Are acute exacerbations of chronic inflammatory appendicitis triggered by coprostasis and/or coproliths?

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Abstract

AIM: To examine the role of coprostasis and coproliths in recurrent appendicitis.

METHODS: We evaluated four hundred and twenty seven consecutive pathology reports of all appendicectomy specimens from January 2003 to December 2004. Findings were categorised as showing acute appendicitis, acute recurrent appendicitis, subacute recurrent appendicitis, chronic appendicitis, or appendices without inflammation. All patients had presented with acute right lower quadrant pain. In 94 instances, there was a history of recurrent similar episodes in the past.

RESULTS: Of the 427 histology reports, 294 were interpreted as showing acute appendicitis, 56 acute recurrent appendicitis, 34 subacute recurrent appendicitis, 28 chronic appendicitis, and 15 non-inflamed appendices.

Coprostasis was observed in 58 patients (13.58%) and the presence of coprolith in 6 (1.4%). Coprostasis, and age, were among the predictors in the final model.

CONCLUSION: Coprostasis but not coproliths seems to be a contributing factor to acute exacerbations of chronic inflammatory appendicitis.

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of General Surgery, Marien Hospital Bottrop, Germany from January 2003 to December 2004. Specimens were categorized as acute appendicitis, acute recurrent appendicitis, subacute recurrent appendicitis, chronic appendicitis, and appendices showing no signs of inflammation. The presence of a coprolith (thickened “stone-like” faces) and coprostasis (appendicular lumen filled with faeces, completely impacted and not just the presence of a little stool) was noted. Clinical details were supplemented by review of selected case notes.

Specimens were doubly evaluated and classified into five categories by two pathologists separately and the presence of coprostasis and coprolith was also recorded. In those cases with discrepancy in the diagnosis or in the presence of a coprolith or coprostasis specimens (n = 4) were reviewed by an experienced independent pathologist.

Patients were divided in 5 groups: Group A for acute appendicitis, group B for subacute recurrent appendicitis, group C for acute recurrent appendicitis, and group D for chronic inflammation of the appendix. Histology reports with normal non-inflamed appendices were classified as group E. Definitions of the pathologic entities were as follows:

**Acute appendicitis (group A):** At early stages the serosa is intensely erythematous due to congestion of the subserosal blood vessels. In advanced stages few intact crypts exist lined with intact mucosal epithelium, lamina propria is hypercellular due to neutrophil infiltration, hemorrhage and ulcers are found at the surface caused by the sloughing off of the inflammatory necrotic tissue.

**Subacute recurrent appendicitis (group B):** This entity is characterized by lympho-follicular hyperplasia, discrete granulocytes, mucocutaneous infiltration and hyperaemic serosa.

**Acute recurrent appendicitis (group C):** In different sections of the appendix, there can be recognized relative diffuse, inflammatory mucocutaneous and appendical wall infiltrations. Primarily neutrophils exist that spread out also within the subserosal tissue. Erosive lesions are additionally observed.

**Chronic inflammatory (group D):** This is characterized by the presence of unequivocal mural granulation tissue, with or without frank fibrosis, partial or total obliteration of the lumen by fibrous tissue and hyperplasia or atrophy of the lymphoid tissue.

**Statistical analysis**

Statistical methods included nonparametric Yates correction chi-square, Fisher’s exact test (two tails) for categorical variables, and Mann-Whitney U test for quantitative variables. The Random Forest test (data mining procedure) was used to disclose the variables for use in regression analysis. The General Discriminant analysis model was used to evaluate the discriminating effect of coprostasis and coproliths on the defined groups. A Receiver Operating Characteristic (ROC) curve was used to define the ideal cut-off separator for continuous predictor variables. A significance level of 0.05 was assigned. Statistica release 7 (Statsoft) was used for statistical analysis.

**RESULTS**

There were 427 appendectomy pathology reports, corresponding to 265 females and 162 males. Mean patient age was 24.40 ± 17.16 years (range, 4-89 years). All patients were referred for acute right lower quadrant pain. In 94 cases, there was a reported history of recurrent similar episodes in the past. Among these 94 patients 56 had acute recurrent, 34 subacute recurrent and 4 chronic appendicitis.

Of the 427 histology reports, 294 were diagnostic of acute appendicitis, 56 of acute recurrent appendicitis, 34 of subacute recurrent appendicitis, 28 of chronic appendicitis, and 15 of non-inflamed appendices.

Coprostasis was observed in 58 patients (13.58%) and the presence of a coprolith was noted in 6 (1.4%) cases. The incidence and the respective percentages of coprostasis and coprolith among separate histology groups are shown in Table 1.

Associated findings were noted in 6 patients: sigmoid cancer in one, corpus luteum cyst in one, and Meckel’s diverticulum in four. Yersinia infection was observed in 1 patient of group B and in one patient of group C. Parasitic infections were diagnosed in 3 patients of group A. Among the 15 cases of group E (non-inflamed appendices), there were four diverticular ruptures, two Meckel’s diverticulitis, one carcinoid tumor, one mesenteric arterial embolism, three adnexitis, two tubo-ovarian abscesses, one endometriosis, and one bilateral ovarian biopsy negative for malignancy.

Prominent pathologic findings were encountered more frequently among group A patients. Appendiceal lumen dilatation greater than 10 mm was noticed in 12 patients of group A, one of group B, and 2 of group C. Forty five appendices of group A were gangrenous, and 38 were perforated. This contrasts with the appendices of patients within groups B and C, which were neither gangrenous nor perforated. The incidence of peri-appendicitis was higher in group A (205/294, 69.38%) than in group B (3/34, 8.82%) and group C (28/56, 50%; Table 2). Appendiceal plastraons were documented in 10 patients of group A and one of group D. There were none among patients of groups B and C.

| Pathology classification | Coprostasis (n = 58) | Coprolith (n = 6) |
|--------------------------|---------------------|------------------|
| Acute                    | 33/294 (11.22)      | 3/294 (1.02)     |
| Subacute recurrent       | 12/34 (35.20)       | 1/34 (2.94)      |
| Acute recurrent          | 9/56 (16.07)        | 1/56 (1.78)      |
| Chronic                  | 3/28 (10.71)        | 0/28 (0.00)      |
| No inflammation          | 1/15 (06.66)        | 1/15 (6.66)      |
In order to find the potential role of coprostasis and coprolith as predictors of the various appendicitis classes as described in methods section, we applied Random Forest classification test (this Data Mining technique - Random Forest algorithm developed by Breiman - can be used for classification problems in order to predict a categorical dependent variable). Importance (from high to low) was attributed to Age = 1, Gender = 0.32, Coprostasis = 0.25, Oxyuriasis and Yersinia cases = 0.12 and Appendicolith = 0.05.

Taking into account the potential predictors suggested from the Random Forest test we proceeded for further analysis. Coprostasis, age, gender and oxyuriasis and Yersinia cases were prognostic factors among the four groups (excluded was the “No inflammation” group of patients) by univariate analysis. The presence of a coprolith did not achieve statistical significance. Coprostasis \( P = 0.0032 \), age \( P = 0.0077 \), and oxyuriasis and Yersinia cases \( P = 0.0354 \), but not the presence of coprolith, were also found to be predictive variables by forward stepwise regression analysis. The level of significance for “coprostasis” in each group is reported in Table 3. The null hypothesis was rejected in groups D \( P = 0.0351 \) and E \( P = 0.0496 \), but substantiated in groups A \( P = 0.6885 \), B \( P = 0.0796 \) and C \( P = 0.1311 \), implying coprostasis as an etiologic factor in acute, subacute recurrent and acute recurrent appendicitis.

A further Discriminant forward stepwise analysis was employed in order to find the predictive model only for subacute recurrent and acute recurrent cases (Table 3). Only age and coprostasis were among predictors in the final model.

A Receiver Operating Characteristic (ROC) curve was used to select the optimum decision threshold for patient age. Patients less or equal to 40 years had a higher prevalence of subacute \( 29/5, P = 0.0012 \) and acute recurrent \( 45/11, P = 0.0003 \) appendicitis. Subacute and acute recurrent appendicitis was also found to be more prevalent in females \( 27/7, P = 0.0083; 39/17, P = 0.0241 \).

**DISCUSSION**

The perception that acute appendicitis might subside spontaneously and re-emerge with bouts of right lower quadrant pain (so-called recurrent appendicitis) has met debate and disbelief. Nonetheless, 10% of patients presenting with acute appendicitis report previous similar physical findings that settled without surgery\(^\text{[7,8]}\). Subsequent appendectomy is remedial\(^\text{[3]}\).

It has been assumed that the likely pathophysiologic

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**Table 2 Pathological findings**

|          | Acute (A: \( n = 294 \)) | Sub-acute recurrent (B: \( n = 34 \)) | Acute recurrent (C: \( n = 56 \)) | Chronic (D: \( n = 28 \)) | \( P \)  |
|----------|---------------------------|-------------------------------------|-----------------------------------|---------------------------|--------|
| Gangrenous | 45                        | 0                                   | 0                                 | 0                         | A vs B, \( P = 0.0101 \), A vs C, \( P = 0.0007 \) |
| Perforated | 38                        | 0                                   | 0                                 | 0                         | A vs B, \( P = 0.0199 \), A vs C, \( P = 0.0019 \) |
| Peri-appendicitis | 205                      | 3                                   | 28                                | 3                         | A vs B, \( P = 0.0031 \), A vs C, \( P = 0.0408 \) |
| Abscess    | 14                        | 0                                   | 0                                 | 0                         |        |
| Other      |                           |                                     |                                    |                           |        |
| Oxyuriasis | 3                         | 0                                   | 0                                 | 0                         |        |
| Yersinia   | 0                         | 1                                   | 1                                 | 0                         |        |

The presence of coproliths did not discriminate among groups. Summary of stepwise regression; variable appendicitis forward stepwise \( P \) to enter, \(< 0.05 \); \( P \) to remove, \( > 0.05 \).

**Table 3 Forward stepwise regression analysis model, only age and coprostasis were among predictors in the final model**

| Steps | Degrees of freedom | \( F \) to remove | \( P \) to remove | \( F \) to enter | \( P \) to enter | Effect status |
|-------|--------------------|-------------------|------------------|---------------|----------------|---------------|
| Age   | Step number 1      | 3                 | 447207           | 0.005081      | Entered        |               |
| Gender| 3                  | 0.880368          | 0.453150         | Out           |                |               |
| Coprostasis | 3              | 3277140          | 0.023264         | Out           |                |               |
| Coprolith | 3              | 0681613          | 0.564865         | Out           |                |               |
| Other pathology | 3            | 1437535          | 0.234958         | Out           |                |               |
| Age   | Step number 2      | 3                 | 421918           | 0.007020      | In             |               |
| Gender| 3                  | 0729353          | 0.536341         | Out           |                |               |
| Coprostasis | 3              | 1119171          | 0.343986         | Out           |                |               |
| Coprolith | 3              | 1059992          | 0.368677         | Out           |                |               |
mechanism of recurrent appendicitis is either incomplete obstruction of the lumen of the appendix or disproportionate mucus production. Except for two cases of yersiniosis associated with coprostasis, we did not observe any disorder involving the gastrointestinal system (such as inflammatory bowel disease, sarcoidosis, tuberculosis, polyarteritis nodosa, endometriosis, parasitosis, changes in neuroendocrine cells) that could account for the chronic or recurrent inflammation of the appendix.

Our study specifically addressed the presence of coprostasis, as opposed to previous series in which only coproliths were considered as causative of either acute or recurrent disease. A radiographically visualized coprolith was considered by many authors as a specific and unquestionable indicator of appendicitis due to obstruction[9]. A growing body of evidence however, suggests that luminal obstruction is not an indispensable factor in the development of appendicitis. Arnbjorsson and Bengmark[10] measured intraluminal pressures in acute appendicitis, and concluded that obstruction was the result rather than the cause of the inflammatory process. The incidence of coproliths in our series was 1.21%. The frequency of coprolith in acute appendicitis according to others ranges from 0.02%[11,12] up to 65%[13]. Our present study also rejects the role of coproliths as causative factors in recurrent appendicitis and imposes the use of high fiber diet after an atypical episode.

The reasons we followed this methodology to trace the relationship of coprostasis to the recurrent appendicitis were: (1) The distinction between subacute and acute recurrent appendicitis helps to better delineate the role of coprostasis as a causative factor since these are two sequential phases of the same entity from its initiation to the well established clinical presentation. (2) The use of data mining procedure disclosed the variables for use in regression analysis. The Random Forest test consists of a collection (ensemble) of simple tree predictors, each capable of producing a response when presented with a set of predictor values. For classification problems, this response takes the form of a class membership, which associates (classifies) a set of independent (predictor) values with one of the categories present in the dependent variable. (3) We had to establish first the predictors of all the patients’ cohort and subsequently to insert them in analysis for the recurrent appendicitis (subacute or acute) group of patients only in order to avoid a type II error.

According to previous reports, the cut-off age after which the incidence of acute appendicitis declines is about thirty years. Based on our observations, the cut-off age in recurrent appendicitis is around forty.

In summary, it seems from our data that coprostasis rather than coproliths could be a contributing factor to acute exacerbations of chronic inflammatory appendicitis, and that its clinical and histologic findings are milder than those of acute appendicitis.

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