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Bioabsorbable Steroid Eluting Stents in the Treatment of Recurrent Rathke's Cleft Cyst

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Abstract

Objectives Bioabsorbable steroid eluting stents may prevent the stenosis of ostia after sinus surgery. We describe a technique utilizing this technology to prevent the reformation of Rathke's cleft cysts (RCC) after transnasal transsphenoidal surgical drainage.

Design This study is based on retrospective review.

Setting The research took place at Tertiary academic medical center.

Participants Patients who underwent endoscopic marsupialization of RCC with stent placement were participated in this study.

Main Outcome Measures Demographics, surgical history, outcomes, and complications were primary measures of this study.

Results Four patients underwent drainage of a recurrent RCC with subsequent stent placement. All patients consented to off-label use of the stent. The mean age of patients was 42 years old and the number of prior drainage procedures ranged from 1 to 3. The stent was placed directly into the opening of the cyst after drainage with no other tissue placed into the cyst cavity or opening. The stents are bioabsorbable and were not removed after surgery but were evaluated endoscopically at 2 and 6 weeks after surgery. The patients have been followed for a mean of 14 months after surgery with no evidence of recurrence on endoscopic exam or imaging. No patient had cerebrospinal fluid leak during or after the operation or permanent endocrinopathy.

Conclusion The use of a bioabsorbable steroid eluting stent had no unanticipated consequences and all drainage pathways of all the RCCs remain patent. The use of this technology may decrease recurrence rates in revision or complex cases where patients have extensive scarring of the operative field from prior drainage procedures. Further follow-up of the current cases and study in a larger cohort are warranted.

Keywords
- Rathke's cleft cyst
- stent placement
- skull base
- steroid eluting stents
- recurrence

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Introduction

Rathke's cleft cysts (RCC) arise when the region between the adenohypophysis and neurohypophysis formed during the 3rd or 4th week of gestation does not regress fully and remains patent, creating an enclosed cyst which manifests as benign sellar and/or suprasellar lesions. The RCC consists of an epithelial membrane, while the inside is filled with mucinous or caseous cystic fluid. Typically, the lesions are asymptomatic but some exhibit growth and compress surrounding neurovascular structures which may lead to headaches as well as visual and endocrine disturbances.

The reported recurrence rate after drainage or resection varies widely in the literature from 0 to 30%, with a recent meta-analysis reporting an 8% rate of recurrence after endoscopic transsphenoidal surgery.[1,2] Risk factors for recurrence include purely suprasellar location,[3,4] inflammation and reactive squamous metaplasia in the cyst wall on pathology or MRI (magnetic resonance imaging),[4–7] large cyst size,[6] and superinfection of the cyst.[8] Additionally, some authors recommend against packing the sellar defect unless a cerebrospinal fluid (CSF) leak is present due to the increased risk of recurrence if residual cyst wall epithelium is prevented from draining into the sphenoid sinus[3,9]

Kinoshita et al suggested that there are three methods for preventing the reaccumulation of RCCs: complete removal of the cyst wall, stopping the secretion of mucus from epithelial cells, and making a permanent marsupialization of the RCC.[6] Extended resection of the cyst wall is not commonly performed due to the high incidence of postoperative endocrine dysfunction and lack of evidence of decreased rate of recurrence for primary lesions.[4–7,10] Several techniques for destroying remnant epithelial cyst lining and preventing the secretion of mucus, such as instillation of alcohol and hydrogen peroxide have not been proven efficacious.[7,11,12] Therefore, we sought to improve the creation of a permanent stoma between recurrent RCCs and the sphenoid.

Bioabsorbable steroid eluting stents have been shown in ethmoid and frontal sinus surgery to decrease the need for postoperative interventions and systemic steroids.[13–16] In frontal surgery, they decrease the rate of restenosis and in ethmoid surgery, the rate of adhesion and synechia formation is decreased.[13–17] The stents are designed to last approximately 30 days. Given the increase in patency and decrease in scarring due to stent placement in sinus surgery, the decision was made to utilize the technology in revision transnasal transsphenoidal (TNTS) marsupialization procedures where patients had significant buildup of scar tissue. Our retrospective review examines the demographics, surgical history, outcomes, and complications of patients who underwent the drainage and stenting procedure.

Methods

The University of California, Los Angeles (UCLA) Institutional Review Board approved this study. We performed a retrospective chart review of the patients who underwent endoscopic TNTS for marsupialization with subsequent stent placement for a recurrent RCC, diagnosed based on histopathologic analysis from prior surgeries or from the most recent procedure. The stents (Propel Mini, Intersect ENT, Palo Alto, California) consist of a bioabsorbable, sustained drug release platform of poly-(DL-lactide-co-glycolide) and polyethylene glycol embedded with 370 micrograms of mometasone furoate which is gradually released over time.[18] Patient demographics (age, gender, past medical and surgical history, and length of follow-up), lesion characteristics (size, imaging), surgical and reconstruction techniques (marsupialization, grafting, stent placement), and outcomes (postoperative endocrinopathy, vision, CSF leak, recurrence on imaging or endoscopic exam, and headaches) were collected.

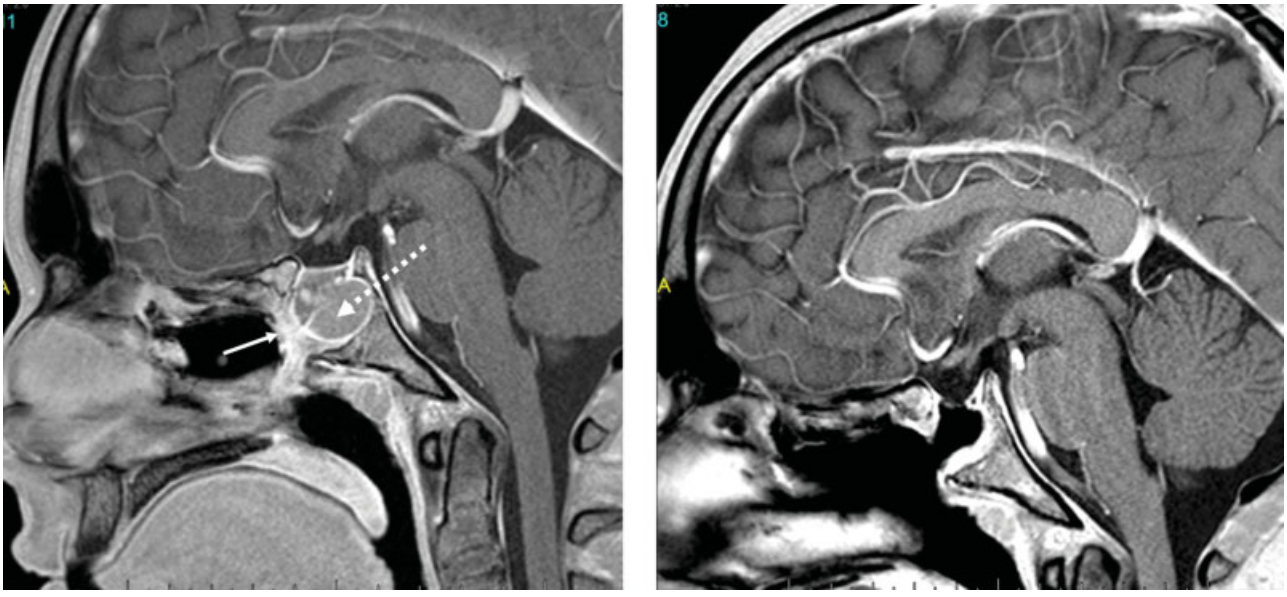

Fig. 1 Left image: second recurrence of Rathke's cleft cyst, marked by dashed arrow, with significant scar tissue buildup marked by solid arrow. Right image: 6-month follow-up MRI with no cyst or stent remaining.

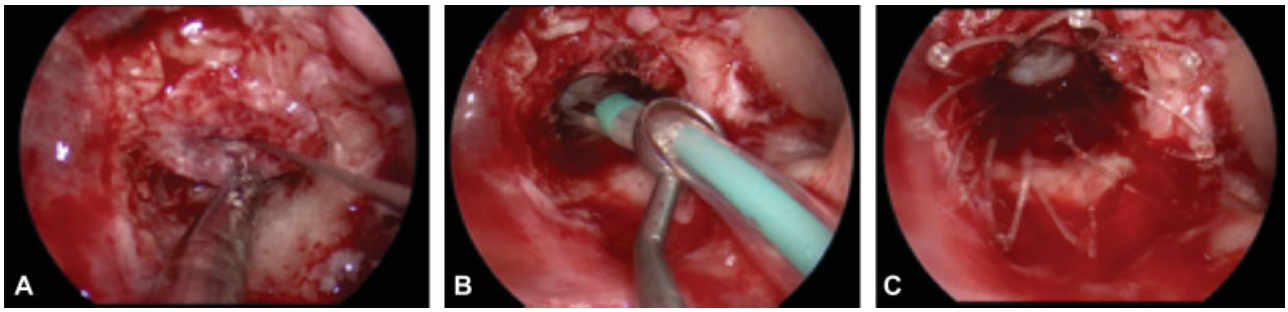

Fig. 2 (A) The recurrent Rathke's cleft cyst is opened, note scar tissue from prior procedures. **(B)** The stent is placed in the cyst opening. **(C)** The stent is well situated and cyst opening is patent.

Due to the small sample size, statistical analysis was limited to descriptive analysis.

Marsupialization

A revision TNTS approach allowed for wide access to the sella (see ►**Video 1**). Scar tissue was removed both bluntly using a Freer elevator and sharply using a feather blade and endoscopic scissors. As all cases were revisions, the bone overlying the sella had previously been removed, but drilling was done to further expand the prior opening, remove osteoneogenesis, and decrease the height of the clivus. Once a wide opening was achieved and scar tissue was removed, a transverse incision was made in the cyst (►**Fig. 2**, also see ►**Video 1**) and the cyst contents were carefully removed using a suction, forceps, and ring curette as needed. The cyst cavity was further exteriorized by removing the anterior wall with scissors, cutting forceps, or Kerrison rongeurs. Hemostasis was obtained with bipolar forceps and a gelatin-thrombin hemostatic matrix (placed around but not into the cyst cavity).

Video 1

Operative video of steroid eluting stent placement in a recurrent Rathke's Cleft Cyst. Online content including video sequences viewable at: www.thieme-connect.com/products/ejournals/html/10.1055/s-0038-1675558.

Stent Placement

A prior publication discussed our institution's typical reconstruction protocol with free mucosal grafting.[1] As the patients had recurred despite this technique or other reconstruction techniques (►**Table 1**), the decision was made to offer them stent placement. The risks and benefits were thoroughly discussed with the patients, and a separate consent form was signed which acknowledged their understanding of the experimental, off-label use of the device. For three patients, the stent was placed using the delivery device either alone or guided by a ring curette (►**Figs. 1** and **2**, also see ►**Video 1**), and for one patient the device was placed with a forceps without the delivery device due to the angle of the sella (see ►**Video 1**). The stent was checked at 2 and 6 weeks after the surgery to ensure continued proper placement and complete dissolution (►**Fig. 3**, also see ►**Video 1**). High-volume, low-pressure nasal irrigations were started within 1 to 2 weeks after surgery to aid in dissolving stents.

Results

Four patients underwent drainage of a recurrent RCC with subsequent stent placement. The mean patient age was 42 years old, and the number of prior drainage procedures ranged from 1 to 3 (►**Table 1**). The patients had undergone prior surgery a mean of 4.8 years previously (range: 0.9–8 years). Two of the four patients had chiasmal compression on MRI with vision change, while the other two patients had headaches as an indication for surgery. All patients had a minimum of one prior drainage procedure at an outside hospital (one patient had two), with or without one prior drainage procedure at UCLA.

The stent was placed directly into the opening of the cyst after drainage with no other tissue placed into the cyst cavity or opening. One patient had had a prior nasoseptal flap which was viable when raised from the sella and so was replaced to reline the sphenoid cavity but did not contact the cyst walls. The stents are bioabsorbable, and were not removed after surgery but were evaluated endoscopically at 2 and 6 weeks after surgery (►**Fig. 3**, also see ►**Video 1**). All patients had patent openings into the sphenoid. All patients had stents in place and not displaced at their 2-week operative visit while no patients had stents remaining at their 6-week visit. None of the patients had crusting or granulation of the cyst fenestration postoperatively.

The patients have been followed for a mean of 14 (range: 3–24) months after surgery with no evidence of recurrence on endoscopic exam or imaging. On endoscopic exam, in all four patients the fenestration remains patent. Two patients had postoperative imaging with no residual cyst. No patient had CSF leak during or after the operation or permanent postoperative endocrinopathy. No patient reported worsening of vision postoperatively.

Discussion

The use of bioabsorbable steroid eluting stents had no unanticipated consequences and the drainage pathways of all the

Table 1 Cases of recurrent Rathke's cleft cyst marsupialization with steroid eluting stent placement

Patient	Gender	Age (in y)	Presenting symptom(s)	Number of prior surgeries	Y since last surgery	Prior reconstruction	Size on MRI (mm)	Reconstruction	Number of mo of follow-up	Postoperative complications	Postoperative imaging
1	M	< 30	Headache, fatigue	2	0.9	Free mucosal graft	21 × 16	Steroid eluting stent	24		No residual cyst at 18 mo
2	F	> 50	Diplopia	3	4.6	None	13 × 14	Steroid eluting stent	18	Diabetes insipidus, resolved without treatment	None available
3	F	30–50	Headache, weight gain, polyuria	2	8	Nasoseptal flap	9 × 11	Steroid eluting stent + Nasoseptal Flap to re-line sphenoid	12		None available
4	F	> 50	Visual changes, headache	1	6	Sella packed with bone, gel sponge, sealant	21 × 14	Steroid eluting stent	3		No residual cyst at 3 mo

Abbreviations: F, female; M, male; MRI, magnetic resonance imaging.

RCCs in this series have remained patent. This is the first report of steroid eluting or bioabsorbable stents being used in RCC. In theory, marsupialization decompresses the cyst and provides a widely opened, relaxed, dependent drainage pathway, and at the same time avoids inadvertent injury to surrounding structures.[1] By working only on the anterior surface of the cyst, the risk of intraoperative CSF leak is also decreased.[1] Bioabsorbable steroid eluting stents may allow the drainage pathway to heal in an open position and decrease the formation of scar tissue, thus decreasing recurrence rates in difficult cases where patients have extensive scarring of the operative field from prior drainage procedures.

After extensive literature review, we could find only one prior abstract which describes the use of a cysto-sphenoid stent.[19] Five patients underwent stenting, two of these patients for recurrent RCC and three for primary RCC.[19] The stents were not bioabsorbable and were removed at 1 month postoperatively in three patients; one patient had an asymptomatic retained stent, and one patient required revision surgery for cyst recurrence and retained stent.[19] One patient also developed a minimal asymptomatic recurrence which did not require revision.[19] The authors concluded that the use of a retrievable stent may decrease restenosis but postoperative scarring may prevent retrieval and contribute to cyst recurrence.[19] The use of a bioabsorbable stent obviates the need for stent retrieval and the use of a steroid eluting stent may help decrease local scar tissue which contributes to cyst recurrence.

Risks of drug eluting stents include displacement and unknown effects of topical steroid exposure close to the pituitary gland. The stents, while elastic and expandable, are soft and conformational due to their lattice pattern and thus are unlikely to cause trauma. We monitored for displacement with serial endoscopy and saw no evidence of displacement in any patient. At 2 weeks after surgery, the stents were less rigid than at insertion and nasal irrigations had begun to increase the speed of stent absorption. The stents in all four patients were fully dissolved by 6 weeks after surgery. In terms of safety of steroid dosing close to the pituitary, no patient demonstrated endocrinopathies on routine postoperative blood tests. During prior safety testing of the technology, five patients had bilateral stents placed in the ethmoid cavity and had blood drawn prior to surgery and at postoperative days 7, 14, 21, and 30.[13] Plasma mometasone furoate concentration was below the quantification limit at all-time points.[13] Mean cortisol concentrations at baseline and at follow-up time points were within normal limits without evidence of adrenal suppression.[13] Further testing is required to ensure that this pattern continues with placement of the stent in the pituitary fossa.

Contraindications to the use of steroid eluting stents include hypersensitivity to the steroid or the polymer component. We would also consider active sphenoid infection and intraoperative CSF leak as relative contraindications for placement. The steroid eluting stent has no antimicrobial properties and placement of the implant in an infected surgical field may lead to biofilm creation and infection of the stent itself. Similarly, placement in a surgical field with active CSF leak could lead to ascending infection, foreign

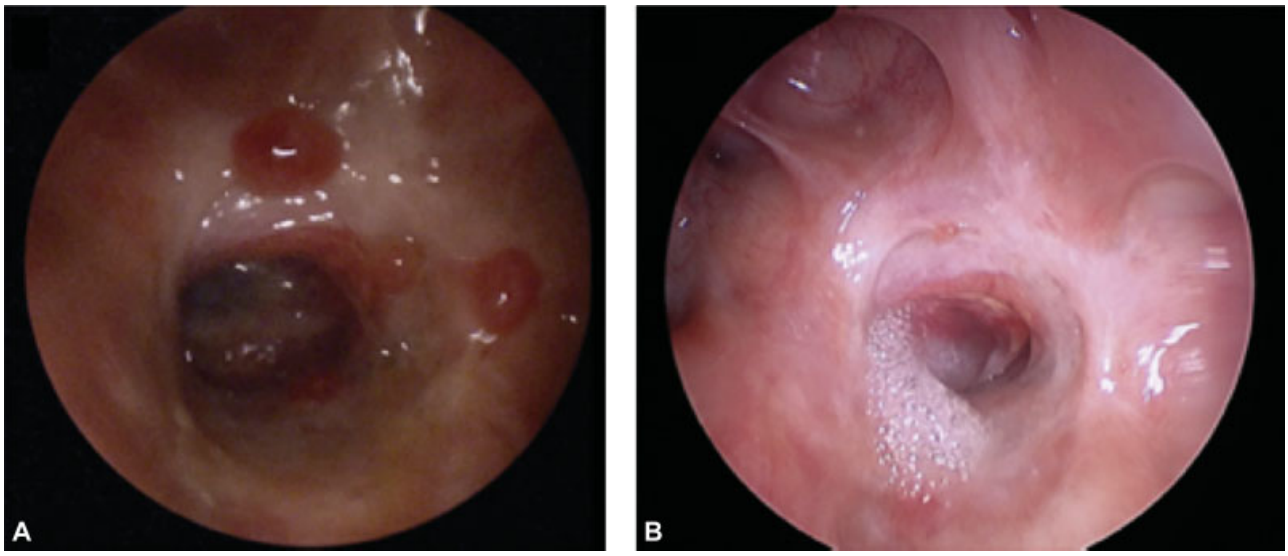

Fig. 3 (A): 6 weeks postoperatively after stent dissolved and **(B)** 6 months postoperatively.

body reaction, or steroid elution directly into the intracranial space. All patients in our series were found to have no CSF leak at the end of the surgery, including with Valsalva to a pressure of 30 mm of mercury, prior to stent placement.

As the diaphragma sella may be thin after surgery, we restrict patients from activities which may lead to increased intracranial pressure, such as scuba diving and lifting weights heavy enough to require Valsalva maneuver or straining. As the sphenoid antrostomy is patent, we also recommend that patients not have blind placement of objects, such as nasogastric tubes or nasal packing in their nasal cavity.

A major limitation of our study is the short follow-up period. The recommended postoperative follow-up period of RCCs is at least a decade.[5,20] One study found that 94% of patients with recurrent RCC were diagnosed within 5 years of surgery.[6] Overall, radiological evidence of recurrence has been reported in 20 to 22% of patients, with symptomatic recurrence in up to 57 to 64% of patients with radiologic findings.[4,21] Further follow-up of the current cases as well as study in a larger cohort is warranted. We also do not routinely obtain cortisol levels postoperatively and so cortisol levels were only available for the patient with diabetes insipidus and were within normal limits on postoperative days 1 and 2. All patients were followed by the Endocrinology team with no clinical evidence of abnormal cortisol levels. Prospective studies with serial cortisol testing are necessary to ensure that no adrenal suppression occurs with placement of the steroid eluting stent.[13] We chose to publish these preliminary findings as there have been no prior reports of utilizing a bioabsorable or steroid eluting stent to improve the maturation of a connection between the RCC and the sphenoid cavity. Moreover, with office endoscopy, we are able to check continued patency of the opening of the cyst into the sphenoid sinus using our described surgical technique (see ►**Fig. 2**) and therefore do not need to rely on serial imaging to determine recurrence. The use of new stenting technology represents a possible solution for patients suffering from multiple, symptomatic recurrences of an RCC.

Conclusion

We report the first four patients, to our knowledge, who underwent bioabsorbable, steroid eluting stent placement after marsupialization of recurrent RCCs in an effort to decrease the risk of scar tissue obstructing the drainage pathway leading to further recurrence. The use of the technology had no unanticipated consequences, no patients had permanent endocrinopathies, and all stents dissolved within the expected timeframe. Further studies are necessary to determine whether steroid eluting stent placement in the drainage pathway of RCC leads to a decrease in the risk of recurrence, especially in patients with recurrent RCC.

Financial Disclosures
The authors have no financial disclosures or conflicts of interest. Of note, none of the authors have or have ever had a consulting or other financial relationship with Intersect ENT.

Conflicts of Interest
None.

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