Post–transanal endoscopic microsurgery (TEM) syndrome: a constellation of symptoms resulting from localized inflammatory changes after TEM

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Background: Transanal endoscopic microsurgery (TEM) is a safe and effective therapy for local excision of rectal lesions, but early postoperative infectious and inflammatory complications are variably defined in the literature. The aim of this study was to describe post-TEM syndrome, a cluster of postoperative symptoms related to a local inflammatory process seen in a subset of patients after TEM.

Methods: We conducted a retrospective cohort study using prospectively collected observational data of all patients who underwent TEM at St. Paul's Hospital in Vancouver, British Columbia, between 2006 and 2017.

Results: During the study period, 795 patients were treated by TEM at the study institution. Of these, 56 patients had postoperative pain or fever and 26 patients were determined to have post-TEM syndrome based on our definition. Sixteen patients presented within the first 2 postoperative days, with all patients presenting within 1 week. All patients who underwent cross-sectional imaging (n = 11) had a combination of inflammatory changes with stranding and free fluid, or with small bubbles of free intraperitoneal, retroperitoneal, or mesorectal air, or with both; they did not have signs of free perforation or abscess at the surgical site. Nearly all patients with post-TEM syndrome (96%) did not progress to further infectious complications. Most patients' (92%) post-TEM symptoms resolved within 1 week of conservative treatment.

Conclusion: We provided a description of post-TEM syndrome, the constellation of symptoms arising from a localized inflammatory response in a subset of patients after TEM. This syndrome is uncommon, and nearly all patients recovered with conservative management without a need for more invasive intervention.

Contexte : La microchirurgie endoscopique transanale (MET) est une modalité sûre et efficace pour l'exérèse locale des lésions rectales, mais la description des complications postopératoires infectieuses et inflammatoires à court terme est variable dans la littérature. Le but de cette étude était de décrire le syndrome post-MET, un ensemble de symptômes postopératoires lié à un processus inflammatoire local observé chez une portion de la patientèle soumise à une MET.

Méthodes : Nous avons procédé à une étude de cohorte rétrospective à partir de données observationnelles recueillies de manière prospective auprès de l'ensemble de la patientèle soumise à une MET à l'Hôpital St-Paul de Vancouver, en Colombie-Britannique, entre 2006 et 2017.

Résultats : Au cours de l'étude, 795 personnes ont été traitées par MET dans l'établissement où se déroulait l'étude. Parmi ces personnes, 56 ont éprouvé des douleurs ou fait de la fièvre après l'intervention et 26 présentaient un syndrome post-MET selon notre définition. Seize personnes ont consulté le lendemain ou le surlendemain de l'intervention; et elles avaient toutes consulté au cours de la première semaine. Chez toutes les personnes ayant subi une épreuve d'imagerie transversale (n = 11), on a noté un ensemble d'anomalies, telles que la présence de filaments et de liquide libre, et de petites bulles d'air libre intrapéritonéales, rétropéritonéales ou mésorectales, ou les deux. Ces personnes ne présentaient pas de signes clairs de perforation ou d'abcès au site chirurgical. La grande majorité des cas de syndrome post-MET (96 %) n'ont pas progressé vers d'autres complications infectieuses. Les symptômes post-MET de la majorité des personnes (92 %) sont rentrés dans l'ordre dans la semaine suivant un traitement conservateur.

Conclusion : Nous avons décrit le syndrome post-MET, l'ensemble de symptômes consécutifs à une réponse inflammatoire locale chez certaines personnes ayant subi une MET. Ce syndrome est peu fréquent et la presque totalité des cas sont rentrés dans l'ordre après une prise en charge conservatrice sans recours à une intervention plus effractive.

Emerging surgical techniques require awareness of both benefits and complications as adoption increases. The use of advanced, minimally invasive platforms for the local excision of rectal neoplasms has become a standard approach to appropriately selected rectal lesions.[1] These techniques can be broadly classified as transanal endoscopic surgery (TES), of which transanal endoscopic microsurgery (TEM) and transanal minimally invasive surgery (TAMIS) are the 2 most common platforms. Several benefits of TES over conventional transanal excision of rectal lesions have been described. For instance, TES is generally associated with improved margin status and local recurrence;[2,3] TES is a well-tolerated procedure, with a reported complication rate of 1.3%–8.3% and a perioperative mortality rate of 0.0–2.8.[4] Several complications of TES have been described, including urinary retention, postoperative bleeding, intraperitoneal entry, abscess, and suture line dehiscence.[3] Infectious complications are relatively uncommon and are heterogeneously reported in the literature.[5–12]

St. Paul's Hospital (SPH) in Vancouver is a high-volume TEM centre, performing an average of nearly 100 procedures a year. Clinicians have noted that a subset of patients develop a localized inflammatory response after TEM, involving a constellation of symptoms and imaging findings not currently described in the literature. A proposed definition for post-TEM syndrome was developed to better define this condition and allow for enhanced reporting in future study. The syndrome encompasses a constellation of symptoms including postoperative abdominal or pelvic pain and fever, along with signs of localized inflammatory changes on blood work and cross-sectional imaging. The aim of this study was to describe the occurrence of this syndrome at SPH and review the current TES literature for reports that fit this definition, with an overview of presentation and management.

Methods

Design and setting

We conducted a retrospective cohort study of all patients who underwent TEM at SPH between 2006 and 2017. At SPH, TEM is the TES procedure performed, using a 40-mm operating endoscope, TEM combination insufflating system, and endomotion articulating arm (Richard Wolf GmbH) with a conventional laparoscopic camera (Storz Medical AG).

Reporting

We adhered to the Strengthening and Reporting of Observational Studies in Epidemiology (STROBE) statement.[13]

Patients and data source

The colorectal surgery group at SPH maintains a prospectively collected database, including all patients who undergo TEM. Demographic, operative, postoperative, and pathology data are recorded and kept using a secure, online database storage and management system (REDCap).[14,15] The day before the procedure, patients are prescribed a full mechanical bowel preparation without oral antibiotics. Immediately before the procedure, patients are given a weight-based dose of intravenous cefazolin and metronidazole. No routine postoperative antibiotics are prescribed. We identified data from patients who presented to 1 of the surgeon's clinics or to SPH with postoperative pain or fever (defined as 38.3°C or higher, the cut-off used to define fever at our institution) within 30 days of surgery. We conducted a detailed chart review of data from these patients.

Variables

To be classified as having post-TEM syndrome, patients had to present with 2 or more of the following signs or symptoms in the postoperative period: pain, fever, leukocytosis, or characteristic imaging findings (Box 1). Patients with a single isolated symptom (e.g., isolated pain) did not meet our definition. In addition, patients could not have an alternate explanation for their symptoms, such as a defined pelvic abscess or objective wound dehiscence. Fever was defined as a single documented temperature measurement of 38.3°C or higher, determined by any route. Pain was as subjectively reported by patients and documented in chart visit data. Imaging findings were as reported in the diagnostic radiology report. All radiologists were certified by the Royal College of Physicians and Surgeons of Canada and licensed by the provincial regulatory authority.

Additional data recorded included date of surgery, length of hospital stay, hospital readmission, the presence of malignancy or high-grade dysplasia, procedural characteristics such as peritoneal entry, and defect closure. We reviewed data from all patients with postoperative fever or pain for complications, which we stratified by Clavien–Dindo classification.[16,17]

Box 1. Diagnostic criteria for post–transanal endoscopic microsurgery (TEM) syndrome

The diagnosis of post-TEM syndrome requires 2 or more of the following signs or symptoms within 7 days of the TEM procedure, and without other explanation for clinical findings (e.g., abscess, leak, frank peritoneal infection):

- **Pain:** pelvic, rectal, or abdominal
- **Fever:** ≥ 38.3°C
- **Abnormal blood work:** leukocytosis ≥ 97.5% upper limit of normal on hospital laboratory-based assay
- **Imaging findings:** inflammatory change with stranding, free fluid or small bubbles of free intraperitoneal, retroperitoneal, or mesorectal air
- No signs of free perforation or abscess at the surgical site.

Postoperative infectious complications included abscess and wound dehiscence. Abscess was defined on imaging (ultrasonography or computed tomography [CT]), as reported by radiologist report, or through direct visualization and operative procedure report, as described by the surgeon. We defined presence of wound dehiscence as reported in written documentation through direct visualization in the operating room or by contrast extravasation on imaging.

Outcomes

Primary outcomes were the characteristics, treatment, and proportion of patients presenting with post-TEM syndrome. Secondary outcomes were causes and treatment of postoperative pain or fever, to distinguish from post-TEM syndrome.

Statistical analysis

We presented results as absolute values and percentages, tabulated using standard descriptive analyses. We generated figures using IBM SPSS version 27.

Ethics approval

We obtained approval from the University of British Columbia research ethics board (no. H17-00514).

Results

Between January 2006 and May 2017, 795 TEM resections were performed at the study site. Of these, 56 patients reported postoperative pain or fever.

Post-TEM syndrome

Overall, 26 patients met our definition for post-TEM syndrome (Table 1), suggesting an incidence of 3.3% in this series. Presentation was variable, as 15 patients (57.7%) presented with fever, 20 patients (76.9%) had pelvic pain, and 3 patients (11.1%) were described as having peritoneal signs on examination (in addition to other signs or symptoms of post-TEM syndrome). Patients also had a variety of other symptoms, including abdominal discomfort, distention, rigors, fatigue, or malaise. Most patients developed symptoms on the same day as the procedure (n = 9, 34.6%) or on the first postoperative day (n = 8, 30.8%). All remaining patients presented within 7 days of surgery, and 9 patients were readmitted to hospital for treatment. The median length of stay was 2 (range 0–6) days. Eleven patients were evaluated with CT. These scans all showed some combination of inflammatory change with stranding and free fluid, or with small bubbles of free intraperitoneal, retroperitoneal, or mesorectal air, or with both; they did not show signs of free perforation or abscess at the surgical site (Figure 1). Most patients with post-TEM syndrome were treated with antibiotics (n = 21, 80.8%). One patient had persistent symptoms at 2 weeks, which resolved with a second course of antibiotics. One patient subsequently developed a pelvic abscess that required drainage and fecal diversion.

Other causes of postoperative pain and fever

Thirty patients with postoperative fever or pelvic pain did not meet our definition of post-TEM syndrome. The Clavien–Dindo classification of all patients presenting with pain or fever is shown in Figure 2. Five patients presented with a defined pelvic abscess requiring drainage, 1 of whom had a wound dehiscence requiring operative repair. Sixteen patients presented with pain as an isolated symptom, with no signs of infection or inflammation. For 3 of these patients, pain was due to postoperative urinary retention. Five patients received diagnoses of perianal pain associated with fecal incontinence. All patients with isolated pain improved over time. In 3 patients who had documented peritoneal entry during the procedure, presentation with abdominal pain and diffuse free air seen on imaging occurred in the early postoperative period. All of these patients' symptoms resolved with time and antibiotics, which were routinely continued in the postoperative period in this scenario. Five patients had isolated postoperative fever. For 3 of these patients, fever was related to urinary retention; fever was not specified as related to specific diagnoses in the remaining 2 patients.

Discussion

Infectious complications after TEM are relatively uncommon, with occurrences ranging widely from 0% to 6.7% reported using a variety of terms.[5–12] In the present study, we reported a cumulative rate of postoperative pain or fever of 56 of 795 patients (7.0%), many of whom required no intervention. We define post-TEM syndrome as an explanation for many of these events.

Post-TEM syndrome is an uncommon complication of TEM, with an incidence of 3.3% in our study cohort. The syndrome represents a constellation of symptoms including fever, pain, leukocytosis, and imaging findings appearing in the early postoperative period, thought to result from a localized inflammatory or infectious process at the surgical site. In this cohort of patients, most symptoms developed within the first 48 hours after the procedure; however, some patients presented with symptoms up to 1 week after surgery. Patients often had evidence of an inflammatory response on laboratory investigations, including leukocytosis. Most patients recovered relatively quickly with supportive care, with a median length of hospital stay of 2 days, ranging from less than 24 hours (day surgery, discharged as planned) up to 6 days. Common findings on cross-sectional

Table 1: Characteristics of patients with post–transanal endoscopic microsurgery syndrome

Year	Fever	Pelvic pain	Peritonitis	Leuko-cyte	POD at diagnosis	Imaging findings	Antibiotics	Pathology	Defect	Peritoneal entry	Other
2007	No	Yes	No	NA	0	Free air bubbles	Yes	ACA	Open	No	
2008	No	Yes	No	NA	0	Retroperitoneal air bubbles	Yes	Ddenoma	Closed	No	High-grade dysplasia
2010	Yes	No	No	High	7	NA	Yes	ACA	Open	No	
2011	Yes	No	Yes	NA	0	NA	No	ACA	Closed	No	
2011	No	Yes	No	High	1	NA	Yes	GIST	Open	No	Positive margin
2011	Yes	Yes	No	NA	1	Free air bubbles	Yes	Ddenoma	Open	No	
2012	Yes	Yes	No	Normal	2	NA	Yes	Adenoma	Open	No	
2012	No	Yes	No	High	1	NA	Yes	Ddenoma	Closed	No	High-grade dysplasia
2013	Yes	No	No	High	2	NA	Yes	ACA	Closed	Yes	
2014	Yes	Yes	No	High	0	NA	Yes	Adenoma	Closed	No	High-grade dysplasia
2014	Yes	Yes	No	High	3	Presacral stranding, free fluid, free air bubbles	Yes	Adenoma	Closed	No	High-grade dysplasia
2014	Yes	Yes	No	Normal	3	Perirectal stranding, free fluid	Yes	Carcinoid	Closed	No	
2014	No	Yes	Yes	Normal	1	Free air bubbles	No	Adenoma	Closed	Yes	Positive margin
2014	No	Yes	No	Normal	2	Free air bubbles	Yes	ACA	Closed	Yes	
2015	Yes	Yes	No	Normal	1	Rectal stranding	Yes	ACA	Open	No	
2015	Yes	Yes	No	High	0	NA	No	Carcinoid	Closed	No	
2015	No	Yes	No	Normal	0	NA	Yes	Adenoma	Closed	No	High-grade dysplasia
2015	No	No	Yes	High	0	NA	Yes	ACA	Closed	No	Bacteremia
2015	Yes	Yes	No	Normal	0	NA	No	ACA	Closed	No	
2016	No	Yes	No	High	1	Rectal stranding, free fluid, free and retroperitoneal air bubbles	Yes	Adenoma	Open	No	
2016	Yes	No	No	High	1	Free air bubbles	Yes	ACA	Open	No	
2016	No	Yes	No	High	1	Mesorectal air	No	Adenoma	Closed	No	
2017	Yes	Yes	No	High	2	NA	Yes	ACA	Closed	No	
2017	No	Yes	No	Normal	4	NA	Yes	Adenoma	Closed	No	Malaise, diaphoresis
2017	Yes	No	No	High	6	Rectal stranding, rectal thickening, free air bubbles	Yes	Carcinoid	Closed	No	
2017	Yes	Yes	No	NA	0	NA	Yes	Adenoma	Open	No	

ACA = adenocarcinoma, GIST = gastrointestinal stromal tumour, NA = not available (diagnostic test not requested), POD = postoperative day.

imaging included inflammatory changes or stranding near the rectum, free pelvic fluid, and small locules of air within the abdomen, retroperitoneum, or mesorectum, with absence of a defined abscess or leak.

As described, post-TEM syndrome is distinct from 2 other clinical scenarios that were present in this patient cohort. A subset of patients developed a degree of isolated pelvic pain or ache after the procedure, some associated with a change in bowel function or incontinence. These patients lacked the other inflammatory symptoms of fever and leukocytosis. This isolated pain usually resolved over time, but over a protracted course of weeks to months and was typically observed among patients whose excision encroached on the anal canal and associated pain fibres in anoderm. This is in contrast to the pain associated with post-TEM syndrome, which resolved quickly along with other associated symptoms within 1–2 weeks.

Some patients developed a defined abscess or leak beside their anastomotic site, likely due to wound dehiscence. These patients presented with a similar constellation of symptoms, but CT showed a rim-enhancing, organized pelvic collection or extravasation of contrast. Dehiscence or abscess may require further intervention in the form of drainage.[3] Small abscesses may resolve with antibiotics alone. Post-TEM syndrome, leak, and abscesses may exist along a continuum of infectious complications. However, within this cohort, most patients with post-TEM syndrome did not appear to progress to abscess formation.

In the TEM literature, local inflammatory and infectious complications are documented using a variety of vague terms, making comparisons between studies difficult. For instance, the term "wound dehiscence" is often used without an indication of how the diagnosis was made,

Fig. 1. Computed tomography image of characteristic findings present in post–transanal endoscopic microsurgery syndrome. Image shows inflammatory change with stranding and a small volume of extraluminal air, without signs of free perforation or abscess at the surgical site.

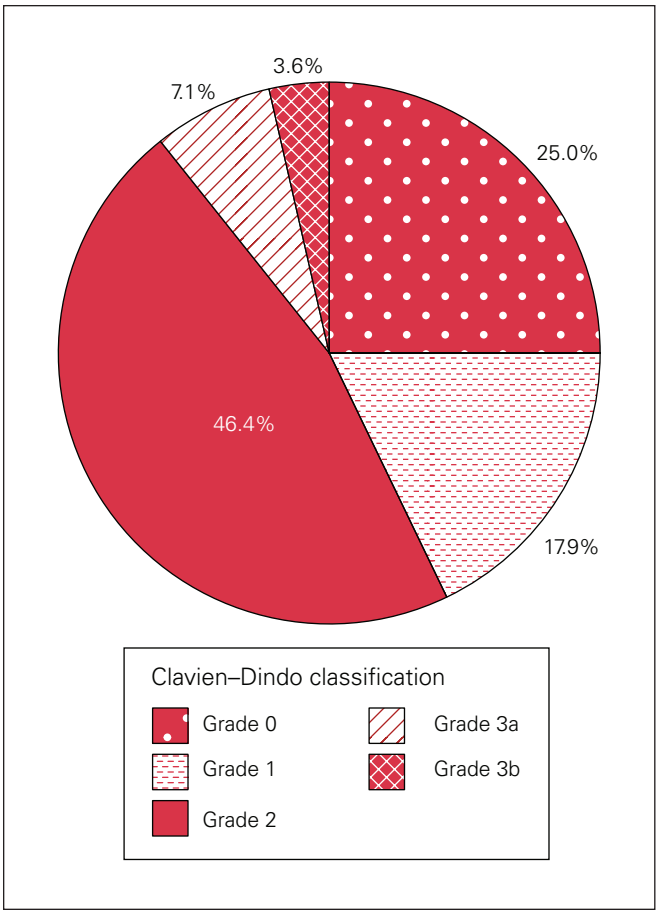

Fig. 2. Clavien–Dindo classification of patients presenting with pain or fever after transanal endoscopic microsurgery (TEM), whereby grade 0 indicates no treatment given (n = 14, 25.0%); grade 1 indicates no need for intervention other than treatment with antipyretics, analgesics, antiemetics, fluids, or electrolytes, with or without admission to hospital (n = 10, 17.9%); grade 2 indicates treatment with antibiotics, but no procedural intervention (n = 26, 46.4%); grade 3a indicates procedural intervention without general anesthetic, including bedside drainage or percutaneous imaging-guided drainage of an abscess (n = 4, 7.1%); grade 3b indicates operative management under general anesthetic, including transanal drainage, repeat TEM, or laparotomy (n = 2, 3.6%); grade 4 indicates care in the intensive care unit (n = 0); and grade 5 indicates death (n = 0).

be it through direct visualization, clinical examination, imaging, or some combination thereof. Based on the findings of the present study, it is possible that this diagnosis may include some patients whom we would define as having post-TEM syndrome. Allaix and colleagues[5] reported a series of 300 consecutive patients who underwent TEM over a 14-year period. The rate of dehiscence and abscess in that series (2%) was higher than in ours (0.8%), and the management was frequently conservative, with 66% managed with antibiotics alone. This is in stark contrast to all patients with abscess and dehiscence in the present study, who required drainage or surgery. Conversely, post-TEM syndrome does not typically require procedural intervention. Post-TEM syndrome may be a catch-all diagnosis that includes most of these cases of dehiscence. Similarly, Tsai and colleagues[7] reported that 8 of 269 patients who had undergone TEM subsequently developed fever that resolved with antibiotics alone. Two additional patients were taken to the operating room for symptoms of a possible dehiscence, where none was found.[7] Finally, Coco and colleagues[8] reported that 5 of 178 patients in their series had undefined dehiscence that was treated conservatively. Other authors reject dehiscence as a postoperative complication. In a series including 325 patients who had undergone TEM, Kumar and colleagues[9] reported that no such events occurred. However, the authors made no reports of postoperative pain or fever either.[9]

A leaking suture is another poorly defined term that has been previously applied and may relate to post-TEM syndrome. Previously, 35 of 588 patients who underwent TEM, performed for benign adenomas, were assigned this diagnosis, which resolved with a local antibiotic and analgesic enema.[10] In a similar series of 425 patients who underwent TEM for rectal cancer, 42 patients were described as having minor complications, which included partial suture line dehiscence. Although stated that patients with partial dehiscence were treated with antibiotics, the exact number of affected patients was not provided. This study contrasted those patients with 3 additional patients who had major complications in the form of a perianal or retroperitoneal phlegmon, which required operative drainage and diversion.[11] Lezoche and colleagues[12] mention a partial leaking suture as a cause for symptoms in 9 patients of their 135-patient cohort, which improved after treatment with antibiotic enemas. Given the previously established equivalency of open versus closed rectal defect after TEM for the purposes of postoperative infection and pain,[18,19] without more information it is difficult to discern

whether an ill-defined loose suture would have caused whatever symptoms ailed those patients. Post-TEM syndrome is an alternative explanation. In this study, several patients classified as having post-TEM syndrome were noted to have had peritoneal entry or an open rectal wall defect. Both are safe,[3,19] and most patients with these features did not develop symptoms. However, sample sizes for these characteristics are small and purely descriptive in nature, so conclusions from these observations cannot be drawn at present.

A local infection is another similar nonspecific complication that has been described, occurring 6 times in a small series of 75 patients in Switzerland. Five of these infections resolved with antibiotics alone.[20] Bach and colleagues[6] reported that 7 of 487 patients treated with TEM developed troublesome pelvic sepsis. Two of these patients required fecal diversion, and 2 rectovaginal fistulas occurred, but no additional clinical details were given.[6] Finally, some smaller series did not comment on infectious symptoms as short-term complications at all.[21,22]

Additional severe complications of TEM have been described, such as wound dehiscence in patients who underwent neoadjuvant therapy before TEM for rectal cancer,[23] or pneumoperitoneum, sepsis, and, ultimately, reoperation and fecal diversion.[24] Patients requiring procedural intervention have more serious perineal sepsis and wound complications, distinct from patients with post-TEM syndrome.

In the present study, most patients with post-TEM syndrome were treated with a course of antibiotics, which seemed to improve symptoms. However, some patients were managed expectantly with admission to hospital, hydration, and pain control, and appeared to have a self-limited course that improved within a few days. Nearly all patients had complete resolution of symptoms with medical management, with no further intervention required. Obvious parallels exist between post-TEM syndrome and the diagnosis of postpolypectomy syndrome after colonoscopy, thought to be related to full-thickness burn injury during endoscopic polypectomy with resulting inflammatory reaction and microperforation.[25] Resection in TEM usually involves full-thickness cautery dissection through the rectal wall, so it is not surprising that a similar symptom constellation would arise in some patients. Management of the 2 syndromes is also similar. However, unlike postpolypectomy coagulation syndrome, which is defined in the absence of extraluminal air, our definition of post-TEM syndrome allows for extraluminal air. For TES, there is often a full-thickness resection of the rectal wall into the perirectal fat; therefore, even without any complication, there may be translocation of air and fluid. This is not the same as a colon polypectomy, where air outside of the colon implies unintended intraperitoneal entry, which can be a separate issue from postpolypectomy coagulation syndrome.

In summary, minor immediate postoperative infectious or inflammatory complications after TEM are infrequent, and poorly described in the surgical literature. We examined a single centre's experience with this technique over an 11-year period, and we suggest a syndromic definition of this condition to provide a common terminology that categorizes a large portion of these occurrences. A review of the literature identified some instances of patients who likely met the criteria.[5–11] Although uncommon, post-TEM syndrome is clinically important, as these patients often require readmission to hospital and supportive treatment. The distinction between post-TEM syndrome and other infectious complications, such as abscess and dehiscence, is important. Although post-TEM syndrome can often be managed medically, other diagnoses commonly require procedural intervention. The proposed definition of post-TEM syndrome allows for commonality of nomenclature and standardized reporting going forward, which may facilitate further research and treatment of this complication.

Limitations

This is a retrospective study, which is subject to potential unknown missing variables. Although data were collected prospectively for the purposes of monitoring complications after TEM, data collection was not designed with this syndrome in mind, and it is possible that important variables were not considered. Furthermore, although every attempt is made to keep this database as accurate as possible, should patients present to alternate hospitals or care providers for their follow-up care, their outcomes may be missing. There were also differences in patient treatment, given the retrospective, observational nature of data collection and the rarity of the condition. Our study sample received care from a single institution with experience using a single TEM platform and similar techniques. The patient population was also derived from a publicly funded, single-payer health care system. Therefore, the generalizability of the treatment strategies employed herein to other centres or health care models is unknown. Finally, despite our relatively long 11-year study period, with a reasonable sample size, the incidence of this syndrome is low (n = 26). This number is too small to make meaningful comparisons, such as of predictors of post-TEM syndrome compared with other infectious complications. Furthermore, some patients recovered without antibiotic therapy. Ultimately, further study is needed to determine whether certain patient factors increase the risk of developing this syndrome, and to determine whether post-TEM syndrome requires antibiotic treatment or can simply be managed expectantly until the inflammatory response resolves.

Conclusion

Infectious complications are relatively uncommon after TEM. We have defined a new syndrome among patients who present with localized and contained inflammatory changes adjacent to the surgical site after TEM. Most patients with post-TEM syndrome do not progress to have further infectious complications. Patients with post-TEM syndrome and concordant imaging findings benefit from a trial of conservative management before more aggressive procedural interventions, with positive outcomes expected in nearly all patients.

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