

Anorectal Disease in Neutropenic Leukemic Patients

Operative *vs.* Nonoperative Management

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PURPOSE: This study was designed to evaluate the spectrum, clinical presentation, management, and outcome of anorectal disease in neutropenic leukemic patients and to compare operative and nonoperative management in neutropenic leukemic patients. **METHODS:** A retrospective review of hospital records was performed. **RESULTS:** One hundred fifty-one of 2,618 (5.8 percent) patients hospitalized with leukemia had concomitant symptomatic anorectal disease. Data from 81 patients were available for analysis. Fifty-two (64 percent) were treated nonoperatively and 29 (36 percent) underwent operative treatment. Fifty-seven (70.4 percent) had absolute neutrophil counts $<1,000/\text{mm}^3$, and 54 (66.7 percent) were severely neutropenic (absolute neutrophil count $<500/\text{mm}^3$). Management and outcomes of 54 severely neutropenic patients were analyzed. In 20 patients who underwent surgery there were 4 deaths (20 percent) and 4 recurrences (20 percent), whereas in 34 patients managed nonoperatively there were 6 deaths (18 percent) and 4 recurrences (12 percent) ($P > 0.05$). **CONCLUSIONS:** Symptomatic anorectal disease afflicted 5.8 percent of hospitalized leukemic patients. In these patients, anorectal sepsis was a major source of mortality. Our data suggest that anorectal abscesses in neutropenic leukemic patients may be safely drained. Because we did not observe excessive morbidity or mortality (20 percent *vs.* 18 percent) in the operated neutropenic leukemics as compared with the nonoperated patients, selected neutropenic leukemic patients should not be denied anorectal surgery when otherwise indicated. [Key words: Anorectal disease; Leukemia; Neutropenia; Anorectal abscess]

Grewal H, Guillem JG, Quan SHQ, Enker WE, Cohen AM. Anorectal disease in neutropenic leukemic patients: operative *vs.* nonoperative management. *Dis Colon Rectum* 1994; 37:1095-1099.

Symptomatic anorectal disease afflicts 2 percent to 32 percent of oncology patients.¹⁻⁷ When septic complications develop, anorectal disease is potentially fatal, especially in neutropenic patients, in

whom mortality rates range from 11 percent to 57 percent.^{1-4, 8-14} Despite studies supporting nonoperative^{1, 4, 13, 15} and operative management,^{2, 8, 9, 16} optimal management of anorectal disease and their infectious complications in neutropenic patients is unclear. Although diverting colostomy and debridement may be life-saving in necrotizing anorectal infections,^{17, 18} there is no consensus on the management of non-necrotizing infections. A previous report from Memorial Sloan-Kettering Cancer Center (MSKCC) recommended low-dose radiation therapy for control of perianal and anorectal complications.¹² However, a subsequent randomized trial did not show any benefit from radiation therapy.¹⁹ A prospective, randomized, controlled trial comparing operative and nonoperative management has yet to be performed. To further define the spectrum, clinical presentation, management, and outcome of anorectal disease in neutropenic leukemic patients, we reviewed the MSKCC records of patients treated for leukemia with associated symptomatic anorectal disease.

METHODS

Study Design

A retrospective review of hospital records was performed. Neutropenia was defined as an absolute neutrophil count (ANC $< 1,000/\text{mm}^3$) and severe neutropenia as an ANC $< 500/\text{mm}^3$. Anorectal disease was classified into four groups: anorectal infection, anal fissure, anal fistula, and hemorrhoids. Outcome assessment was based on a description of the anorectal condition and classified as 1) *resolution*, control of signs and symptoms; 2) *recurrent*, recurrence of signs or symptoms after resolution was documented, and 3) *death*. Outcomes of operated (OR) *vs.* nonoperated (non-OR), severely neutropenic patients were analyzed.

Read at the meeting of The American Society of Colon and Rectal Surgeons, Chicago, Illinois, May 2 to 7, 1993.

Dr. Guillem is recipient of a Career Development Award from the American Cancer Society and a Grant from the Richard Molin Foundation.

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Patient Selection

Inclusion into the study required hospitalization at MSKCC between 1980 and 1990 with a diagnosis of leukemia and symptomatic anorectal disease.

Patient Exclusion

Seventy patients were excluded from the study (34 incomplete or unavailable charts, 24 patients with chronic asymptomatic anorectal disease, 6 patients with previous treatment at another hospital, and 6 coding errors).

Statistical Analysis

Chi-squared, Fisher's exact test, and Student's *t*-test were used. *P* values < 0.05 were considered significant.

RESULTS

One hundred fifty-one of 2,618 (5.8 percent) leukemics admitted to MSKCC had a concomitant diagnosis of benign anorectal disease. Data on 81 patients were available for analysis. There were 50 males and 31 females, with ages ranging from 1 to 68 (mean, 45.3) years. Sixty-four (79 percent) patients had acute leukemia (myeloblastic, 36; lymphoblastic, 22; acute unclassified, 6) and 17 (21 percent) had chronic leukemia (myeloblastic, 14; lymphoblastic, 3). Leukemia was in remission in 46 percent, in relapse in 35 percent, and newly diagnosed or active in 19 percent. At the time of admission, 53 percent of patients were receiving chemotherapy, and 25 percent had received chemotherapy within one month of admission. In addition, 21 percent of patients were receiving ste-

roids. Forty-seven percent had a past history of anorectal complaints, and nine percent had undergone previous anorectal surgery.

Clinical Characteristics

Anorectal pain was the most common complaint (86 percent), and local tenderness was the most frequent physical finding (44 percent). Although erythema and cellulitis were present in 42 percent, purulent discharge and fluctuation were uncommon (13.5 percent). Fever ($\geq 38^\circ$) was present in 80 percent of patients on hospitalization. Four groups were identified: anorectal infections (39); anal fissures (22); inflamed or prolapsed hemorrhoids (12); anal fistulas (8).

Laboratory Data

Results of hematologic tests, blood cultures, and anorectal cultures are summarized in Table 1. Blood and anorectal cultures were positive in 30 and 22 patients, respectively. The most common organisms cultured from blood and anorectum were *Escherichia coli* and *Pseudomonas aeruginosa*.

Management

Seventy-six (94 percent) patients were treated with intravenous antibiotics upon admission to the hospital, with a mean duration of treatment of 25.7 (range, 1–125) days. Twenty-nine (36 percent) underwent OR management and 52 (64 percent) were treated non-OR. Twenty (69 percent) patients from the OR group and 34 (65 percent) from the non-OR group were severely neutropenic (ANC < 500/mm³). The opera-

Table 1.
Laboratory Data of 81 Leukemic Patients with Anorectal Disease

Groups	Anorectal Infection	Anal Fissure	Anal Fistula	Hemorrhoids
Hematocrit (%)	20.3–37.0	27.5–42.9	27.6–45.0	21.0–35.0
Range (mean)	(27.9)	(32.8)	(30.8)	(26.1)
Hemoglobin (g/dl)	9.9–13.0	6.8–13.1	8.5–15.0	6.6–11.7
Range (mean)	(9.3)	(10.2)	(10.3)	(8.8)
Platelet count ($\times 10^3/\text{mm}^3$)	7.0–416.0	9.0–455.0	19.0–310.0	3.0–1588.0
Range (mean)	(69.7)	(69.8)	(116.0)	(174.0)
WBC ($\times 10^3/\text{mm}^3$)*	0–67.4	0.1–134.0	0.2–3.8	0.2–288.0
Range (mean)	(9.3)	(11.2)	(1.7)	(54.4)
ANC				
<1000/mm ³ †	28	16	5	9
<500/mm ³	24	16	5	9
Positive blood cultures	17	8	2	3
Positive anorectal cultures	21	—	—	1

* WBC = white blood count.

tive procedures performed are shown in Table 2. Incision and drainage in 14 and sphincterotomy in 7 patients were the most frequently performed procedures. In the non-OR group, all patients received local care, including sitz baths, stool softeners, local medication, and analgesics. In addition, five patients received low-dose perineal radiation therapy (300–600 cGy).

Outcome

There were 13 (16 percent) deaths (OR, 4; non-OR, 9). Resolution was documented in 58 (72 percent) patients, whereas 10 (12 percent) had recurrence of their condition. Mean hospital stay was 25.2 days in the OR group and 24.6 in the non-OR group ($P > 0.05$). In the OR group there were two (7 percent) complications related to the operation. One patient had bleeding from his colostomy requiring transfusion, whereas the second patient had transient hypotension during induction of anesthesia.

Analysis of Outcome in Severely Neutropenic Patients

Hematologic data of severely neutropenic OR and non-OR groups were similar, although the OR group had a slightly higher mean ANC than the non-OR group ($P < 0.05$) (Table 3). Outcomes of severely neutropenic OR and non-OR groups are shown in Table 4. There were four deaths (20 percent) and four recurrences (20 percent) in the OR group as compared with six deaths (18 percent) and four recurrences (12 percent) in the non-OR group ($P > 0.05$). Three of four deaths (75 percent) in the OR group and five of six deaths (83 percent) in the non-OR group were in patients with anorectal infections.

DISCUSSION

The 5.8 percent prevalence of anorectal disease in hospitalized leukemic patients in our study is

Table 3.
Comparison of Hematologic Data of OR and Non-OR Severely Neutropenic Patients

Variable (mean \pm S.D.)	OR group (no. = 20)	Non-OR group (no. = 34)
Hematocrit (%)	29.8 (± 6.7)	26.9 (± 4.1)
Hemoglobin (g/dl)	10.1 (± 1.9)	9.1 (± 1.3)
Platelet ($\times 10^3/\text{mm}^3$)	51.8 (± 69)	50.3 (± 75)
ANC ($/\text{mm}^3$)*	137.3 (± 157)	69.8 (± 97)

* $P < 0.05$ by Students *t*-test.

consistent with the reported 2 to 8 percent from previous series.^{1, 2, 4} Our overall 18.5 percent mortality from anorectal disease in severely neutropenic leukemic patients compares favorably with rates of 20 percent to 57 percent in previously reported series,^{1, 3, 4, 10–14} all of which included patients who were not severely neutropenic. Our data, showing similar outcomes and mortality (18 percent *vs.* 20 percent) in the OR and non-OR groups, do not resolve the issue of which management approach is better. However, it does indicate that in selected severely neutropenic patients OR management does not result in excessive morbidity and mortality when compared with non-OR management.

Severe neutropenia was present in two-thirds of our patients and appears to increase the risk for anorectal infectious complications. This is supported by previous reports of an increased incidence of these complications in association with neutropenia.^{2, 8, 9, 14} A striking feature in these patients is the absence of classical signs of abscess formation. In our patients, fever and local pain were the most common presenting complaints. On physical examination, tenderness and erythema were present in the majority of patients. However, fluctuation and purulent drainage were uncommon. This has also been observed in previous reports.^{2, 16, 20} Absence of classical signs of abscess formation, along with risk of progressive necrotizing

Table 2.
Operative and Nonoperative Management of Anorectal Disease in 81 Leukemic Patients

Groups	Anorectal Infection	Anal Fissure	Anal Fistula	Hemorrhoids
No.	39	22	8	12
Non-OR (no.)	24	15	3	10
OR (no.)	15	7	5	2
Procedure	I&D, 15; (I&D with colostomy, 1)*	Sphincterotomy, 7; (sphincterotomy with hemorrhoidectomy, 1)	Fistulotomy, 5; (fistulotomy with sphincterotomy, 3)	Hemorrhoidectomy, 2; (hemorrhoidectomy with sphincterotomy, 1)

* I&D = incision and drainage.

Table 4.
Outcome of Operative vs. Nonoperative Management of 54 Leukemics with Severe Neutropenia

Groups (Outcome)	Anorectal Infection	Anal Fissure	Anal Fistula	Hemorrhoids	Total No. (%)
OR (no.)	11	4	3	2	20 (100)
Death	3	0	0	1	4 (20)
Resolved	5	3	3	1	12 (60)
Recurred	3	1	0	0	4 (20)
Non-OR (no.)	13	12	2	7	34 (100)
Death	5	0	1	0	6 (18)
Resolved	6	11	0	7	24 (71)
Recurred	2	1	1	0	4 (12)

infections,^{18, 21, 22} mandates a high index of suspicion for anorectal disease in neutropenic leukemics with fever and local pain. An adequate local examination, including digital rectal and proctoscopic examination, is necessary to arrive at a diagnosis in these extremely sick patients. We did not observe an increased complication rate associated with digital rectal and proctoscopic examination.

Intrarectal ultrasound may be useful in diagnosing perianal abscesses in patients with uncertain perirectal disease,^{23, 24} as well as in patients with anorectal complications of Crohn's disease.²⁵ Magnetic resonance imaging (MRI) may also help in diagnosing perianal abscesses in Crohn's disease.²⁶ Currently we are exploring the utility of these diagnostic modalities in neutropenic patients with unexplained anorectal complaints. Until the reliability of these and other noninvasive studies is determined, when local pain, tenderness, and sphincter spasm prevent adequate evaluation, we recommend an examination under anesthesia to exclude an occult anorectal abscess.

E. coli and *P. aeruginosa* were the most common bacteria isolated from both blood and anorectal cultures, which is similar to previous reports.^{1, 4, 8, 10, 14} This is in contrast to anorectal abscesses in non-neutropenic patients, in whom gram-positive bacteria are more commonly isolated.²⁷ A combination of neutropenia, colonization of perineal skin by enteric flora, and break in mucosal integrity of the anorectum may be responsible for increased frequency of gram-negative infections in this group of patients. Antibiotic treatment for suspected anorectal infections should, therefore, provide coverage against gram-negative as well as gram-positive bacteria.²⁸

CONCLUSIONS

A total of 5.8 percent of leukemic patients hospitalized at MSKCC had concomitant anorectal disease,

which when infectious was a major source of mortality. Anorectal abscesses in severely neutropenic leukemic patients may be drained without incurring a higher mortality than that noted in nonoperated patients. Because we did not observe excessive morbidity or mortality in operated neutropenic leukemic patients as compared with nonoperated patients, selected neutropenic leukemic patients should not be denied anorectal surgery when otherwise clinically indicated.

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