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ORIGINAL ARTICLE

Endoanal ultrasonography may distinguish Crohn's anal fistulae from cryptoglandular fistulae in patients with Crohn's disease: a cross-sectional study

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Abstract
Background The aim of the study was a cross-sectional investigation into the types of anal fistulae in patients with Crohn's disease using 3-dimensional endoanal ultrasonography.
Methods The study population consisted of 45 patients with established Crohn's disease referred in a 2-year period for treatment of anal fistula. The fistulae were classified according to the presence of three criteria: 1. bifurcation or secondary extension; 2. cross-sectional width $\geq$3 mm; and 3. content of hyperechoic secretions.
Results The fistulae of 24 patients (53%) satisfied two or three criteria and were classified as true Crohn's fistulae, while the fistulae of 21 patients satisfied one or none of the criteria and were the cryptoglandular type. The fistulae in the two or three criteria group had been in existence for 8.4 years on average and those in the cryptoglandular group for 4.5 years on average ($P = 0.283$). The corresponding numbers of previous operations for fistula were 5.7 (range 0–32) and 1.5 (range 0–6), respectively ($P = 0.0211$). The presence of colitis or proctitis was similar across the groups, but the perianal Crohn's disease activity index was higher with a Crohn's type of fistula ($P = 0.0097$). Also, a larger proportion had been treated with anti-TNF-monoclonal antibody (0.0169).
Conclusions Endoanal ultrasonography was capable of discerning two subgroups of fistula in Crohn's patients. These groups were clinically different indicating that the prospect of surgical cure is also different.

Keywords Fistula · Perianal · Cyptoglandular · Crohn's disease · Endoanal ultrasound

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Introduction

Patients with anal fistulae due to Crohn's disease suffer physical and emotional distress because the fistula may be painful and persistent. Many such fistulae have an appearance and course that is markedly different from the fistulae seen in the non-Crohn population [1]. Other fistulae in Crohn's patients are successfully treated with means designed for ordinary cryptoglandular fistulae [2]. The recent developments in surgical techniques and the addition of biological therapy have resulted in a 'call to action' for treatment of perianal disease in Crohn's patients [3].

Our experience with the apparent differences in the behaviour of anal fistulae in patients with Crohn's disease suggested that the fistulae may represent two types of fistulae rather than a continuous spectrum of increasing severity. This hypothesis was explored by examination of the fistulae under endoanal ultrasonography. For this study, three ultrasonographic criteria were devised that take into account the clinical observations that seem to distinguish the complex fistula from the simple one in Crohn's perianal disease. The criteria included the bifurcation of the fistula tract, the width of the tract and its content of hyperechoic debris. A cohort of patients with anal fistula and Crohn's disease were investigated to study the presence and implication of these signs.

Materials and methods

Forty-five patients with a diagnosis of Crohn's disease established with the usual criteria were referred for surgical treatment of perianal disease between January 2007 and December 2008. All patients were examined with 3-dimensional endoanal ultrasound using a Pro Focus 2202 model equipped with a type 2050 13 MHz rotating transducer (BK Medical, Herlev, Denmark). The examinations were performed with the patient in the lithotomy position without anaesthesia. The images were downloaded for subsequent examination and classification. The examiner (KS) performs approximately 100 endoanal studies per year for anal fistula.

Using three predetermined criteria, the fistulae were subclassified into two groups. The criteria were (1) the presence of bifurcation or secondary extension, (2) a tract that was 3 mm or more in diameter and (3) a tract that was filled with hyperechoic secretions or debris (Fig. 1). Examinations with two or three positive criteria were designated Crohn's fistula, while those with one or no criterion were designated cryptoglandular fistula. The investigator also provided a global assessment of her impression of the fistula type based on the general appearance of the dynamic examinations. These fistulae could be both high and low fistula, but no specific effort was made to determine the particular anatomy in this respect. Some patients had more than one external opening. Most patients had had previous surgical treatment of the fistula, and some had in situ seton at the time of investigation. All patients were subsequently subjected to examination under anaesthesia for drainage procedures (incision or loose seton) in preparation for attempted definitive treatment.

Table 1 Characteristics of 45 patients with established Crohn's disease examined for subsequent perianal disease

Sex distribution, male/female	27/18
Age, years, mean (range)	39.9 (17–75)
Duration of Crohn's disease, years, mean (range)	13.8 (1–44)
Duration of fistula, years, mean (range)	6.7 (1–36)
Previous surgery of current fistula, operations (range)	3.7 (0–32)
Number with previous abdominal surgery for Crohn, (%)	19 (42)
Treatment with infliximab/adalimumab*, number (%)	22 (49)

* Previous or current

From the case notes, information was retrieved about each patient's age at diagnosis of Crohn's disease, the presence of proctitis or colitis, years since first diagnosis of perianal disease, number of previous abdominal and anal surgical procedures, and previous or current treatment with biological medication (infliximab, Remicade® or adalimumab, Humira®). A modified perianal Crohn's disease activity index (PCDAI) [4] was calculated for each patient excluding the sexual activity dimension, which was not available (Table 1).

Statistical analysis

Dichotomous variables were compared with Fisher's exact test and ordinal variables with the Mann–Whitney *U* test with a two-tailed *P*-value of less than 0.05 as a significance

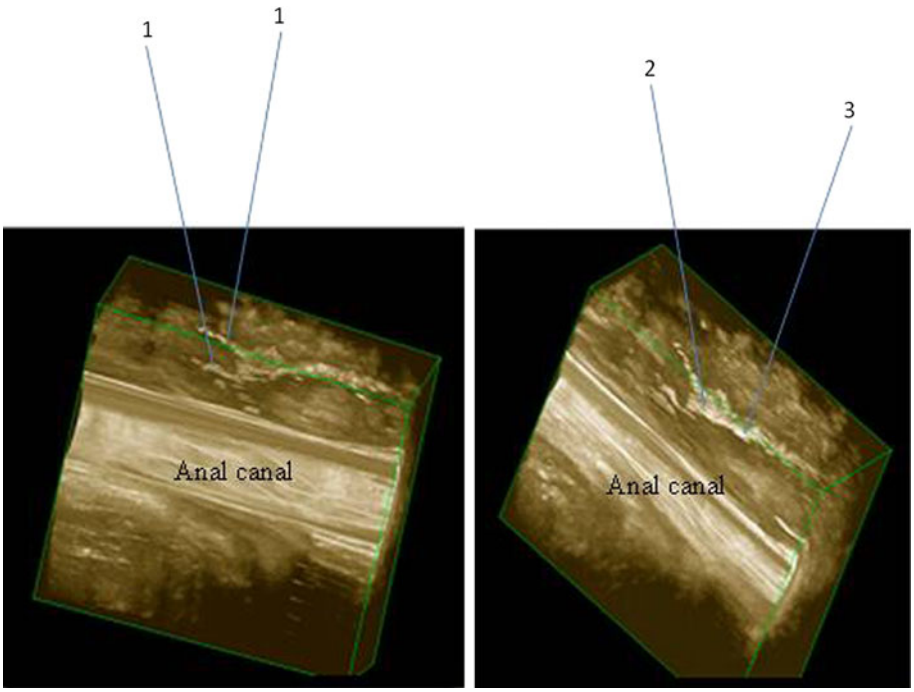

Fig. 1 Three-dimensional endoanal ultrasound with installed hydrogen peroxide demonstrating three criteria of a Crohn's fistula: (*1*) the presence of bifurcation or secondary extension, (*2*) a tract 3 mm or more in cross-sectional measurement and (*3*) a tract filled with debris

level (Statistica™, Statsoft, Tusla, USA). No permission from the ethics committee was required for this study as it involved no intervention beyond the regular clinical follow-up.

Results

Twenty-four (53 %) of the fistulae, when examined, satisfied two or three criteria and were designated Crohn's fistula, while 21 satisfied only one or no criterion and were designated cryptogenic fistula (Table 2). The investigator's global assessment of the subtype of fistula revealed that 23 of the 24 Crohn's type fistulae had a convincing ultrasonographic appearance of Crohn's fistula. The exception was a patient who had had no surgery for the fistula although it had been present for 8 years. The average length of time Crohn's disease had been present in the two or three criteria group and in the cryptogenic group was 15.4 and 11.8 years, respectively, while perianal disease had been present for 8.9 and 4.4 years, respectively. These differences did not reach statistical significance.

The number of previous operations for fistula was 5.7 (median 3, range 0–32) and 1.5 (median 1, range 0–6), respectively, for patients with the Crohn's type and the cryptogenic type ($P = 0.0211$). An acute incision for drainage of abscess had been performed in 18/24 versus 6/21 cases ($P = 0.0028$), and the PCDAI was significantly higher in patients with a Crohn's type of fistula ($P = 0.0097$). The clinical correlates showed a similar presence of colitis and proctitis across the two types of fistula, while previous or current treatment with biological medication was significantly more common in patients with Crohn's fistula ($P = 0.0169$) (Table 2). Documentation showed that the majority (73%) had had one or more courses of cortisone with no intergroup difference.

Discussion

Based on these data, we propose that two subtypes of anal fistula in Crohn's patients may be distinguished by means of endoanal 3-dimensional ultrasonographic examination. It should also be evident from our results that patients with Crohn's disease may develop fistulae of a type that is indistinguishable from the ordinary cryptoglandular fistulae observed in the non-Crohn's population. The three criteria used for the subclassification were arbitrarily devised but derived from long experience with fistula treatment and endoanal examination of such patients. Whether these criteria are fulfilled is easily assessed with modern 3-dimensional ultrasonography.

The examination of the clinical correlates demonstrated an equal presence of proctitis in patients with the two types of fistulae. A higher PCDAI and more frequent use of biological treatment as well as more frequent surgical procedures showed that Crohn's fistulae were indeed more severe.

Scientifically, these findings may be little more than a signal to increase awareness that in Crohn's patients with anal fistulae there may be two or more subtypes of fistula that appear to be clinically different with diverse prospects of cure. Ultrasonographic findings showing that satisfaction of two or all three criteria are satisfied may simply represent the sequel of more severe disease of longer duration that had been subjected to repeated unsuccessful surgery. It has been proposed that the hyperechoic content of the fistula tract is a sign of inflammatory activity of the fistula tract or of perianal disease as a whole [5, 6]. The same type of secretions inside the fistula can also be observed by means of magnetic resonance imaging [7].

We also do not know if our findings represent a natural course of progression from simple to more complex fistulae, which may be inferred from the difference in the length

Table 2 Fistula type according to endoanal ultrasonographic criteria and clinical correlation

	Fistula type[a]		
	Two or three signs	One sign or none	P[b]
Number of patients	24	21	
Global assessment of Crohn's fistula[c]	23	0	<0.001
Proctitis/colitis	18	18	0.467
Treatment with infliximab/adalimumab[d]	16	6	0.0239
Number of fistula operations	5.7	1.5	0.0211
Perianal Crohn's disease activity index, mean (range)[e]	7.6 (2–12)	5.0 (2–13)	0.0097

[a] Three criteria: *1* secondary tracts, *2* tract width ≥3 mm, *3* secretions or debris in the fistula

[b] Fisher's exact test or Mann–Whitney *U* test

[c] Investigator's global assessment of ultrasonographic fistula type

[d] Previous or ongoing treatment

[e] Modified from Irvine [4]. Maximum score 16 points

of time the fistulae had been in existence, or if the findings represent instead a selection process in which some patients with cryptogenic fistula were cured by treatment elsewhere, and therefore not referred, while those with active inflammatory fistulae were referred. The data can be interpreted both ways, and only a careful longitudinal cohort study would be able to provide adequate information.

Persistent inflammatory activity of the fistula is probably a main determinant for failure of any surgical treatment of a Crohn's fistula. Surgeons, however, have been more concerned with aspects of continence than with measuring the degree of inflammatory activity and correlating it with outcome after surgery [8, 9]. The modified PCDAI excluding sexual activity evaluates fistula discharge, induration, associated pain and type of perianal disease [4]. We found that the presence of proctitis or colitis was equally common in patients with the two types of fistulae, while a clear difference was observed as regards discharge, pain and induration. These features in the presence of the proposed ultrasonographic criteria would suggest that only drainage procedures, including seton, should be attempted for as long as the inflammation remains active. In the absence of active inflammation according to the PCDAI, and non-fulfilment of the ultrasonographic criteria, attempts to treat the fistula by means of fistulotomy, bioprosthetic plug or advancement flap may be successful.

Conclusions

The presence or absence of three easily observed signs on endoanal ultrasonography was used to subclassify anal fistula in patients with Crohn's disease. Patients with two or three signs had had fistulae for a longer time, more operations and a worse activity index, while in those with none or only one sign, fistulae were indistinguishable from the cryptoglandular fistulae in non-Crohn's patients. We intend to perform a prospective longitudinal study with endoanal ultrasonography to examine their course.

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