Diagnostic Value of C-Reactive Protein in Acute Appendicitis

Eugene Albu, M.D., Barnett M. Miller, M.D., Young Choi, M.D., Sanjiv Lakhanpal, M.D., R. N. Murthy, M.D., Paul H. Gerst, M.D.

From the Departments of Surgery and Pathology, Bronx-Lebanon Hospital Center, Bronx, New York

Serum C-reactive protein was measured in 56 patients hospitalized with a suspected diagnosis of acute appendicitis. Based on these determinations, four groups of patients were defined: Group A = 26 patients with acute appendicitis who had a C-reactive protein level higher than 2.5 mg/dl. Group B = 4 patients with a C-reactive protein level lower than 2.5 mg/dl who, after surgery based on a presumed diagnosis of acute appendicitis, were found to have a normal appendix. Group C = 22 patients with nonspecific abdominal pain, 18 (72 percent) of whom had an elevated C-reactive protein level, although in only 4 (7.1 percent) were these levels higher than 2.5 percent mg/dl. Group D = 4 patients who had diseases other than acute appendicitis. It is concluded that an increase in C-reactive protein levels to more than 2.5 mg/dl is not a definite indicator of acute appendicitis. However, if the C-reactive protein level in blood drawn 12 hours after the onset of symptoms is less than 2.5 mg/dl, acute appendicitis can be excluded. [Key words: C-reactive protein; Appendicitis; Diagnosis]

Albu E, Miller BM, Choi Y, Lakhanpal S, Murthy RN, Gerst PH. Diagnostic value of C-reactive protein in acute appendicitis. Dis Colon Rectum 1994;37:49–51.

Within a few hours after exposure to an acute inflammatory stimulus, there is a sharp increase in the serum concentration of C-reactive protein, an acute-phase protein, in the body.[1] Until recently, methods to quantify this protein were not available. The nephelometric immunocytochemistry system, which provides exact quantification of C-reactive protein, appears to be a promising aid in evaluating the clinical and prognostic significance of serum concentrations of C-reactive protein. The doubling time of this protein varies from 4 to 11 hours and peak levels occur two to three days after acute injury.[2] Serum concentrations of C-reactive protein are higher when inflammation and tissue destruction are more extensive. However, in the absence of superimposed bacterial infection, C-reactive protein levels rarely exceed 6 to 8 mg/dl. It has been proposed that C-reactive protein levels can be used to differentiate inflammation from infection or acute myocardial infarction from atypical angina.[2]

Address reprint requests to Dr. Albu: Department of Surgery, Bronx-Lebanon Hospital Center, 1276 Fulton Avenue, Bronx, New York 10456.

At present, pathologic confirmation of a preoperative diagnosis of acute appendicitis is anywhere from 25 to 85 percent.[3,4] Negative exploration carries a morbidity of 5 to 15 percent.[3–6] The aim of our study was to ascertain the diagnostic value of C-reactive protein levels in patients suspected of having acute appendicitis.

PATIENTS AND METHODS

The subjects for this double-blind prospective trial were 56 patients between the ages of 4 and 31 (average age, 16) years who were admitted to our institution with a suspected diagnosis of acute appendicitis. Only patients whose symptoms had persisted for more than 12 hours were included. In all cases, acute appendicitis could not be ruled out on the basis of history, physical examination, routine laboratory tests, and radiographs. Serum C-reactive protein was measured by the nephelometer (Array protein chemistry; Beckman Instruments, Fullerton, CA). Normal C-reactive protein levels (Bronx-Lebanon Hospital Center Laboratory) range from 0.08 to 0.8 mg/dl. The results of the measurements were not made available to the treating surgical teams at any time during the hospitalization of the patients.

Depending on the results of examination by an attending surgeon, patients were observed, underwent surgery for acute appendicitis, were treated conservatively, or were transferred to a different specialty service. The patients fell into the following groups: Group A = 26 patients whose surgery and histopathologic findings confirmed acute appendicitis. Group B = 4 patients who underwent surgery with a diagnosis of acute appendicitis; however, histopathology disclosed a normal appendix. Group C = 22 patients in whom symptoms could not be attributed to any specific cause. These patients were categorized as having benign nonspecific abdominal pain. Group D = 4 patients who were diagnosed as having a definite condition other than acute appendicitis.

There was no statistically significant age or sex differences among the patients in any of these groups (Group D excluded). Group comparisons were carried out using Student's *t*-test. Probability levels of less than 0.05 were taken as significant.

RESULTS

A preoperative diagnosis of acute appendicitis was made in 34 (60 percent) of the 56 patients. Laparotomy was performed on 30 of these patients. In 26 (87 percent) of those patients who underwent surgery, histopathologic examination of the resected specimens confirmed acute appendicitis. Four patients (Group D) were subsequently diagnosed as having specific pathologies other than acute appendicitis. Three patients had pelvic inflammatory disease and one had a twisted right ovarian cyst.

The mean C-reactive protein values of the four groups (Figs. 1 and 2) were as follows: Group A: mean, 12.22 mg/dl (range, 2.85–29.1 mg/dl). Within this group, the mean C-reactive protein value in the 17 patients with acute appendicitis was 7.26 mg/dl (range, 2.85–21.6 mg/dl). The mean value in the 6 patients with a perforated appendix was 10.1 mg.dl (range, 4.74 to 19.60 mg/dl). The mean value in the 3 patients with a gangrenous appendix was 19.3 mg/dl (range, 10.3- 29.1 mg/dl) (Fig. 1). Group B: mean, 1.36 mg/dl (range, 0.6–2.1 mg/dl). Group C: mean, 1.61 mg/dl (range, 0.6–8.9 mg/dl). Group D: mean, 11.63 mg/dl (range, 6.6–18.7 mg/dl).

After serial analyses of different C-reactive protein levels and the correlation of these levels with acute inflammatory changes in the appendices, it was observed that patients with a C-reactive protein level higher than 2.5 mg/dl had an ongoing inflammatory process; they were categorized as having a positive test. Patients with a C-reactive protein level lower than 2.5 mg/dl were considered to have a negative C-reactive protein test.

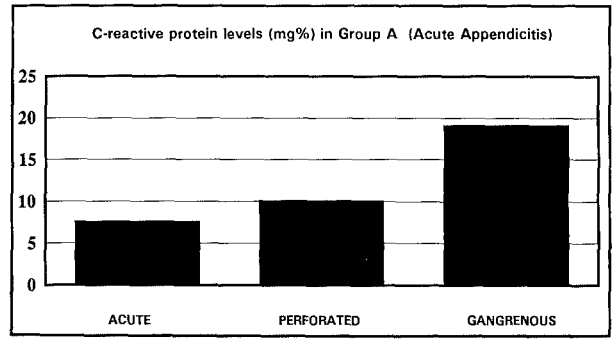

Figure 2. Levels of C-reactive protein in Group A.

The sensitivity of the C-reactive protein test was calculated as 100 percent and the specificity was 84.6 percent. The positive predictive value of the test was 86.6 percent and the negative predictive value was 100 percent (Table 1).

DISCUSSION

The value of serum C-reactive protein level as an indicator of acute appendicitis and, more specifically, as a guide to surgical intervention has been debated.[4, 7–9] Previous investigations have shown that C-reactive protein levels are increased in patients with acute appendicitis[7–9] and other inflammatory diseases.[10] Mikaelsson and Arnbjornsson[7] found abnormally high C-reactive protein levels in 47 percent of their patients with acute appendicitis. Peltola *et al.*[8] noted elevation in 72 percent of their patients.

In our study, C-reactive protein levels were sub-

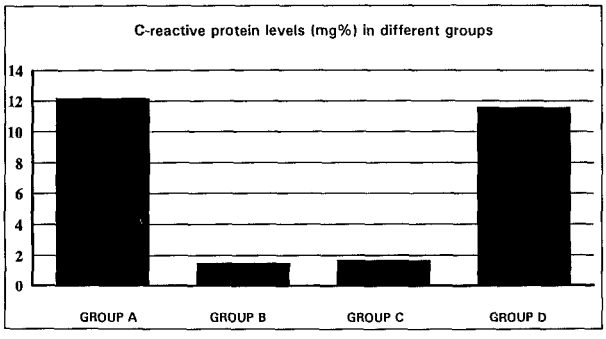

Figure 1. Levels of C-reactive protein in the different groups.

Table 1.
Correlation Between C-Reactive Protein Levels and Histopathologic Findings

CRP Test	Appendicitis		Total No. of Patients
	Present	Absent	
Positive	26	4	30
Negative	0	22	22
Total tested	26	26	52*

C-reactive protein test (levels > 2.5 mg/dl considered positive).

* Four patients from Group D were excluded because they had diseases other than acute appendicitis.

stantially elevated in all patients with acute appendicitis. The same was found by Thimsen *et al.*[9] and Ingram *et al.*[11] C-reactive protein levels increase within 12 hours after the onset of symptoms and reach a peak at 24 to 48 hours, with a mean doubling time of 7.3 ± 1.8 hours. It is possible, therefore, that the time interval between the appearance of symptoms and the actual testing for C-reactive protein levels had some bearing on the results of Mikaelsson and Arnbjorsson[7] and Peltola *et al.*[8]

Four of our patients with benign nonspecific abdominal pain (Group C) had a C-reactive protein level in the same range as that of patients with acute appendicitis (Group A). In two of these patients, these elevated levels were attributed to upper respiratory infection. However, the cause of the C-reactive protein elevations in the other two patients could not be ascertained. In Group C the abnormally high C-reactive protein levels may have been caused by the placement of intravenous lines and other medical procedures. Previous studies have found elevated C-reactive protein values in high percentages of patients with a normal appendix.[9, 10]

Among the Group A patients with uncomplicated acute appendicitis, the C-reactive protein levels were less elevated than those in patients with gangrenous appendicitis. The C-reactive protein values among patients with a perforated appendix fell between these two extremes, for reasons we could not determine.

Both the negative predictive value and the sensitivity of the serum C-reactive protein test were 100 percent. Thus, if this test had been used as a basis for deciding whether or not to perform surgery, four unnecessary laparotomies could have been avoided. In all patients with a C-reactive protein level of less than 2.5 mg/dl at 12 hours after the onset of symptoms, the symptoms resolved spontaneously.

CONCLUSIONS

C-reactive protein levels can be used as an indicator of acute appendicitis. To be sure, the time-tested clinical signs must still serve their purpose. However, when there is doubt about the diagnosis, a low serum C-reactive protein level should be used as a basis for the decision to defer surgery.

REFERENCES

1. Morley JJ, Kushner I. Serum C-reactive protein levels in disease. Ann N Y Acad Sci 1982;389:406–18.
2. Kushner I. C-reactive protein and the acute phase response. Hosp Pract [Off] 1990;25:13–28.
3. Jess P, Bjerregaard B, Brynitz S, Holst-Christensen J, Kalaja E, Lund-Kristensen J. Acute appendicitis: prospective trial concerning diagnostic accuracy and complications. Am J Surg 1981;141:232–4.
4. Mason LB, Deyden WE. Primary appendectomy. Am Surg 1976;42:239–43.
5. Chang FC, Hogle HH, Welling DR. The fate of the negative appendix. Am J Surg 1973;126:752–5.
6. Lewis FR, Holcroft JW, Boey J, Dunphy JE. Appendicitis: a critical review of diagnosis and treatment in 1,000 cases. Arch Surg 1975;110:677–84.
7. Mikaelsson C, Arnbjornsson E. The value of C-reactive protein determinations in patients with suspected acute appendicitis. Ann Chir Gynaecol 1984;73:281–4.
8. Peltola H, Ahlqvist J, Rapola J, *et al.* C-reactive protein compared with white blood cell count and erythrocyte sedimentation rate in the diagnosis of acute appendicitis in children. Acta Chir Scand 1986; 152:55–8.
9. Thimsen DA, Tong GK, Gruenberg JC. Prospective evaluation of C-reactive protein in patients suspected to have acute appendicitis. Am Surg 1989;55:466–8.
10. Gewurz H, Mold C, Siegel J, Fiedel B. C-reactive protein and the acute phase response. Adv Intern Med 1982;27:345–72.
11. Ingram RR, Mohammed R, Tillman J. C-reactive protein and acute appendicitis. J R Coll Surg Edinb 1988;33:115–6.