic accuracy of peak serum NSE concentration. Poor neurological outcome was defined as a best achieved CPC of 4 (persistent coma).

When this study was started in the year 1998, an institutional review approval for this observational investigation was not required by the local ethics committee and the need for informed patient consent was waived.

**Statistical analysis**

Data with normal or asymmetric distribution are described by mean and standard deviation (SD) or median and inter-quartile range, respectively. Differences between groups involving not normally distributed data were analysed by the Mann-Whitney U-test and those involving proportions by Fisher’s exact test (two-tailed). To adjust the alpha level for multiple comparisons, Bonferroni’s correction was used in the evaluation of daily NSE measurements.

The diagnostic accuracy of peak NSE values in predicting poor neurological outcome was evaluated by receiver operating characteristic (ROC) analysis. To avoid any false positive predictions of persistent coma (CPC 4), sensitivity, positive and negative predictive value, and predictive accuracy of the test with its corresponding 95% confidence intervals (CI) were calculated for the lowest (i.e. most sensitive) cutoff value of peak NSE concentration that resulted in a specificity of 100% in our study population. A bootstrap procedure was performed to estimate a 95% CI for this cutoff value. To allow limited validation, we used a split sample approach randomly dividing our data set into two equal halves and calculating the corresponding cutoff values for peak NSE. Logistic regression (method Wald) was performed to detect effects of various variables on neurological outcome: age, gender, location of cardiac arrest, bystander initiated CPR, first monitored rhythm, time from collapse to ROSC, use of therapeutic hypothermia, and peak NSE concentration. Results are presented as odds ratios (OR) and 95% CI. A two-sided P-value < 0.05 was considered statistically significant. All calculations were performed with SPSS statistical software (Version 13.0, SPSS Inc., Chicago, IL, USA).

**Results**

**General characteristics**

We enrolled a total of 227 consecutive patients (143 men, 84 women; mean age, 65 ± 15 years; range, 16–93 years) according to our inclusion criteria. The first monitored rhythm on the scene of CPR was ventricular fibrillation (or pulseless ventricular tachycardia) in 119 patients, asystole in 47, and pulseless electrical activity in 61. The presumed etiology of circulatory arrest could be attributed to a cardiac origin in 137 patients, to a non-cardiac origin in 79, and was unknown in 11. Time to ROSC varied between 1 and 60 min (median, 15; inter-quartile range, 5–25).

Sixteen of the 227 patients were excluded from the study due to incomplete NSE data: lack of serial analysis of serum NSE concentration due to technical errors in three patients, due to transfer to another hospital within 24 h after admission in two, and due to awakening within 24 h with early transfer to a step-down unit in the remaining 11. Another 34 patients were excluded because they died while under analgesia sedation before their neurological outcome could be reliably evaluated. Baseline data of the remaining 177 analysed patients are compiled in Table 1. The median duration of intensive care was 8 days (inter-quartile range, 4–17 days) in patients regaining consciousness (CPC 1–3) and 8 days (inter-quartile range, 5–11 days) in those remaining comatose (CPC 4). Therapeutic hypothermia was performed in 20 (11%) of our 177 analysed patients. In two patients (1%) an IABP was inserted and in 24 patients (14%) CVVH was performed during days 0–4 after CPR. During their stay on the intensive care unit, a do-not-resuscitate (DNR)-order was issued in 33 patients (19%) without any other restrictions of intensive care.

**Outcome variables**

A total of 118 patients (67%) regained consciousness, with good or moderately impaired cerebral performance (CPC 1–2) in 90 patients (51%) (CPC 1 in 46 patients, CPC 2 in 44 patients) and with severely impaired cerebral
performance (CPC 3) in 28 patients (16%), whereas 59 patients (33%) remained comatose (CPC 4). Total mortality within 6 months after CPR was 31% for patients with CPC 1–3 (in-hospital mortality 15%) and 93% for those with CPC 4 (all of whom died during their hospital stay after a median of 10 days, inter-quartile range 6–17 days).

Serum NSE levels

Peak NSE concentrations were significantly higher in patients with poor neurological outcome (CPC 4) (median, 132 ng/mL; inter-quartile range, 49–215) compared with those who regained consciousness (CPC 1–3) (median, 19 ng/mL; inter-quartile range, 14–29) \((P < 0.001)\) (Figure 1). A peak NSE concentration of 80 ng/mL (95% CI 63–93 ng/mL) was the lowest cutoff value with 100% specificity for the prediction of persistent coma. Of the 59 patients with poor neurological outcome, 37 (63%) showed a peak NSE concentration above this threshold. Neither the exclusion of patients with IABP or CVVH nor the exclusion of those with a DNR-order affected this cutoff value. No significant difference in peak NSE concentrations could be observed between patients with CPC 1–2 (median, 19 ng/mL; inter-quartile range, 14–26) and those with CPC 3 (median, 23 ng/mL; inter-quartile range, 15–34) \((P = 0.188)\).

Serial NSE determinations after cardiac arrest showed varying temporal profiles depending on the neurological outcome of the patients (Figure 2). Patients with CPC 1–2 and CPC 3 showed almost identical time courses of NSE with only minor median elevations of this biochemical marker. In contrast, in patients with CPC 4 median NSE concentrations increased considerably during the first 2 days after CPR. Individual peak NSE values were usually recorded between the second and fourth day resulting typically in a bell-shaped time course pattern. The cutoff value of 80 ng/mL was first exceeded on day 0, 1, 2, 3, 4 after CPR in one (2%), nine (15%), 23 (39%), three (5%), and one (2%) of our 59 persistently comatose patients, respectively. If these patients were discharged to a step-down unit as soon as this threshold was surpassed, the total number of intensive care days of 502 in this subgroup would be reduced by 186 (37%; 95% CI 33–41%). Significant differences in the levels of NSE between patients with CPC 4 and those with CPC 1–3 were observed during the entire study period \((P < 0.001, \text{for all days 0–4 after CPR with an adjusted alpha level of 0.0033})\). However, no significant differences in NSE concentrations could be observed between patients with CPC 1–2 and those with CPC 3.

Figure 3 shows the frequency of different neurological outcome categories in relation to the individual peak NSE concentrations of our patients. Whereas a peak NSE concentration beyond the cutoff value of 80 ng/mL was invariably associated with persistent coma, lower values did not always predict return of consciousness. However, the lower the peak NSE concentration of an individual patient, the higher was the probability of a better neurological outcome.

Results for sensitivity and specificity for the prediction of persistent coma were calculated for different cutoff values of peak serum NSE concentrations and are depicted as ROC curve showing an area under curve (AUC) of 0.931 (95% CI

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Baseline data of all 177 analysed patients</th>
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<tbody>
<tr>
<td></td>
<td>Out-of-hospital cardiac arrest ((n = 100))</td>
</tr>
<tr>
<td>Age, years</td>
<td>61 ± 15</td>
</tr>
<tr>
<td>Male gender, n (%)</td>
<td>59 (59.0)</td>
</tr>
<tr>
<td>First monitored rhythm, n (%)</td>
<td></td>
</tr>
<tr>
<td>Shockable</td>
<td>64 (64.0)</td>
</tr>
<tr>
<td>Non-shockable</td>
<td>36 (36.0)</td>
</tr>
<tr>
<td>Etiology of arrest, n (%)</td>
<td></td>
</tr>
<tr>
<td>Cardiac origin</td>
<td>66 (66.0)</td>
</tr>
<tr>
<td>Non-cardiac origin</td>
<td>27 (27.0)</td>
</tr>
<tr>
<td>Unknown</td>
<td>7 (7.0)</td>
</tr>
<tr>
<td>Bystander initiated CPR, n (%)</td>
<td>39 (39.0)</td>
</tr>
<tr>
<td>Time to ROSC, min</td>
<td>20 (10–30)</td>
</tr>
<tr>
<td>Blood lactate on admission, mmol/L</td>
<td>8.9 ± 3.6</td>
</tr>
<tr>
<td>Blood glucose on admission, mg/dL</td>
<td>255 ± 126</td>
</tr>
</tbody>
</table>

Values are expressed as number, percentage, mean ± SD, or median (inter-quartile range) as appropriate.
At a specificity of 100% (95% CI 97–100%), a peak serum NSE concentration of more than 80 ng/mL after CPR predicted persistent coma (CPC 4) with a sensitivity of 63% (95% CI 49–75%), a positive predictive value of 100% (95% CI 91–100%), a negative predictive value of 84% (95% CI 77–90%), and a predictive accuracy of 88% (95% CI 82–92%). No significant difference in any measure of diagnostic accuracy could be found between patients with therapeutic hypothermia and those not undergoing this procedure (predictive accuracy 85% vs. 88%; $P = 0.719$).

Split sample validation showed cutoff values for peak NSE of 73 and 80 ng/mL with corresponding AUC values of 0.914 (95% CI 0.832–0.996) and 0.951 (95% CI 0.911–0.991), respectively.

Logistic regression (Table 2) confirmed peak NSE concentration, first monitored rhythm and location of cardiac arrest as independent predictors of neurological outcome. The remaining tested variables usually associated with neurological outcome (age, gender, bystander initiated CPR, time to ROSC, therapeutic hypothermia) had either no effect or lost their independent predictive ability in the multivariable model because their influence on outcome seemed almost completely represented by the extent of post-arrest rise in NSE. The predictive accuracy of this model was 91% (95% CI 86–95%) compared to 88% (95% CI 82–92%) with the use of peak NSE concentration (at cutoff...
subject to inter-observer variability, whereas biochemical analysis. Additionally, clinical examinations are generally time-consuming. In contrast to neuroimaging techniques, the determination of biochemical markers requires no risky transport of unstable patients outside the intensive care unit.

In our study population, one case of intracerebral haemorrhage and another case of subdural haematoma were detected. Both patients died after 3 days in coma due to massive cerebral edema without any prior neurosurgical intervention, showing peak NSE concentrations of 110 and 188 ng/mL, respectively.

### Discussion

We explored the prognostic value of serum NSE in a large cohort of consecutive cardiac arrest victims who were unconscious on admission to the intensive care unit. The prevalence of poor neurological outcome (persistent coma, CPC 4) within 6 months follow-up was 33% in our 177 analysed patients. At a specificity of 100%, the most sensitive cutoff value of peak serum NSE concentration for the prediction of persistent coma was 80 ng/mL. Logistic regression revealed that a higher peak NSE concentration, a non-shockable first monitored rhythm, and an out-of-hospital cardiac arrest increased significantly the probability of persistent coma. However, the incremental value of this multivariable model regarding predictive accuracy was clinically negligible compared to the use of peak NSE concentration alone. Although limited by the small proportion of patients undergoing therapeutic hypothermia in our study, we could not confirm the results of a recent investigation where the diagnostic accuracy of serum NSE seemed to be lower in hypothermic compared to normothermic patients.

Prolonged time to ROSC, pathological brain stem reflexes, and a low Glasgow Coma Scale score several days after CPR are widely used predictors of poor neurological outcome. However, time to ROSC may be uncertain if the collapse was not witnessed. Moreover, analgesia and sedation severely interfere with the neurological evaluation of the patients, but may be unavoidable for prolonged periods of time predominantly in those with convulsions or multi-organ failure, necessitating mechanical ventilation of longer duration. Additionally, clinical examinations are generally subject to inter-observer variability, whereas biochemical analyses are much more unbiased in this regard.

Bilateral absence of N20 on SSEP is accepted as poor neurological outcome, whereas the classification as poor outcome can be disputed for any other study population to 87% and simultaneously diminished the number of patients with a better neurological course.

Table 2 Predictors of persistent coma (logistic regression)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Unit</th>
<th>OR (95% CI)</th>
<th>P-value</th>
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<tbody>
<tr>
<td>Peak NSE concentration</td>
<td>1 ng/mL</td>
<td>1.07 (1.04–1.11)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>First monitored rhythm</td>
<td>non-shockable vs. shockable</td>
<td>10.10 (2.30–44.24)</td>
<td>0.002</td>
</tr>
<tr>
<td>Cardiac arrest location</td>
<td>out-of-hospital vs. in-hospital</td>
<td>5.38 (1.12–25.86)</td>
<td>0.036</td>
</tr>
<tr>
<td>Age</td>
<td>1 year</td>
<td>1.02 (0.98–1.06)</td>
<td>0.389</td>
</tr>
<tr>
<td>Gender</td>
<td>male vs. female</td>
<td>1.85 (0.53–6.47)</td>
<td>0.337</td>
</tr>
<tr>
<td>Bystander initiated CPR</td>
<td>no vs. yes</td>
<td>1.74 (0.50–6.08)</td>
<td>0.390</td>
</tr>
<tr>
<td>Time to ROSC</td>
<td>1 min</td>
<td>1.03 (0.98–1.08)</td>
<td>0.310</td>
</tr>
<tr>
<td>Therapeutic hypothermia</td>
<td>no vs. yes</td>
<td>1.97 (0.31–12.39)</td>
<td>0.472</td>
</tr>
</tbody>
</table>

Compared to other investigations dealing with serum NSE after CPR sensitivity (at 100% specificity) for prediction of persistent coma in our study lies in the middle of the published range of ~40–90%, whereas our cutoff value for NSE seems to be rather high in comparison to other studies with reported thresholds between 25 and 120 ng/mL. There are several reasons for these discrepancies. First, criteria for definition of poor neurological outcome differed between investigations. Some studies classified patients with CPC 3 together with CPC 4 as poor neurological outcome, accordingly their cutoff values for NSE were consistently lower than ours. We did not use this approach, because only persistent coma (with or without subsequent death) is generally accepted as poor neurological outcome, whereas the classification as poor outcome can be disputed for any other neurological state. Secondly, various laboratory assays for the determination of serum NSE may yield deviating results. Therefore, our proposed cutoff value may not be applicable if one of the other commercially available tests is used. To provide interchangeable results with assays from different manufacturers, an internationally accepted standard for serum NSE determination is imperative. Thirdly, selection bias has been introduced in two recently published studies which consequently cannot provide an unbiased estimate of the diagnostic accuracy of peak NSE concentration. In both investigations, decisions about treatment withdrawal in comatose patients were made after 3 days of intensive care primarily depending on the absence of N20 on SSEP. Therefore, these studies explored the sensitivity of NSE not independently of SSEP results. One investigation included only patients who were still unconscious at 24 h after CPR. This approach artificially increased the prevalence of poor outcome in the study population to 87% and simultaneously diminished the number of patients with a better neurological course. Consequently, the probability to detect patients awakening despite NSE values above the chosen cutoff value of 33 ng/mL was substantially reduced which affects negatively the practical advantage of biochemical markers lies in the ease of data acquisition. In contrast to electrophysiological testing, no sophisticated technical equipment has to be transported to the bedside. Moreover, SSEP may not always be readily available, appear relatively time-consuming and may be prone to potential sources of electrical interference in the setting of a busy intensive care unit.
certainty of the reported 100% specificity for this threshold. Of note, if we had adopted this repeatedly proposed cutoff value for NSE, 5, 14–16 17 (9.6%) of our 177 analysed patients would have been falsely classified as poor neurological outcome, whereas in fact nine of these patients scored eventually as CPC 1–2 and the remaining eight patients as CPC 3.

Single outliers of high NSE concentrations should always be viewed with caution because visible but overlooked haemolysis in a single serum sample may be the true reason for this phenomenon leading to a potentially fatal misclassification of a patient’s prognosis. Extreme caution should be applied to NSE values determined while intra- or extracorporeal pumping systems (IABP, CVVH, ventricular assist devices, cardiopulmonary bypass) are in operation which may cause mechanical destruction of blood cells with consecutive release of NSE. 19 We suggest paying attention to this problem even if we could not confirm its presence in our study population including only a small number of patients with IABP or CVVH.

In the exceptional patients with a primary intracranial origin of their cardiac arrest, the relative contributions of the intracraniatal mass lesion and the diffuse anoxic damage to the rise in serum NSE concentrations may be difficult to separate. However, earlier studies 5 showed that the prognostic value of a high serum NSE concentration due to cerebral origin seems to be largely independent of its particular cause as exemplified by our two patients with combined incidents.

Although extremely rare, the coincidental occurrence of NSE producing tumours such as small-cell lung carcinoma, neuroblastoma, or carcinoid tumours should be kept in mind when using this method for prognostic assessment after cardiac arrest. However, in these cases the time course of serial NSE determinations is expected to show a persistent elevation rather than the typically bell-shaped pattern of patients with a poor neurological outcome after CPR.

Limitations

Physicians were not blinded for the potential prognostic variables studied. Moreover, there was no defined minimal time period of optimum treatment. However, we eagerly avoided any influence of known NSE values on clinical treatment decisions in the intensive care unit, because we were well aware of the serious risk of self-fulfilling prophecy if decisions would have been influenced by the test results. Although this study was prospective, our reported cutoff value for NSE was data-derived. However, the method to obtain this threshold was clearly defined in advance requiring a specificity of this test procedure of 100% to predict persistent coma. Nonetheless, a large prospective and blinded validation study with defined endpoints in terms of treatment duration and intensity seems still warranted, particularly for the growing number of patients undergoing therapeutic hypothermia after CPR.

Conclusion

A peak serum NSE concentration exceeding 80 ng/mL is a highly specific but only moderately sensitive marker for a poor neurological outcome after CPR. Although a simple, reliable, and readily available test, clinical decisions with potentially irreversible consequences should never rely on a single marker but only be made in the context of all available prognostic information.

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References

Clinical vignette

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Echocardiographic detection of intracardiac non-metallic foreign body complicated by infective endocarditis

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An 11-year-old boy was referred for unexplained fever of 3 months. Laboratory tests showed elevated white blood cell count with a left shift, and decreased haemoglobin level. Blood cultures at admission were negative. Chest radiograph displayed no abnormal findings. The illness responded poorly to antibiotics. Echocardiography revealed moderate-sized, highly mobile, non-homogeneous masses in both atria, with ‘stalk’ attached to each side of the interatrial septum (Panel A). The mass in the left atrium protrudes into the left ventricular inflow tract during diastole (Panel B). The ‘stalk’ of the masses appeared like a ‘fragment of a catheter’ penetrating the septum (Panel C). At open-heart surgery, the masses were successfully excised, together with a small portion of the muscular part of the septum around the point of attachment (Panel D). Surprisingly, a 6 cm-long and 0.1 cm-diameter bamboo stick (Panel D) was discovered in the left atrium with one of its tips pointing towards the septum where the masses attached. The bamboo stick was removed followed by septum repair.

On further investigation, it was learnt that the boy had a history of falling over himself and chest injury 1 year before, but without known injury of his heart. Cultures from the removed masses grew Serratia marcescens. Histopathological examination confirmed the masses to be vegetations. Cefminox and Etimicin were prescribed for antibiotic therapy. The boy recovered rapidly and was discharged uneventfully. On follow-up visits, he showed complete recovery from the disease without recurrence of fever 6 months after the operation.