Surgical treatment of perianal and rectal fistula
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Chapter 5

*Histological identification of epithelium in perianal fistulas; a prospective study*

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*Colorectal Disease*, 2009
ABSTRACT

Background
A procedure often performed following fistulotomy and advancement flap is curettage of the fistula tract after fistulotomy or after closing the internal opening. Epithelialization of the fistula tract might prevent closure of the fistula tract. The aim of this study was to assess the incidence and origin of epithelialization of the fistula tract in patients with perianal fistulas undergoing fistulotomy.

Methods
Only patients with low perianal fistulas that were surgically treated by fistulotomy were included. Surgical biopsies were taken from the fistula tract from three different locations; on the proximal side at the internal opening, in the middle of the fistula tract and near the distal end close to the external opening.

Results
In the study period, 18 patients with low perianal fistulas were included. In 15 of the 18 patients, squamous epithelium was found at least in one of the biopsies taken from the fistula tract. Epithelium was predominantly found near the internal opening. There was no relation between the duration of fistula complaints and the presence of epithelialization (p=0.301). The amount of epithelium was not related to the presence of a history of fistula surgery (p=1.000).

Conclusions
The study demonstrated epithelialization in the fistula tract in the majority of the patients surgically treated by fistulotomy for low perianal fistulas. Curettage of perianal fistulas must therefore be considered an essential step in the surgical treatment of perianal fistulas.
INTRODUCTION

The aim of fistula surgery is eradication of the fistula tract by closing or removing the internal opening without endangering continence. Although there are many different treatment options, perianal fistulas remain difficult to treat. In patients with low perianal fistulas, located in the lower third of the external sphincter, fistulotomy results in low recurrence rates and relatively little impact on continence. The recurrence rates of fistulotomy vary and range from approximately 2-9%. A division of the anal sphincter of more than 30-50% leads to significant continence disorders. The treatment of choice for high perianal fistulas of cryptoglandular origin currently is the mucosal advancement flap. The success percentages reported in the literature have an average of about 60%. A procedure often performed following fistulotomy and advancement flap is curettage of the fistula tract after division or after closing the internal opening respectively. The rationale is that epithelialization prevents complete closure of the fistula tract. In a series of 18 patients published in 1995 by Lunniss et al., biopsies were taken to assess the amount of epithelium present in the fistula tract. They found that in 13 of the 18 patients epithelialization was present. The aim of this study was to assess the incidence and origin of epithelialization of the fistula tract in patients with low perianal fistulas undergoing fistulotomy.

METHODS

Between April 2007 and September 2008, a consecutive series of patients were prospectively enrolled in the study. Only patients with low perianal fistulas that were surgically treated by fistulotomy were included. Low perianal fistulas were defined as fistulas in which the fistula tract was submucosal, intersphincteric, or located in the lower third of the external anal sphincter muscle and a fistulotomy could be performed without endangering continence. The complete procedure was done in day case setting. All patients had an enema on the day of surgery. All procedures were performed under general or locoregional anaesthesia in the lithotomy position. Broad spectrum antibiotics were administered perioperatively. The fistulotomy was done according to the following technique. The internal fistula tract opening was identified by probing the external fistula opening. During surgery the amount of sphincter involved was judged by palpation of the
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puborectal sling and the inferior edge of the external sphincter complex. The tissue was divided by laying open the complete fistula tract from the internal to the external opening. After the division of the fistula, surgical biopsies were taken from the fistula tract from three different locations, respectively on the proximal side close to the internal opening, in the middle of the fistula tract and near the distal end close to the external opening. When the fistula tract was too short to take multiple biopsies only one biopsy in the middle of the tract was taken. Care was taken to obtain biopsies from the fistula tract and not from the tissue surrounding it. After taking the biopsies the fistula tract was curetted to remove potentially present epithelial lining. Only patients with low perianal fistulas were included as it is very difficult to obtain biopsies from high perianal fistulas from different locations. Routine H&E staining was performed using a standardized protocol. No additional immunohistochemical staining techniques were used. Multiple sections were made and the evaluation was done by a pathologist unaware of any clinical characteristics of the patients, i.e. duration of the fistula and clinical outcome. The amount and the type of epithelium and granulation present in the fistula tract were assessed.

All patients visited the outpatient’s clinics frequently during the follow-up period. Patient’s clinical records were reviewed and data were collected on demographic data, previous fistula surgery, fistula duration, complications and fistula recurrence rate. Previous fistula surgery was defined as surgery aimed to permanently repair the fistula. Duration of the fistula was defined as the time from when the complaints started until the present operation. In case of multiple interventions for the same fistula the time from the latest intervention was taken until the present surgical procedure.

Statistical analysis

Continuous data are presented as median values (range) unless otherwise specified. Categorical data are presented as frequencies or percentages. Differences between groups were tested using Mann-Whitney U test for continuous data. For the comparison of categorical variables, the Chi-squared or Fisher exact test was used. A p-value of 5% or lower was considered statistically significant. Statistical analysis was done using the SPSS version 15.0.1 for Windows (SPSS, Chicago, Illinois, USA).
RESULTS

In the study period 18 patients with low perianal fistulas were included. Patient characteristics are presented in Table 5.1. The median age was 46 years (range 23-76). Eleven patients were male (61%). The majority of the fistulas were cryptoglandular (16 patients, 89%). There was one patient with a perianal fistula in Crohn’s disease and one with human immunodeficiency virus (HIV). Previous fistula surgery was performed in ten patients (56%). Patients had a fistula for a median of six months (range 1-24). None of the patients underwent seton drainage previous to the fistulotomy. There were no intra- or postoperative complications. The median follow-up duration was nine months (range 1-19). In one out of the 18 patients the fistula persisted (6%).

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<td>Previous fistula surgery (n)</td>
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<td>Recurrence</td>
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<td>Follow-up (months, range)</td>
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Pathological results

In 18 patients biopsies were taken. A median of three biopsies were taken from the fistula tract (range 1-3). In 15 of the 18 patients squamous epithelium was found at least in one of the biopsies taken from the fistula tract (Table 5.2). A picture of epithelialization was presented in Figure 5.1. In none of the patients cylindrical epithelium was found. In the majority of the biopsies a larger part of the surface was denuded. Epithelium was predominantly found near the internal opening. In 9 out of the 12 patients with several biopsies, epithelium was found at the proximal end of the fistula tract. In the middle biopsy this was the case in four patients, compared to only two patients with epithelium found in the distal biopsy. In none of the patients epithelium was found in all three locations. In the majority of the patients (17 of the 18) an active inflammatory response was visible. This ranged from a mild to severe inflammation. No skin appendages were found in either of the
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**Legend:**
- Crypto = Cryptoglandular fistula
- Crohn = Crohn's disease
- HIV = Human Immunodeficiency Virus

**Notes:**
- Table 5.2 - Distribution of epithelium in the fistula tract.
Histological identification of epithelium in perianal fistulas.

There was no relation between the duration of fistula complaints and the presence of epithelialization \((p=0.301)\). The amount of epithelium was not related to the presence of a history of fistula surgery \((p=1.000)\).

**Figure 5.1** – Biopsy from a fistula tract with routine haematoxyline-eosine staining \((25x)\). In the smaller picture keratin immunohistochemistry staining \((25x)\) was used to present the keratin in the biopsy.

**DISCUSSION**

The present study assessed the incidence and origin of epithelialization of the fistula tract in a consecutive series of patients undergoing fistulotomy for low perianal fistulas. In these series in 15 out of the 18 patients epithelium was found by the pathologist after obtaining surgical biopsies from the fistula tract after performing the fistulotomy. Epithelium was predominantly located close to the internal opening at the proximal location of the fistula tract. There were only two patients with epithelial lining of the distal part of the fistula tract. None of the biopsies were taken from the anal skin as no skin appendages were found by the pathologist. Epithelialization was not found more often in patients with a previous fistula surgery. Perianal fistulas remain difficult to treat and often a fistula persists after surgical treatment especially in high transsphincteric fistulas. A possible explanation for the
persistent or recurrent fistula is the existence of epithelialization in the fistula tract which prevents the fistula to close. Williams et al. recently stated that the presence of epithelialization may be more important for the persistence of a fistula than the chronic infection.\(^4\) The question arises whether there is a relation between the recurrent or persistent fistula and the presence of epithelium. Furthermore it is not clear where the epithelium originates from. In a histological study by Parks et al. from 1961, 30 specimens were examined for epithelialization among other things.\(^6\) Epithelium was found in 13 out of 30 patients. Lunniss et al. described in their series of 18 specimens 13 patients with epithelium originating from the anal canal.\(^5\) Presumably this was the result of ingrowth of anal epithelium into the internal opening. In the present series a comparable result was found as the majority of the epithelium was seen close to the internal opening. In only two of the patients’ epithelium was found at the distal segment of the fistula tract. When there was epithelium in the middle there was always epithelium in the proximal biopsy taken close to the internal opening. In these two patients no epithelium was found in the biopsy taken from the middle of the fistula tract. It might be that the amount of epithelium in the middle of the fistula tract was low and the biopsy did not contain this epithelium. Epithelium located near the internal opening in the anal canal could potentially be cylindrical or squamous epithelium depending on the height of the internal opening. Surprisingly however, in the patients reported in the present series no cylindrical epithelium but only squamous epithelium was found at the proximal end close to the internal opening. Metaplastic degeneration of cylindrical epithelium as result of the chronic inflammatory response may explain this.

In this study no information could be provided on the role of the seton in the development of epithelialization of the fistula tract. As all patients had low perianal fistulas and none of them were treated by seton drainage before to ensure optimal drainage. Hypothetically there may be more epithelialization in fistulas which exist longer and are drained by a seton.

There is also the possibility of malignant transformation of the chronically retained epithelium in the fistula tract.\(^7\) The incidence of a perianal mucinous adenocarcinoma is low and ranges from 3-11\% of all anal carcinomas. In literature there are only case reports reporting this phenomenon.\(^8\) The anal fistula plug appears a promising device for the treatment of high peri-
Histological identification of epithelium in perianal fistulas

anal fistulas. The results reported by Champagne et al. were very good with a success percentage of 83%. Overall the success percentages appear to be around 50-60% in the literature. However, these rates vary a lot in the different studies. Randomized clinical trials can provide information on the true effectiveness of the anal fistula plug. In the product instructions of the plug provided by the manufacturing company the advice is not to perform debridement, curettage of brushing of the tract. At a consensus conference on this subject held in Chicago in 2007, the advise was not to perform any debridement of the tract to prevent increase of the fistula tract diameter. By flushing the tract with hydrogenperoxide all loose debris should be sufficiently removed. The presence of epithelial lining in the fistula tract shown in this study might be an explanation for the less successful outcome of the anal fistula plug in some patients. Removal of any epithelial lining would be of added value to the plug installation. The plug may grow into the tissue more easily which leads to increased closure rates without leading to substantial increase in the fistula diameter. In conclusion, the present study demonstrated a degree of epithelialization in the fistula tract in the majority of the patients surgically treated by fistulotomy for low perianal fistulas. There was no relation with the duration of the fistula. Curettage of perianal fistulas after closure may prevent recurrent and persistent fistulas and should be used in all surgical treatment options, i.e. the anal fistula plug. The question remains whether curettage of the fistula tract is sufficient to remove all epithelial lining.

REFERENCES


