

Is the Incidence of Appendicitis Reduced in Patients With Sickle Cell Disease?

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ABSTRACT. *Background.* Patients with sickle cell disease (SCD) often present with abdominal pain, usually attributable to vasoocclusion. Experience at a single institution suggested that appendicitis was a rare cause of abdominal symptoms in this population.

Objective. We sought to determine whether the incidence of appendicitis was significantly lower in patients with SCD than in the population at large.

Methods. A 17-year retrospective chart review was performed at Rainbow Babies and Children's Hospital, Cleveland, OH, to determine the approximate incidence of acute appendicitis (AA) in patients with SCD. In addition, we performed a statistical analysis comparing the incidence of AA among SCD patients enrolled in the Cooperative Study of Sickle Cell Disease with that in the general population.

Results. Only two patients with SCD with pathologically confirmed AA were identified among ~200 patients followed at our institution during a 17-year period (~3500 patient-years), yielding an incidence rate of 5.7 cases per 10 000 patient-years. Among 3765 patients with SCD enrolled in the Cooperative Study of Sickle Cell Disease followed for a mean of 5.3 years (19 886 patient-years), a maximum of 9 cases of AA were identified, yielding an incidence rate of 4.5 cases per 10 000 patient-years. Based on data from the National Hospital Discharge Survey of 1978 to 1981, the incidence rate of AA in the general population (0 to 44 years of age) is ~16 per 10 000 patient-years. Paired *t* test analysis demonstrated a highly significant difference ($P < .001$) when comparing the incidence of AA among patients enrolled in the Cooperative Study of Sickle Cell Disease and the population at large.

Conclusion. AA is an unusual event in patients with SCD. The likelihood of developing appendicitis in SCD patients is less than one third of that for the population at large. Conservative therapy is warranted in the large majority of patients with SCD who present with acute abdominal pain. Surgical exploration is best limited to patients with clear evidence of potential surgical pathology or progressive findings during a period of observation. The biologic basis of our findings remains unknown. *Pediatrics* 1998;101(1). URL: <http://www.pediatrics.org/cgi/content/full/101/1/e7>; *sickle cell disease, appendicitis*.

ABBREVIATIONS. SCD, sickle cell disease; AA, acute appendicitis.

Pain caused by microvascular occlusion is among the most common clinical expressions of sickle cell disease (SCD).¹ Abdominal pain often represents a substantial diagnostic challenge in this population of patients. Although most often attributable to vasoocclusion, symptoms and signs may mimic acute surgical processes, particularly appendicitis.² In such circumstances, patients may undergo surgical exploration, often yielding no evidence of gross or microscopic pathology.

Anecdotal observations made by the senior pediatric surgeons at Rainbow Babies and Children's Hospital over several decades suggest that acute appendicitis (AA) is a rare event in children and adolescents with SCD. These observations prompted us to review our single-institution experience, as well as to perform a retrospective review of data accumulated from a large multicenter study of the natural history of SCD (Cooperative Study of Sickle Cell Disease, Phase I).³

We hypothesized that the incidence of AA is significantly lower in patients with SCD than in the general population.

METHODS

Observations at Rainbow Babies and Children's Hospital

We retrospectively reviewed a 17-year experience at our institution, during which 12 patients were identified with a hospital discharge diagnosis of SCD and appendectomy. This period included an estimated 3500 patient-years. Among the 12 patients identified, the majority had incidental appendectomies at the time of other abdominal operative procedures. Only 2 patients had pathologic evidence of AA (approximate incidence of 5.7 cases per 10 000 patient-years). Histologic findings in all other appendices studied were normal. The 2 patients with documented AA involved a 16-year old male with mild SCD, and a 17-year old female receiving chronic transfusion therapy because of cerebral vascular disease.

Cooperative Study of Sickle Cell Disease Data

This dataset included 3765 patients between birth and 82 years of age, followed at 23 clinical centers between 1978 and 1988. Mean length of follow-up was 5.3 years (± 2.0 years), representing 19 886 patient-years.⁴ Nine nonincidental appendectomies were performed among this group (nonincidental appendectomies were defined as primary operative procedures performed in cases of suspected AA). Unfortunately, in a majority of cases, pathologic data was unavailable for review; hence, for the purposes of this study, all cases were considered to represent AA, although it is likely that some appendices would have been pathologically normal. The incidence of appendicitis in this population is, therefore, ≤ 4.5 cases per 10 000 patient-years.

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Appendicitis in the General Population

The incidence of AA in the general population was calculated using data accumulated by the National Hospital Discharge Survey of 1978–1981.^{5,6} This survey provides data on a representative sample of discharge diagnoses recorded in all short-stay, nonfederal hospitals in the United States. Data are weighted to derive national estimates of disease incidence. Among individuals 0 to 44 year of age (a range that closely approximates the SCD population database), the incidence of appendicitis was ~16 cases per 10 000 patient-years.^{5,6}

Statistical Analysis

Comparison of the incidence of AA in the SCD population with that of the general population using the paired *t* test yielded a highly statistically significant difference ($P < .001$). The likelihood of developing AA in patients with SCD was less than one third of that of the population at large.

DISCUSSION

Review of available data supports the hypothesis that the occurrence of AA is substantially lower in patients with SCD than in the general population. We were able to demonstrate this difference with a high degree of statistical significance.

The biologic basis for this observation is unknown and deserves additional study. Possible considerations include alterations in the immune/inflammatory response in patients with SCD, a decrease in lymphoid tissue proliferation in the gastrointestinal tract leading to a lower likelihood of obstruction of appendiceal lumen, and/or an effect of prophylactic antibiotic therapy on gastrointestinal tract flora.

It has been suggested that the incidence of AA is lower in the nonwhite population, although precise data are not available. Addiss and coworkers⁷ estimate that whites are ~1.5 times more likely to develop AA than nonwhites. However, this racial difference does not appear to account for our findings.

Our observations have considerable implications in the approach to the patient with SCD and acute abdominal pain. In the absence of florid and clear evidence of potential surgical pathology, a cautious, expectant approach seems warranted. Conservative treatment, including effective pain management, hy-

dration, and other supportive measures, appears warranted in the majority of patients before contemplating surgical intervention. Patients with SCD and intraabdominal vasoocclusion often manifests signs suggesting surgical disease, ie, abdominal wall muscle rigidity and distention.⁸ The potential for overinterpretation of these findings in the SCD population exists, particularly among physicians and surgeons with limited experience in the treatment of children and adults with hemoglobinopathy. Although relatively unusual, AA does occur in patients with SCD; hence, progressive abdominal findings during the period of observation warrants consideration of AA or other surgical complications.

In summary, our observations and analysis of available data demonstrate that AA is far less common in patients with SCD than in the population at large. The biologic basis of our findings remains unknown.

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