Initial Experience With a New Biodegradable Airway Stent in Children: Is This the Stent We Were Waiting for?

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Summary. Objective: To report our experience with a new type of biodegradable airway stent in the setting of severe tracheobronchial obstruction in children. Design and Methodology: We conducted a retrospective and prospective (since June 2014) study of pediatric patients with severe airway obstruction treated with biodegradable stents in our institution between 2012 and 2015. The following data were collected: demographics, indication for stenting, bronchoscopic findings, insertion technique complications, clinical outcome, stent related complications, re-stenting, and time of follow-up. Results: Thirteen custom-made polydioxanone stents were placed in four infants (mean age, 4 months) with severe tracheobronchial obstruction: tracheomalacia (two patients), bronchomalacia (1), and diffuse tracheal stenosis (1). All the stents were bronchoscopically inserted uneventfully. Immediate and maintained clinical improvement was observed in every case. No major stent related complications have occurred and only mild or moderate granulation tissue was observed during surveillance bronchoscopy. Two patients required repeated stenting as expected. All the patients are alive and in a good respiratory condition with a follow-up ranging from 5 to 40 months. Conclusions: Biodegradable airway stents seem to be safe, effective, and cause fewer complications than other types of stents. They can be an alternative to the classic metallic or plastic stents for severe tracheal stenosis or malacia in small children. More experience is needed in order to establish the definite clinical criteria for their use in pediatric patients. **Pediatr Pulmonol.**

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INTRODUCTION

Tracheobronchial obstruction is a rare condition in the paediatric age group and is usually due to malacia or stenosis. Management varies from a conservative approach to complex surgical procedures depending on the clinical situation of the patient and the type and extension of the disease.[1] Endoscopic treatment of airway obstruction with metallic stents was first reported by Filler et al. in 1995,[2] since then several groups have reported their experience with stenting with variable results.[1,3–5] In our institution, 39 children with severe tracheobronchial obstruction have been treated with intraluminal stents in the last 22 years. Most of the patients (23/58.9%) were treated with metallic balloon-expandable Palmaz stents (Johnson & Johnson Interventional Systems, Warren, NJ) and 12 (30.7%) with plastic or hybrid stents. Increasing experience with airway stenting together with the awareness of possible severe stent related complications have led us to try a new biodegradable stent.[6]

The aim of this study is to show our initial experience with absorbable airway stents in children, with special concern on safety and clinical effectiveness.

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MATERIALS AND METHODS

The clinical charts of patients treated with biodegradable stents in our unit, from March 2012 to July 2015, were retrospectively reviewed. The following data were collected: demographics, indication for stenting, bronchoscopic findings, insertion technique complications, clinical outcome, stent related complications, re-stenting, and time of follow-up. In order to compile as much information as possible and record the experience of other institutions, a prospective national airway biodegradable stent database has been instituted since June 2014. This study was approved by our institutional ethics and research committees, and informed consent was obtained from the parents of every patient.

We have used biodegradable self-expanding stents (ELLA-CS, Hradec Kralove, Czech Republic) which were custom-made according to the patient́s airway size and needs. The decision to perform stenting was made by the staff of our multidisciplinary pediatric airway team considering the clinical situation of the patient and the information obtained from both bronchoscopic exploration and CT-scan study. These data were also useful in order to obtain the cross-sectional measurements of the stent. In our unit, stenting is not a first line treatment and other therapeutic options are considered, or tried, before deciding to use an airway stent.

The SX-ELLA biodegradable stent consists on a polydioxanone (PDS) monofilament, which is a semicrystalline polymer that degrades by random hydrolysis. It has its own dedicated delivery system which comprises a hollow plastic guiding tube with an olive at the end.[7] The stent was placed under general anesthesia, with rigid bronchoscopy and fluoroscopic control. When deployed, the stent has some degree of shape memory and tends to coil, achieving its nominal diameter after a few hours. This stent maintains its full mechanical strength for the first 6–7 weeks after placement and degrades completely after 14–15 weeks. More detailed biomechanical and physical properties have been described elsewhere.[6,7]

RESULTS

Thirteen biodegradable stents were placed in four infants (mean age, 4 months) with severe tracheobronchial obstruction: tracheomalacia (TM) (two patients), bronchomalacia (BM) (one patient), diffuse tracheal stenosis (one patient). All the stents were bronchoscopically inserted uneventfully. Immediate and maintained clinical improvement was observed in every case. No major stent related complications have occurred and only mild or moderate granulation tissue was observed during surveillance bronchoscopy. Two patients required repeated stenting as expected. All the patients are alive and in a good respiratory condition with a follow-up ranging from 5 to 40 months. More detailed information of these four patients is given below.

Patient 1

This 2-month-old girl was referred to our unit for surgical treatment. She had a diagnosis of congenital tracheal stenosis (CTS) and left pulmonary artery sling. Preoperative bronchoscopy and CT-scan showed that the entire trachea was severely stenotic (2 mm diameter) (Fig. 1). Slide tracheoplasty (STP) and left pulmonary artery reimplantation were performed under cardiopulmonary bypass. Due to the length of the stenosis, tracheal reconstruction had some degree of anastomotic tension albeit surgical release manoeuvres. Subtotal dehiscence of the anastomosis occurred and the patient was re-operated in the 4th postoperative day performing a new STP. Again, bronchoscopy disclosed anastomotic failure so the endotracheal tube was advanced to the carina in order to stent the whole trachea and promote secondary healing. Follow-up bronchoscopy 2 weeks after demonstrated healing of the dehiscent trachea with a diffuse severe re-stenosis.

Repeated endoscopic balloon dilations (3.5–6 mm) did not yield satisfactory results so we decided to place a tracheal stent. Recent experience with biodegradable airway stents reported by the National Service for Severe Tracheal Disease in Children from Great Ormond Street Hospital in London encouraged us to try them in this particular patient.[7] A custom-made self-expanding PDS stent (5 mm diameter × 15 mm length, SX-ELLA) was inserted in the distal trachea 3 months after STP. Definite clinical respiratory improvement made discharge possible soon after. As expected, repeated stenting after stent absorption has been necessary in seven more occasions

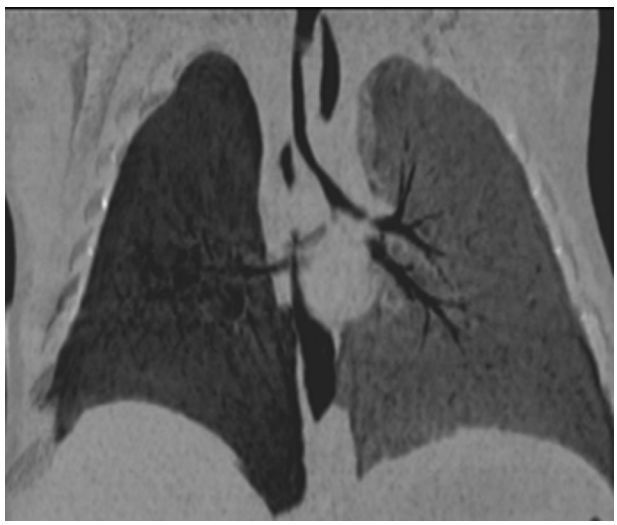

Fig. 1. Initial CT-scan study disclosing a diffuse and severe congenital tracheal stenosis.

(total, eight stents). Every new stent was inserted when degradation of the previous one was almost complete, between 3 and 4 months after placement. We have gradually increased stent diameter (5–8 mm) and length (15–35 mm) in order to provide internal support to the entire trachea. Follow-up bronchoscopies have shown good tissue tolerance with only mild granulation tissue. Currently, the patient́s trachea is not stented and she has an almost normal life for her age 40 months after the first stenting intervention. A control thoracic CT-scan has shown tracheal growth with an enhanced tracheal diameter (narrowest cross section, 6 mm) (Fig. 2).

Patient 2

This full-term female baby with oesophageal atresia and distal tracheoesophageal fistula (EA & TEF) was operated soon after birth in her hometown hospital. Although the fistula was successfully closed and esophageal integrity achieved, she showed apnoeic-near death episodes (ALTE) due to severe associated TM. She was referred to our institution for evaluation and surgical treatment. Aortopexy was performed at the age of 3 months with only partial clinical improvement. Postoperative bronchoscopy disclosed residual severe segmental TM (Fig. 3). Re-do aortopexy was disregarded due to the inherent surgical risks and a temporal tracheostomy was offered by our team but rejected by the patient's parents. Despite our limited experience with biodegradable airway stents, this therapeutic possibility was extensively discussed with the baby's parents and finally selected as the most appropriate option.

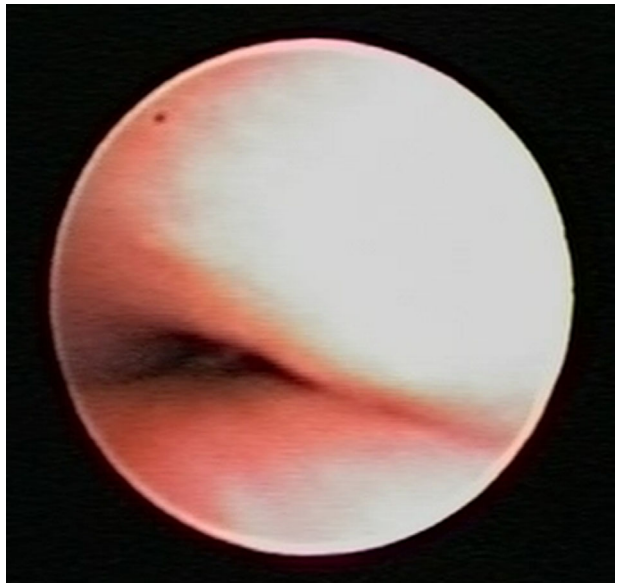

Fig. 3. Bronchoscopic view: persistent tracheal collapse after aortopexy.

A PDS biodegradable stent (8×30 mm) was bronchoscopically placed in the patient's trachea at the age of eight months (Fig. 4). Insertion was uneventful and clinical improvement was immediate. As expected, the patient required a second similar stent 4 months after because of recurrence of respiratory symptoms. Bronchoscopy showed nearly complete stent resorption, mild granulation tissue and persistent tracheal collapse. Her clinical status improved after this second stent but

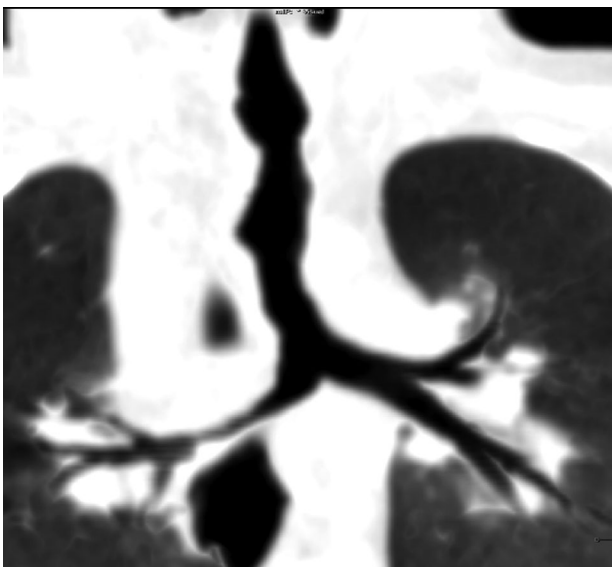

Fig. 2. Follow-up CT-scan after eight consecutive biodegradable stents showing tracheal growth with an enhanced diameter.

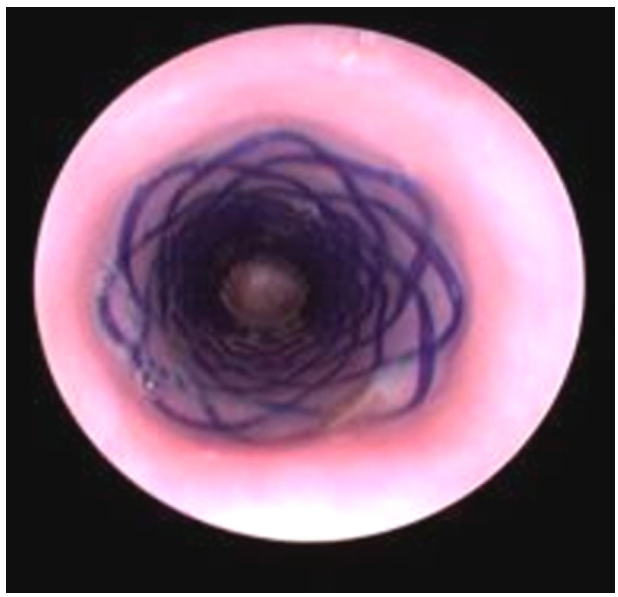

Fig. 4. Biodegradable PDS tracheal stent after bronchoscopic insertion.

15 weeks later the patient showed symptoms related to airway obstruction. A bronchoscopy was performed disclosing moderate granulation tissue at the level of the stent gold marks which was treated with balloon dilation. A third custom made PDS biodegradable stent (8×30 mm), with no gold marks, was endoscopically inserted a few days later with complete resolution of symptoms. Surveillance bronchoscopy performed 5 months after showed mild tracheal collapse with no granulation tissue. Currently, the patient is 2 years old and remains in good clinical condition, without a tracheal stent, 9 months after the last stenting procedure.

Patient 3

This 3-month-old male infant was referred to our unit because of severe respiratory symptoms secondary to a presumed TM. Bronchoscopy and CT scan showed segmental distal tracheal collapse due to vascular compression. Aortopexy and innominopexy, with intraoperative bronchoscopic control, were performed through a median sternotomy. In the postoperative period, failure to extubate the patient led us to perform a bronchoscopy that showed absence of tracheal collapse but severe bronchomalacia (left main bronchus). A 5×15 mm PDS biodegradable stent was ordered and placed bronchoscopically 2 weeks later (Fig. 5). The respiratory situation of the patient improved dramatically and extubation was possible 24 hr after. Surveillance bronchoscopy performed 3 months after stent insertion disclosed a patent left main bronchus with mild granulation tissue and an almost completely degraded stent. At present, no further stenting has been necessary (5 months follow-up).

Patient 4

This 2-month-old female infant showed a severe cardiovascular malformation consisting on a vascular ring with hypoplasia of the distal right aortic arch and an aberrant left subclavian artery, plus ventricular and atrial septal defect (VSD, ASD) and anomalous systemic vein return. This complex vascular anomaly caused external airway compression with total collapse of the distal trachea and left main bronchus. An aortic arch repair together with pulmonary artery (PA) banding and percutaneous VSD closure were performed by the cardiac team. Nevertheless, tracheobronchial collapse was not relieved and the patient remained intubated and ventilated.

Initial airway management consisted on a tracheostomy with a long adjustable tube in order to stent the distal trachea and provide a more effective ventilation. This approach was unsuccessful due to the difficulty on maintaining the tube exactly in the carina and obstructive respiratory episodes occurred. Because a second surgical procedure was necessary in order to remove the PA banding, repair left pulmonary veins stenosis and relieve tracheal vascular compression, we decided to insert a biodegradable stent (8×25 mm) as a "bridge" treatment to improve the patient's clinical situation and permit the definitive surgical intervention. This stent was placed in the distal trachea, next to the carina, and the tip of tracheostomy tube lied inside the upper end of the stent (Fig. 6). Although lung ventilation improved and the obstructive episodes disappeared, granulation tissue was a concern and bronchoscopic removal including laser photoresection was necessary in two occasions. Frequent secretion aspirations through the tracheostomy tube may have played a role in granulation tissue formation.

Three months after stent placement the final surgical intervention was accomplished. This included PA debanding, left pulmonary veins repair with a sutureless technique, direct ASD closure, translocation of pulmonary branches (Lecompte maneuver), distal tracheopexy and left main bronchopexy. Postoperative bronchoscopy showed a substantial improvement of the tracheobronchial collapse with nearly complete resorption of the stent. At present, the patient is almost ventilator independent (follow-up, 5 months).

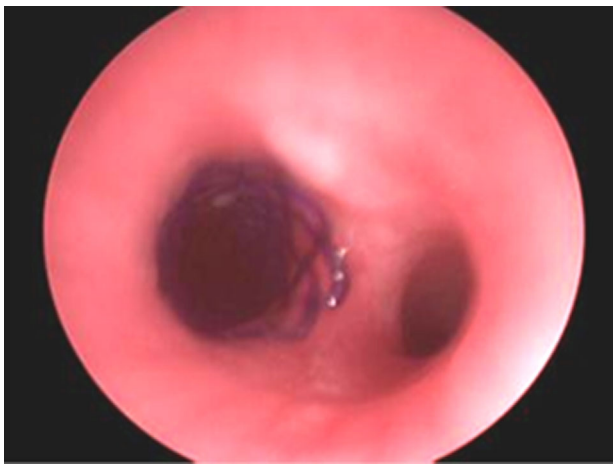

Fig. 5. Bronchoscopic view of a biodegradable stent in the left main bronchus.

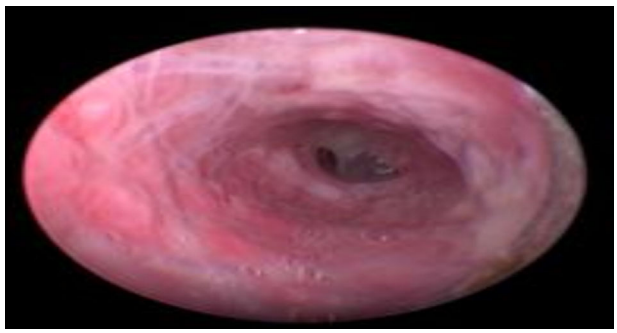

Fig. 6. Bronchoscopic view: PDS tracheal stent 7 weeks after placement.

DISCUSSION

Several surgical or endoscopic techniques have been described for the treatment of severe tracheobronchial obstruction in children.[8–12] Stent therapy aims to give internal support to the airway and keep the lumen open. In most cases it is a temporary measure until the airway regains its structural integrity with growth, or other therapeutic alternatives are available.[1]

As a general rule, airway stenting in children is not a first line treatment and it is usually used when other surgical or endoscopic procedures have failed or are not indicated.[12] Various stenting options are currently available for the pediatric airway. In our practice, we have used balloon-expandable metallic stents, plastic-silicone devices and hybrid stents.[1] Each one has its own pros and cons, so the "ideal" airway stent is not yet available.

Palmaz metallic stents seem to be the most widely used in children.[1,12,13] They can be easily placed through a rigid bronchoscope, or an endotracheal tube, and are balloon expanded to the desired diameter. This type of stent does not interfere with mucous clearance and migration is infrequent. On the other hand, granulation tissue formation is a matter of concern and most authors consider metallic stents permanent once inserted.[12,13] Severe complications such as: excessive granulation tissue formation, arteriobronchial fistulas, or airway perforation have been reported.[12,14,15] Conversely, other authors communicate satisfactory long-term outcomes in treating infants with airway metallic stents.[16] Our own experience (seven patients with metallic stents in place for more than 5 years) demonstrates fewer complications than expected in the long-term and a mild to moderate impact in the quality of life related to respiratory health (non published data). Nevertheless, the difficulty or impossibility of stent removal after a few weeks and the need to keep dilating the stent as the child grows are important issues that limit their use in children.

Silicone-type stents are the most frequently used in adult patients. Placement and removal are relatively easy and they are usually well tolerated. On the other hand, they can become obstructed by thick secretions and stent migration is a frequent issue.[1,5] Hybrid stents try to get together the advantages of metallic and plastic devices while diminishing their drawbacks. Their limited availability in the pediatric size as well as the usually bulky delivery system required for placement have significantly restricted their use in small children.[12]

In order to avoid, or decrease, complications related to airway stenting research has focused on the development of absorbable stents.[6,17,18] Currently, there are several biodegradable materials available for making this type of device, and it has already been tested in other organs such as esophagus, biliary duct or the vascular system.[6,19] Polydioxanone airway stents were initially used in adult patients with bronchial stenosis after lung transplantation.[20] This limited, but encouraging experience, together with ongoing research studies, have expanded their use to other clinical settings such as benign tracheal stenosis, tracheobronchomalacia, or as an internal support of the donor graft in pediatric tracheal transplantation.[7] Common complications of airway stenting are mucous plugging, granulation tissue formation, stent migration, and erosion.[12,21] Despite the scarce clinical experience with this new biodegradable stent, it seems that fewer complications occur compared to other types of stents. Moreover, biocompatibility and tissue tolerance seem to be their main features.[7] On the other hand, degradation of the stent in a relatively short period of time may require repeated stenting and limit their use in long-standing or chronic diseases. This fact was a matter of concern when we decided to use it for the first time in an infant with a diffuse and very severe tracheal re-stenosis. Being a desperate case, we consulted with international tracheal transplant experts to see if she could be a candidate for tracheal substitution. This procedure was finally disregarded due to the complexity of the technique and the limited experience. We tried balloon dilation of the stenosis but proved ineffective when dealing with very severe tracheal narrowing, so stenting emerged as the best option for the maintenance of tracheal lumen patency. Available metal or plastic stents did not seem to be the most adequate in this particular case so we tried the new biodegradable stent. Following the initial experience reported by Vondrys et al.[7] we ordered a 5×15 mm custom made stent that was bronchoscopically inserted in the patient's trachea at the age of 5 months. The patient's clinical situation improved significantly although, as predicted, repeated stenting has been necessary. Re-stenting was performed when respiratory symptoms appeared, or worsened, and this usually occurred between the 10th and 15th week after insertion. In fact, placement of a new biodegradable stent overlapping a previous one, not completely resorbed, was performed uneventfully. At present, the patient's trachea is not stented (7 months since the last stenting procedure) and, although she may need another stent in the future, several definite advantages have resulted from this approach: (1) the patient is alive, at home and ventilator independent; (2) her respiratory status has progressively improved over time; (3) fewer stent-related complications have occurred compared with other type of stents; and (4) we buy time until the stenosis gets stabilized, as it seems to be happening, or other therapeutic alternatives become available.[22]

Severe TM secondary to congenital TEF is probably the best indication for biodegradable stenting. Because spontaneous improvement usually occurs in the second or third year of life, as the trachea grows and gets stiffer,

absorbable stents may be a good option. Aortopexy is a highly successful technique when properly indicated but requires a thoracotomy, or median sternotomy, and diverse surgical complications have been reported.[23] Two or three consecutive biodegradable stents providing internal support to the trachea during the most critical period of time may be a reasonable alternative, as it happened in our second patient after a failed aortopexy. With more experience, this technique even may become a first line treatment in this selected group of patients.

Tracheo-bronchial collapse due to vascular external compression is a relatively common clinical condition in patients with severe congenital cardiovascular anomalies. As a general rule, airway stenting is not used if there is a feasible surgical procedure to relieve airway compression.[7] In this setting, biodegradable stents can play a role as a "bridge" treatment until a definitive surgical correction is performed, allowing a more stable clinical situation or even weaning the patient from mechanical ventilation. This was the case in patient 4 of our series, in whom together with vascular repairing techniques, tracheopexy and bronchopexy achieved permanent airway patency.

Airway stenting in children is a controversial topic. Some authors state that the currently available stents for children can cause a high rate of severe complications that may supersede the airway compromise that necessitated their initial placement.[14,15] Other reports show satisfactory outcomes with metallic and /or plastic stents.[1,3,16] At the end, there seems to be a basic general agreement that stents may play a role in selected cases in which there are no surgical alternatives, or be a life-saving procedure in extremely sick patients.[12] It is clear that although we do not have yet the "ideal" stent, some children may benefit from this non-invasive therapeutic option.[1,12]

Despite our limited experience, we consider that biodegradable stents are safe, effective, and cause fewer complications than other types of stents. Certainly, more experience is needed in order to establish the clinical criteria for their use in children, and research should address relevant issues such as: the eventual histologic changes in the stenotic or malacic airway while the stent is in place and after resorption, or the design of new devices with a longer useful life. If all these matters are elucidated, we possibly may hypothesize that this is the stent we were waiting for.

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