



**Figure 1.** Postintubation subglottic stenosis and confirmation of proper placement for the Vergnon silicone stent

In this report, the bronchoscopy revealed tracheal stenosis. Not only early diagnosis but also early stent placement was possible in this patient with subglottic tracheal stenosis. The early placement of tracheal silicone stents may prevent the need for major surgical interventions.

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## Anaphylaxis during cardiac surgery for hypertrophic cardiomyopathy: pathophysiological and therapeutic considerations

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Sir,

In a very interesting report published in *Anaesthesiology Intensive Therapy* [1], a 40-year-old female patient suffering from hypertrophic obstructive cardiomyopathy and being on metoprolol therapy developed anaphylaxis with profound hypotension and cutaneous manifestations while being scheduled for an elective, surgical septal my-

ectomy. Chlorhexidine was used for skin disinfection prior to the insertion of an arterial line. The patient received phenylephrine, midazolam, fentanyl, propofol and rocuronium both before and during the anaesthesia induction. Subsequently, she was treated with epinephrine boluses, hydrocortisone, diphenhydramine and salbutamol via the ventilatory circuit. However, a transesophageal echocardiographic examination showed that the epinephrine boluses had caused obstruction of the left ventricular outflow tract and the patient went clinically into cardiogenic shock. With an urgent cardiopulmonary bypass, protamine directly into the aorta and cefazolin administration, she had an excellent surgical result and favourable clinical improvement. Although a skin prick test was negative for rocuronium, he was confirmed to have an allergy to chlorhexidine.

While this report is interesting, it raises important questions related to the cause of anaphylaxis in anaesthesia, the

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role of anaesthetic drugs and the treatment of anaphylaxis in patients with hypertrophic obstructive cardiomyopathy.

1. Anaphylaxis in anaesthesia: Diagnosing anaphylaxis in anaesthesia becomes problematic due to the fact that cutaneous manifestations such as flushing, urticaria, or angioedema may be absent, while several substances commonly used in the perioperative setting have been implicated in inducing anaphylaxis. These substances include drugs such as antibiotics, neuromuscular blocking drugs, latex, and disinfectants. A recent study has shown that 68% of patients who experienced anaphylaxis in the operating room had a history of atopic diathesis [2]. Apart from the grading system classification from 1 to 5 [3] and the 'mild', 'moderate', or 'severe' system [4], a new classification of perioperative anaphylaxis has been suggested recently that comprises the following [5]: Grade a — moderate, grade b — life-threatening and grade c — cardiac arrest with or without respiratory arrest. According to the latter, the above-described patient had developed grade c anaphylaxis to antiseptic chlorhexidine associated with cutaneous involvement.
2. The role of anaesthetic drugs: The reported patient was administered 5 different drugs for the induction of anaesthesia, namely phenylephrine, midazolam, fentanyl, propofol, rocuronium together, chlorhexidine topically for skin disinfection. Although two drugs were administered for the treatment of anaphylaxis, namely epinephrine and salbutamol, the patient went clinically into cardiogenic shock. All these anaesthetic drugs have been incriminated as inducing mild or severe allergic reactions [6–11]. Thus, physicians and anaesthetists should always remember that the more allergens a patient is exposed to, the easier and quicker anaphylactic shock and Kounis syndrome appear [12].

Furthermore, bronchodilator treatment with salbutamol (albuterol) can induce cardiovascular collapse as occurred in a 77-year-old woman with an asthma exacerbation [13]. In this patient, an echocardiogram revealed hyperdynamic ventricles with obliteration of the left ventricular cavity during systole that was associated with systolic anterior motion of the mitral valve compatible with hypertrophic cardiomyopathy. There was also mild concentric left ventricular hypertrophy and slight asymmetric hypertrophy of the basal septum. Therefore, this case has some similarities with the reported patient.

On the other hand, while epinephrine is life-saving in anaphylaxis, it usually contains sodium metabisulphite as a preservative. The latter also behaves as an allergen [12]. The question that arises in this report is whether or not the above-described patient was sulphite-sensitized. Only few physicians are aware of this hazardous association.

3. Anaphylaxis in patients with hypertrophic obstructive cardiomyopathy: Treating anaphylaxis in patients

with this type of cardiomyopathy may be dangerous. Anaphylactic events create acute decrease in preload, decrease afterload, increase the heart rate and increase myocardial contractility that could exacerbate dynamic left ventricular outflow obstruction. Anaphylaxis can induce myocardial ischemia from coronary vasospasm and Kounis syndrome that appear to play a significant role in the etiology of myocardial ischemia in patients with hypertrophic cardiomyopathy [14],

It has been recently found that patients with hypertrophic cardiomyopathy are associated genetically with atopic diathesis. Indeed, hypertrophic cardiomyopathy associated genes have been found to contribute to the development of eosinophilic esophagitis, a disease in which chest pain can be the primary symptom [15]. Furthermore, patients with this type of cardiomyopathy may present hypersensitivity myocarditis towards the drugs they are taking, a life-threatening but also a potentially treatable complication [16].

Therefore, anaesthetists and surgeons should take consideration on all of the above while additional monitoring with an intraoperative transesophageal echocardiogram examination would be helpful in managing anaphylaxis in such patients with such hemodynamic responses to anaesthetics administered during surgery.

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## In response to: Anaphylaxis during cardiac surgery for hypertrophic cardiomyopathy: pathophysiologic and therapeutic considerations

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We are most appreciative for the comments from Dr. Nicholas G. Kounis [1] and his colleagues regarding our recent publication describing the challenging case of anaphylactic shock in patients suffering from hypertrophic obstructive cardiomyopathy (HOCM) scheduled for surgical treatment, namely myectomy [2]. Their letter raises several important concerns regarding anaphylaxis in anaesthesia and particularly in patients with HOCM. Before we address each point, we would like to mention that several topics discussed by authors were mentioned in our case report but could not be described in detail due to space limitations. In this context, several comments made by Dr. Kounis provide excellent complimentary information to our case reports.

The authors of this letter have indicated that the diagnosis of anaphylaxis may be difficult while the patient is under general anaesthesia and subsequently during emergence from anaesthesia [3]. In the described case, patient presented several symptoms typical for severe anaphylactic reaction: arterial hypotension, high airway pressures, airway swelling and skin rash. Additionally, after initiating a cardiopulmonary bypass which stabilized patient hemodynamic collapse, we obtained a blood sample to test for mast cell tryptase. This approach is in agreement with current practice of diagnosing anaphylaxis during the perioperative period [3, 4]. The test came positive, confirming the occurrence of severe anaphylactic reaction. Finally, after recovery following cardiac surgery, the patient was referred to an allergologist

and additional skin tests confirmed a strong sensitivity to chlorhexidine.

Concerns were also raised about the role of anaesthetic drugs in the development of anaphylaxis. Indeed, several medications used to induce and maintain general anaesthesia have been described as strong allergens. The most common are non-depolarizing muscle relaxants and antibiotics [2, 3]. Dr. Kounis and colleagues have suggested that salbutamol could aggravate hemodynamic collapse; this is an excellent point as this beta mimetic certainly causes tachycardia, which can worsen hemodynamic compromise in patients suffering from HOCM. Additionally, they suggested that preservatives present in ampoules of epinephrine (for example, sulphites) may also contribute to allergic reactions. We checked the contents of epinephrine ampoules used in our hospital and they are preservative-free. Finally, the authors of the letter asked the question about possibility of Kounis syndrome, which is defined as the concurrence of acute coronary syndromes with conditions associated with mast cell activation, involving interrelated and interacting inflammatory cells, and including allergic or hypersensitivity and anaphylactic or anaphylactoid insults [5–7]. Again, it is an excellent point and all anaesthesiologists should be aware of this phenomenon. However this diagnosis was unlikely in the presented patient since a transesophageal echocardiography demonstrated excellent contractility of both ventricles without any features of regional wall motion abnormalities.

Dr. Kounis and colleagues pointed out another important genetic association — HOCM and atopic sensitivity. This is again an excellent point and one which alludes to our conclusions that patients suffering from this rare genetic disorder (HOCM) should be treated in tertiary referral centres, which can offer extracorporeal support in cases of hemodynamic collapse induced by anaphylactic reaction including Kounis syndrome.

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