

Perianal Sepsis in Hematologic Malignancy: MR Imaging Appearances and Distinction from Cryptoglandular Infection in Immunocompetent Patients¹

Andrew A. Plumb, MRCP, FRCR
Steve Halligan, MD, FRCP, FRCR
Gauraang Bhatnagar, MBBS, FRCR
Stuart A. Taylor, MD, MRCP, FRCR

Purpose:

To use magnetic resonance (MR) imaging to document the appearance of perianal infection in patients with a hematologic malignancy (HM) compared with that in immunocompetent control patients.

Materials and Methods:

After an ethical waiver was obtained, 38 patients with an HM were matched by age and sex to 38 control patients with no history of immunocompromise or Crohn disease. Both groups had undergone MR imaging for perianal symptoms and/or systemic sepsis. Two radiologists who were blinded to the diagnosis independently reviewed the MR images and recorded the size and distribution of abscesses and/or fistula tracts, the extent of perianal edema, and the likely diagnosis. Groups were compared by using the Mann-Whitney-Wilcoxon, χ^2 , or Fisher exact test. Receiver operating characteristic (ROC) curves were constructed to estimate the ability of MR imaging to help distinguish patients with an HM from control patients.

Results:

Patients with an HM had significantly greater perianal edema than did control patients (mean arc angle of anal canal involved, 220° vs 60°; $P < .001$). However, they had significantly lower rates of fistula (15 [39.5%] vs 35 [92.1%] of 38; $P < .001$). Abscesses were similar in frequency (10 [26.3%] vs 17 [44.7%] of 38; $P = .15$) and were unrelated to the degree of neutropenia ($P = .71$) or the use of chemotherapy ($P = .10$). Surgical treatment was rarely required in patients with an HM, either during the acute illness (four [10.5%] of 38) or thereafter (three [7.9%] of 38). MR imaging had an excellent ability to help discriminate patients with HM from immunocompetent patients (areas under the ROC curve, 0.91 and 0.97).

Conclusion:

Perianal infection in patients with an HM is more likely to cause diffuse perianal edema and is less likely to cause fistulas than in immunocompetent patients. MR imaging can help distinguish patients with an HM from those without immunocompromise.

©RSNA, 2015

Online supplemental material is available for this article.

¹From the Centre for Medical Imaging, University College London, Podium Level 2, University College Hospital, 235 Euston Rd, London, NW1 2BU. Received July 31, 2014; revision requested September 17; revision received November 19; accepted December 11; final version accepted December 23. Address correspondence to A.A.P. (e-mail: aaoplumb@doctors.net.uk).

Hematologic malignancies account for almost 10% of new cancer diagnoses annually in the United States (1) and represent abnormal proliferation of hematopoietic or lymphoid cell lines (2). Patients with these malignancies are immunocompromised because of the clonal expansion of malignant cells in the bone marrow that disrupts normal immunologic function. Furthermore, treatment for hematologic malignancies is commonly immunosuppressive, whether through chemotherapy or marrow irradiation or after bone marrow transplantation (3). Additionally, chemotherapy may compromise the normal barrier function provided by the skin—a compromise that is manifest clinically as oral and

perianal mucositis, which predisposes to infection (4).

Perianal infection occurs in approximately 5%–10% of patients with acute leukemia (5–8) and may occasionally be the presenting complaint (9). The underlying pathophysiology is believed to be no different from that in immunocompetent patients—that is, infection begins in the intersphincteric anal glands (10). However, the clinical manifestation may be modified by immunocompromise and impaired pus formation due to neutropenia. This results in diffuse perianal swelling, edema, and erythema rather than the more typical fluctuant collection (11). Although clinically obvious abscesses require prompt drainage to prevent systemic sepsis or even death (6), clinicians may be reluctant to examine the anus and rectum of immunocompromised patients for fear of provoking bacteremia and deterioration. Indeed, consensus guidelines prohibit digital rectal examination of patients with neutropenia (12). This causes a diagnostic dilemma: Occult infection requires prompt identification and treatment, particularly with an attenuated host immune response, but detailed physical examination is relatively contraindicated. Magnetic resonance (MR) imaging can help resolve this by demonstrating the presence, extent, and distribution of perianal sepsis, allowing surgical intervention to be appropriately planned (13).

Here, we test the hypotheses that (a) perianal abscess formation is less common in patients with hematologic malignancies than in immunocompetent individuals and (b) that diffuse perianal edema is more common. We aimed to use MR imaging to document the distribution and morphology of

perianal disease in patients with hematologic malignancies and in immunocompetent control patients.

Advances in Knowledge

- Patients with hematologic malignancies and perianal symptoms had considerably greater perianal edema than did immunocompetent patients with cryptoglandular disease (58.7% vs 13.4% of anal canal height inflamed).
- Perianal fistulas were less common in patients with hematologic malignancies with perianal symptoms (21 [55.3%] of 38) than in immunocompetent patients (35 [92.1%] of 38).
- Patients with hematologic malignancies and perianal symptoms formed perianal and pelvic abscesses in 26.3% of cases (10 of 38), even in the presence of neutropenia.
- Acute surgical treatment was required in only approximately 10% of patients (four of 38) with hematologic malignancies and perianal symptoms.
- MR imaging can help discriminate between the appearance of perianal infection in patients with hematologic malignancies and that in immunocompetent patients in most cases (areas under the receiver operating characteristic curve, 0.91 and 0.97).

Implication for Patient Care

- MR imaging can be used successfully to depict perianal inflammation, abscesses, and fistulas in patients with hematologic malignancies and perianal symptoms and to distinguish such patients from immunocompetent individuals.

Materials and Methods

Ethical permission and patient consent are not required by our institution for retrospective review of imaging series acquired during normal patient care.

Patient Selection

Using the hospital radiology information system, we identified patients who had undergone anorectal MR imaging between January 2007 and March 2014 (inclusive) after being referred by a hematologist. Patients were included if they had been given a diagnosis of hematologic malignancy according to their electronic patient record and if they were imaged for the evaluation of perianal symptoms and/or systemic sepsis. Exclusion criteria were a diagnosis of Crohn disease or nonhematologic malignancy or previous anorectal surgery. Thirty-eight patients with hematologic malignancies underwent 50 MR imaging examinations during the study period. Because we expected repeat examinations in the same patient to be more similar than those from different individuals (ie, clustered), only the earliest MR imaging study was used for initial analysis. However, we subsequently

Published online before print

10.1148/radiol.15141662 **Content codes:** GI MR

Radiology 2015; 276:147–155

Abbreviations:

AUC = area under the ROC curve
 CI = confidence interval
 ROC = receiver operating characteristic
 STIR = short inversion time inversion recovery

Author contributions:

Guarantors of integrity of entire study, A.A.P., G.B.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; manuscript final version approval, all authors; agrees to ensure any questions related to the work are appropriately resolved, all authors; literature research, A.A.P., S.H., S.A.T.; clinical studies, all authors; statistical analysis, A.A.P.; and manuscript editing, all authors

Conflicts of interest are listed at the end of this article.

Table 1

MR Imaging Parameters

Parameter	1.5-T Imaging Units		3.0-T Imaging Units	
	Coronal/Axial STIR Sequence	Sagittal/Axial T2-weighted TSE Sequence	Coronal/Axial STIR Sequence	Sagittal/Axial T2-weighted TSE Sequence
Field of view (cm)	18–24	18–24	18–24	18–24
No. of sections	25/40	25/40	25/35	25/35
Repetition time (msec)	3470/5650	4910/8370	4400/5075	3890/5075
Echo time (msec)	21/30	97/99	60/60	100/85
Inversion time (msec)	150/150	NA	200/200	NA
Echo train length	7/7	13/15	12/12	20/17
Image matrix	256 × 159/256 × 173	256 × 256/256 × 173	244 × 192/244 × 192	256 × 244/348 × 205
Section thickness (mm)	4/4	6/4	3/3	3/3
Section gap (mm)	5/4.4	6/4.4	4/4	4/3.3
No. of signals acquired	1/1	3/3	2/2	3/2

Note.—NA = not applicable, TSE = turbo spin echo.

inspected follow-up MR imaging studies to determine if imaging features changed over time.

For each patient, we chose a control patient, defined as the next sex- and age-matched patient (to within 5 years) who underwent imaging after the study patient. Control patients had been imaged for perianal symptoms and/or systemic sepsis but had no preceding diagnosis of malignancy, immunocompromise, or Crohn disease according to their electronic patient record. Control patients were followed up for a median of 4.3 years (interquartile range: 2.1–5.8 years; range, 1.6–7.5 years) to confirm that these diseases did not develop subsequently.

Clinical Data Recorded

For patients with hematologic malignancies we recorded the following: (a) age and sex; (b) the hematologic diagnosis; (c) current or recent (<3 months) use of chemotherapy; (d) any previous bone marrow transplantation and, if relevant, its type; (e) the lowest neutrophil count at the time of imaging (within 2 weeks of the examination date); (f) perianal symptoms; (g) requirement for immediate (≤ 1 week) surgical drainage; and (h) any subsequent need for re-drainage, examination under anesthesia, or specific treatment for perianal fistula. For control

patients, we recorded a and f–h from the above list.

Imaging Protocol and Viewing Conditions

All patients were imaged with one of five MR imaging units: three units with a 1.5-T field strength (Avanto or Symphony; Siemens, Erlangen, Germany) and two with a 3.0-T field strength (Ingenia or Achieva, Philips, Best, the Netherlands). Imaging protocols comprised sagittal and axial oblique T2-weighted turbo spin-echo sequences, as well as axial oblique and coronal oblique short inversion time inversion recovery (STIR) imaging, angled to the central axis of the anal canal (Table 1).

Images were viewed independently in a random order with a picture archiving and communication system (Impax 6.4.0.4551; Agfa Healthcare, Mortsel, Belgium) by two abdominal radiologists (A.A.P. [radiologist 1] and G.B. [radiologist 2], with 7 and 6 years of experience in abdominopelvic MR imaging, respectively). Randomization was performed separately for each radiologist by using statistical software (14). Although the radiologists were aware that they would be interpreting findings in patients with and patients without hematologic malignancies and that there was a clinical suspicion of perianal sepsis, they were blinded to clinical information and results of prior

imaging examinations. They were asked to record the presence of the following: (a) discrete fluid collections or abscesses and their number, size, and location; (b) any internal enteric opening in the anal canal; (c) fistulous or sinus tracts and their type (according to classification system of Parks et al [15]); and (d) any extensions from this primary tract, including their location. An abscess was defined as a localized, rounded collection of predominantly fluid signal intensity that exhibited a mass effect on adjacent structures, and a fistula was defined as an elongated tubular structure with an internal enteric and external opening. The anal canal was defined as that part of the gastrointestinal tract running between the anorectal junction at the level of the puborectalis sling and the external anal margin. Each radiologist made the assessment separately, and disagreements were subsequently resolved in consensus. The radiologists also estimated the proportion of the anal canal and the perianal region that exhibited MR imaging features of inflammation, defined as high signal intensity distinct from that of normal blood vessels on STIR images (16). This assessment was made by using (a) the axial section judged to be most abnormal, with extent described as the number of hours of an imaginary clock face centered on

the anal canal, and (b) the coronal section judged to be most abnormal, with extent described as the percentage of the length of the anal canal that appeared inflamed. Finally, the radiologists were asked to classify the patient as having a hematologic malignancy or not by using a 101-point scale. They were informed that existing clinical literature suggested that diffuse perianal inflammation was common in immunocompromised patients (11), but they were not required to use specific MR imaging criteria—instead, they were asked to give their overall clinical opinion. A score of 100 was assigned when the radiologists were certain of the diagnosis of hematologic malignancy; scores of 50 or greater were used to indicate preference for that diagnosis. A score of 0 indicated certainty that the patient was an immunocompetent control patient; scores of less than 50 were used when this was believed to be more likely.

Statistical Analysis

Data were collated by using Excel for Macintosh (Microsoft, Redmond, Wash) and were analyzed by using R, version 2.15.1 (R Foundation for Statistical Computing, Vienna, Austria). Between-group comparisons were performed by using the Mann-Whitney-Wilcoxon test. To determine which MR imaging features were more commonly seen in immunocompetent control patients and which predominated in patients with hematologic malignancies, we compared the proportion of patients in each group using the χ^2 test (or the Fisher exact test where expected cell counts were ≤ 5), considering $P < .05$ to indicate a significant difference. We used the consensus interpretation of the two radiologists to define the true presence or absence of a particular MR imaging feature. Agreement between radiologists was assessed by means of percentage agreement for binary variables and by means of Bland-Altman limits of agreement for quantitative variables (17). To determine the ability of MR imaging to help distinguish patients with hematologic malignancies from control patients, we constructed

Table 2

Demographic Data, Clinical Features, and Subsequent Treatment for Patients with Hematologic Malignancy and Matched Control Patients

Parameter	Patients with Hematologic Malignancy (n = 38)	Control Patients (n = 38)	PValue
Baseline parameters			
Age (y)*	38.9 ± 18.5	41.5 ± 14.7	.41
No. of men	25 (65.8)	25 (65.8)	>.99
Neutrophil count ($\times 10^9/L$)*	1.09 ± 1.92
Hematologic diagnosis			
Acute myeloid leukemia	21 (55.3)
Acute lymphoid leukemia	3 (7.9)
B-cell lymphoma	3 (7.9)
Other	11 (28.9)
Clinical features			
Pain	34 (89.5)	28 (73.7)	.14
Fever	18 (47.4)	8 (21.1)	.03
Discharge	5 (13.2)	19 (50.0)	.001
Swelling	6 (15.8)	6 (15.8)	>.99
Subsequent treatment			
Incision and drainage	4 (10.5)	8 (21.1)	.34
Examination under anesthesia	6 (15.8)	34 (89.5)	<.001
Seton	1 (2.6)	18 (47.4)	<.001
Other fistula treatment	2 (5.3)	15 (39.5)	<.001
Lay-open procedure	2 (5.3)	10 (26.3)	.03
Fistula plug	0	3 (7.9)	.24
Advancement flap	0	2 (5.3)	.47

Note.—Unless otherwise specified, data are numbers of patients, with percentages in parentheses.

* Data are means ± standard deviations.

receiver operating characteristic (ROC) curves for each reader using their individual confidence scores (18). Empiric curve thresholds were taken above and below each confidence score, and smoothed curves used the binormal assumption. Areas under the ROC curve (AUCs) were calculated by using the trapezoidal method; 95% confidence intervals (CIs) for empiric AUCs were constructed according to the method of DeLong et al (19), and smoothed AUCs were calculated with the percentile method from 2000 bootstrap replicates.

Results

Clinical Characteristics

Patient demographics and clinical features are shown in Table 2. Men outnumbered women at a rate of approximately two to one. The mean age was

38.9 years in the study group and 41.5 years in the control group. Neutrophil counts were available for 37 of 38 patients with hematologic malignancies: 28 (75.7%) had neutrophil counts of less than $1.0 \times 10^9/L$, indicating moderate neutropenia, and 24 (64.9%) were severely neutropenic (neutrophil count, $<0.5 \times 10^9/L$) (20). Only one patient had a normal neutrophil count ($>2.5 \times 10^9/L$). Seven (18.4%) of the 38 patients had previously undergone bone marrow transplantation (five allografts and two autografts). Twenty-six (68.4%) of the patients were undergoing chemotherapy at the time of the MR imaging examination, and 33 (86.8%) had undergone chemotherapy within 3 months.

The most common symptom provoking MR imaging was pain, in both the study group (34 [89.5%] of 38) and the control patients (28 [73.7%] of

Table 3

MR Imaging Findings in Patients with Hematologic Malignancy and Control Patients

Finding	Patients with Hematologic Malignancy (n = 38)	Control Patients (n = 38)	P Value
Abscess			
No. of patients with an abscess	10 (26.3)	17 (44.7)	.15
Location of abscess*			
Intersphincteric	9 (23.7)	10 (26.3)	>.99
Ischioanal	1 (2.6)	7 (18.4)	.18
Supralevator	1 (2.6)	1 (2.6)	>.99
Subcutaneous	1 (2.6)	0	>.99
Mean diameter of abscess (cm)	2.0	2.1	.69
Fistula tracts			
No. of patients with a visible internal opening	21 (55.3)	35 (92.1)	<.001
No. of patients with a fistula	15 (39.5)	35 (92.1)	<.001
No. of patients with a fistula who also had extensions	4 (26.7)	11 (31.4)	>.99
Classification of primary fistula			
Intersphincteric	12 (80.0)	20 (57.1)	.22
Transsphincteric	3 (20.0)	15 (42.9)	...
Perianal inflammation			
Mean no. of hours of the clock involved (axial)	7.2	1.9	<.001
Mean percentage of the anal canal height involved (craniocaudal)	58.7	13.4	<.001
Radiologist 1 diagnosis			
Correct	27	37	...
Incorrect	11	1	...
Radiologist 2 diagnosis			
Correct	25	38	...
Incorrect	13	0	...

Note.—Unless otherwise specified, data are numbers of patients, with percentages in parentheses.

* One patient with hematologic malignancy and two control patients had abscesses in more than one anatomic compartment.

38). Fever was more common among patients with hematologic malignancies (18 [47.4%] of 38) than among control patients (eight [21.1%] of 38; $P = .03$), whereas control patients were more likely to have discharge (five patients [13.2%]; 19 control patients [50.0%]; $P = .001$).

MR Imaging Features

MR imaging appearances in patients with hematologic malignancies and control patients are summarized in Table 3. There was good agreement between the two radiologists regarding the presence of abscess (agreement in 71 [93.4%] of the 76 total patients) and fistula (agreement in 62 [81.6%] of the 76 total patients). At subsequent consensus

interpretation, patients with hematologic malignancies were observed to have a lower rate of abscess formation (10 [26.3%] of 38) than did control patients (17 [44.7%] of 38), but this difference was not statistically significant ($P = .15$). There was no difference in the average size of abscesses when present (patients with hematologic malignancies: 2.0 cm; control patients: 2.1 cm; $P = .69$). There was no discernible relationship between neutrophil count and the presence of abscesses in patients with hematologic malignancies (patients without an abscess, median neutrophil count = $0.49 \times 10^9/L$ [interquartile range, $0.07-1.09 \times 10^9/L$]; patients with an abscess, median neutrophil count = $0.44 \times 10^9/L$ [interquartile

Figure 1

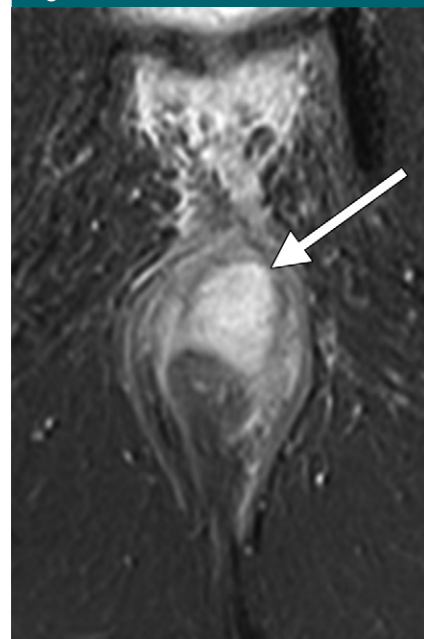


Figure 1: Axial STIR MR image (repetition time msec/echo time msec/inversion time msec, 5650/30/150) through the anal canal in a 57-year-old man with mantle cell lymphoma shows an intersphincteric abscess (arrow).

range, $0.08-0.69 \times 10^9/L$]; $P = .71$). Similarly, there was no significant difference in rates of abscess formation between patients who had and those who had not undergone bone marrow transplantation (two [28.6%] of seven patients who had undergone transplantation had an abscess, while eight [25.8%] of 31 patients who had not undergone transplantation had an abscess; $P > .99$) or between patients who had and those who had not recently (<3 months) received chemotherapy (recent chemotherapy: seven [21.2%] of 33 patients had an abscess; no recent chemotherapy: three [60.0%] of five had an abscess; $P = .10$, Fig 1).

Fistulas were less common in patients with hematologic malignancies than in control patients, occurring in 15 (39.5%) of 38 such patients versus 35 (92.1%) of 38 control patients ($P < .001$). An internal opening was visible for 21 (55.3%) patients with hematologic malignancies and 35 (92.1%) control patients ($P < .001$). Considering

Figure 2

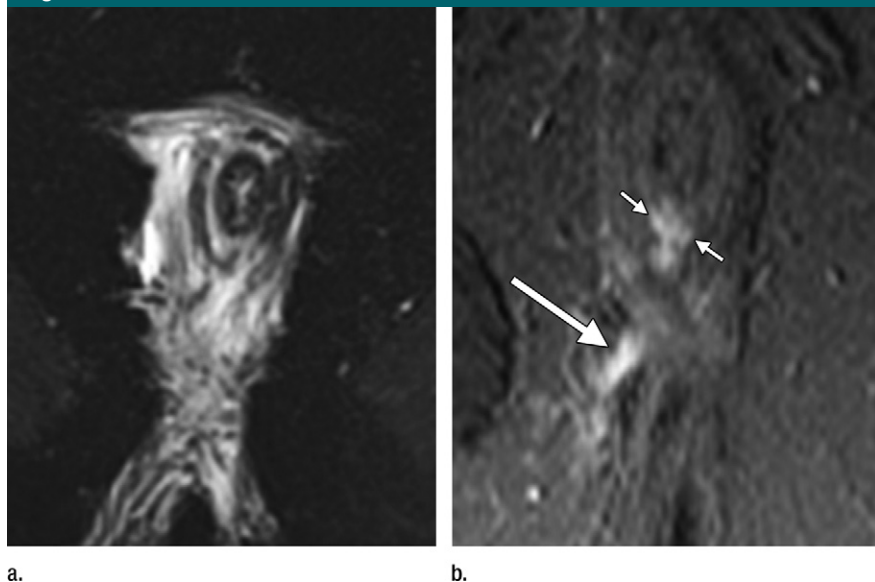


Figure 2: (a, b) Axial STIR MR images (5650/30/150) through the anal canal in (a) a 51-year-old man with acute myeloid leukemia who was scored as having circumferential edema of the anal canal (ie, edema in all 12 hours of an imaginary clock face) by both radiologists and (b) the corresponding control patient, a 49-year-old man who was scored as having inflammation (small arrows) over 2 hours of the clock face by both radiologists. Large arrow = fistula tract.

only those individuals with a fistula, the proportion of individuals with extensions from the primary tract did not differ between patients with hematologic malignancies and control patients (four [26.7%] of 15 vs 11 [31.4%] of 35; $P > .99$). Intersphincteric fistulas were the most common fistula type in both groups (patients with hematologic malignancies: 12 [80.0%] of 15; control patients: 20 [57.1%] of 35; $P = .22$). A single patient with a hematologic malignancy subsequently was observed to have developed an intersphincteric fistula at follow-up MR imaging (performed 4 months after the index examination). No other fistulas were observed to have developed in the follow-up MR imaging studies.

The amount of abnormal perianal MR imaging signal intensity on the STIR images was considerably greater for patients with hematologic malignancies than for control patients (Fig 2; Figs E1, E2 [online]). The mean number of hours of the clock face showing high signal intensity on STIR images was 7.2 for patients with hematologic malignancies

(approximately a 220° arc angle), versus 1.9 for control patients (approximately a 60° arc angle, $P < .001$). Similarly, a longer segment of the anal canal was inflamed in patients with hematologic malignancies (mean, 58.7% length inflamed) than in control patients (mean, 13.4% inflamed; $P < .001$). There was good agreement between the two radiologists when estimating the amount of abnormal high signal intensity on STIR images for both the clock face estimate (mean difference, 0.039 hours of a clock [1.2° arc angle]; Bland-Altman limits of agreement, 3.3 hours of a clock [98.1°]; Fig 3a) and the percentage length of anal canal involvement (mean difference, -0.59%; Bland-Altman limits of agreement, 27.3%; Fig 3b).

Radiologist 1 classified 37 (97.4%) of 38 control patients correctly (ie, assigned a confidence score of < 50), whereas radiologist 2 classified all control patients correctly. The single control patient believed to have a hematologic malignancy by radiologist 1 had a 1.8-cm intersphincteric collection and

diffuse anal edema. Patients with hematologic malignancies were categorized correctly in 27 (71.1%) of 38 cases by radiologist 1 and in 25 (65.8%) of 38 cases by radiologist 2. The overall ability of MR imaging to help discriminate patients with hematologic malignancies from control patients was good: AUCs were 0.97 (95% CI: 0.93, 1.00) for the empiric curve and 0.97 (95% CI: 0.90, 0.98) for the smoothed curve for radiologist 1 and 0.90 (95% CI: 0.83, 0.98) for the empiric curve and 0.91 (95% CI: 0.81, 0.97) for the smoothed curve for radiologist 2 (Fig 4). The sensitivity, specificity, positive predictive value, and negative predictive value for hematologic malignancies, respectively, were 71.1%, 97.4%, 96.4%, and 77.1% for radiologist 1 and 65.8%, 100%, 100%, and 74.5% for radiologist 2. A total of 16 patients with hematologic malignancies were incorrectly categorized as immunocompetent control patients by at least one radiologist. Incorrectly categorized patients were more likely to have a fistula (incorrect: 10 [62.5%] of 16 had a fistula; correct: five [22.7%] of 22 had a fistula; $P = .032$) and had significantly less edema than correctly categorized patients (mean height inflamed for incorrectly categorized patients, 35.8% of anal canal; mean height inflamed for correctly categorized patients, 81.6%; $P < .001$).

Subsequent Treatment

Overall, requirement for acute incision and drainage of an abscess did not differ significantly between the two groups (patients with hematologic malignancies: four [10.5%] of 38; control patients: eight [21.1%] of 38; $P = .35$). However, subsequent performance of examination under anesthesia was significantly less frequent for patients with hematologic malignancies (six [15.8%] of 38) than control patients (34 [89.5%] of 38, $P < .001$). Only a single patient (2.6%) with a hematologic malignancy required a seton (ie, insertion of a suture along the fistula tract to encourage drainage of pus), whereas 18 control patients (47.4%) did ($P < .001$). Only two (5.3%) of

Figure 3

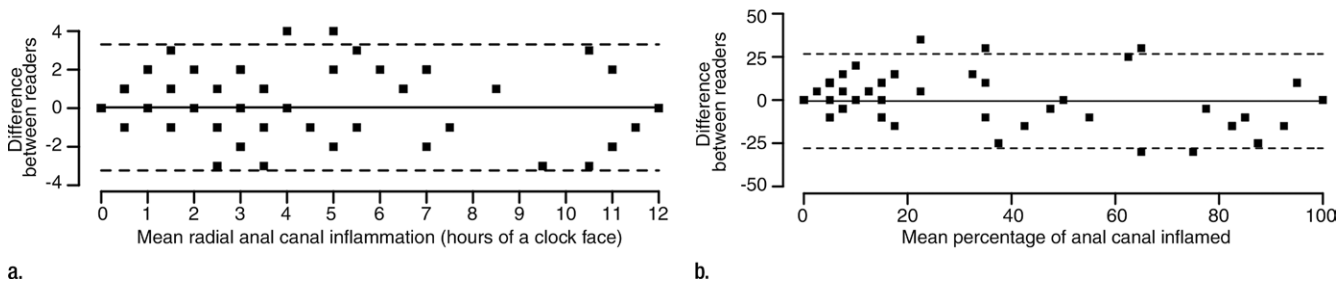


Figure 3: (a, b) Bland-Altman plots show agreement between the two radiologists in the assessment of (a) radial inflammation of the anal canal (measured in hours of an imaginary clock face) and (b) the height of anal canal inflammation (percentage height of anal canal inflamed). Solid line = mean difference, dashed lines = 95% limits of agreement.

Figure 4

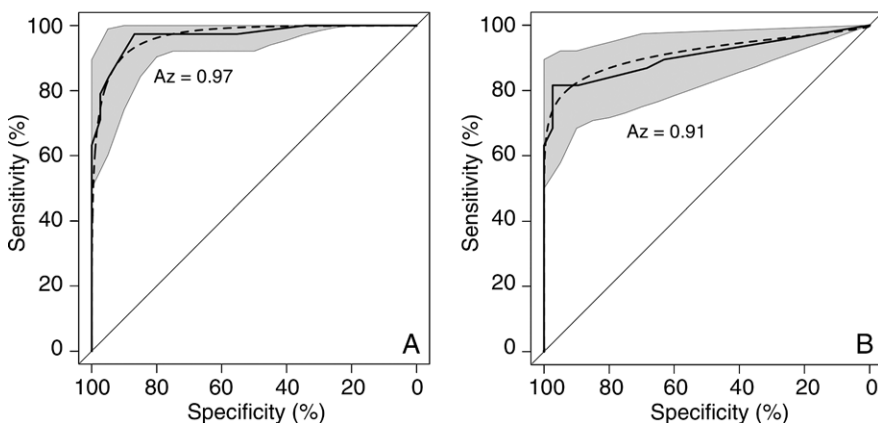


Figure 4: A, B, Empiric (solid line) and smoothed (dashed line) ROC curves for the distinction of patients with hematologic malignancies from control patients for, A, radiologist 1 and, B, radiologist 2. Shaded area = 95% CIs around the summary curve.

38 patients with hematologic malignancies had a fistula tract laid open, versus 10 (26.3%) of 38 control patients ($P = .025$). Additionally, three control patients underwent placement of a fistula plug, and two required an advancement flap (subsequently repeated for recurrence in one case). No patient with a hematologic malignancy died within 4 weeks of their MR imaging examination—that is, the lack of surgical treatment was not due simply to patient death.

Discussion

More than 135 000 patients are given a diagnosis of a hematologic malignancy each year in the United States

(21). Although intensive chemotherapy regimens (often supplemented by bone marrow transplantation) are frequently curative, the resulting immunocompromise may be profound, and serious infections commonly occur. Perianal sepsis occurs in 5%–10% of patients with hematologic malignancies and causes substantial morbidity and, occasionally, death (8). MR imaging is well established as a valuable technique for assessing perianal infection in patients with cryptoglandular infection and Crohn disease, and surpasses surgical examination under anesthesia because it reveals sites of infection that are clinically occult (13,16). Because of this, we anticipated that the utility of MR imaging would be

similarly high in patients with hematologic malignancies.

We found that, contrary to our expectation, perianal abscesses were relatively common in patients with hematologic malignancies, including those with neutropenia. Although the ability to form pus is impaired by neutropenia (22), our data suggest that this is not absolute—we found no significant difference in rates of abscess formation between patients with hematologic malignancies and control patients, and no effect of the degree of neutropenia on the frequency of abscess formation. The size and location of abscesses was also no different between the two groups, supporting the hypothesis that the underlying pathophysiology (cryptoglandular sepsis) is the same in the two groups. Importantly, the MR imaging finding of an abscess does not exclude hematologic malignancy as an underlying etiology.

Reports describing findings of clinical examination have suggested that diffuse edema and induration are common manifestations of perianal disease in hematologic malignancies (11). Supporting this, using imaging, we found a significantly greater degree of abnormal perianal high signal intensity on STIR images at MR imaging in patients with hematologic malignancies. On average, more than half of the anal canal showed abnormal high signal intensity on STIR images (approximately 60% of both height and radial extent), in comparison to approximately 10%–15% for control patients. The reason

for this difference is unclear, but the two main possibilities are either alterations in the host immune response or, alternatively, different microorganisms opportunistically infecting the immunocompromised host and causing a different clinical phenotype. The former seems more likely, as results in microbiologic series (5,6,8,23) suggest that the pathogens isolated from patients with hematologic malignancies are gut commensals such as *Enterobacteriaceae*—no different from those in immunocompetent patients. Irrespective of the precise reason, MR imaging appearances clearly differ in patients with hematologic malignancies from those in control patients, and these imaging features do not mandate surgical intervention. This corroborates historical surgical series (23), in which 55%–88% of cases of perianal infection in patients with hematologic malignancies were controlled by antibiotics alone. In our study, a subset of patients with hematologic malignancies were erroneously believed to be immunocompetent control patients at MR imaging. Such patients had a simple, noninflamed fistula tract, causing the appearances to be similar to those in immunocompetent individuals.

We found that defined fistula tracts were less common in patients with hematologic malignancies (21 of [55.3%] of 38 patients) than in control patients (35 [92.1%] of 38 patients). Accordingly, the rate of performance of examination under anesthesia, seton placement, or other fistula treatment was lower in patients with hematologic malignancies. We propose that recovery from the nadir of neutropenia (eg, after cessation of chemotherapy) allows perianal healing without the need for subsequent treatment, explaining the lower rates of fistula. Conversely, control patients developing perianal sepsis have already developed chronic infection that is beyond the immune system's ability to control and cannot escalate the host response any further. An alternative possibility is that patients with hematologic malignancies were imaged with less severe disease

than control patients, meaning that prompt treatment prevented fistulation. This seems unlikely, because we found no difference in the rate of abscess formation, and the inflammatory reaction (as judged by the extent of signal intensity change on STIR images) was greater, implying a more severe initial disease process.

Our study had limitations. First, our cohort was retrospective, although sizeable for a relatively uncommon group. We treated all patients with hematologic malignancies as a single group, whereas in reality, there may be differences in immune function between patients with different subtypes of hematologic malignancies undergoing various treatments. The study was conducted in a Western hemisphere tertiary oncology center: Results may not generalize more widely. All MR imaging studies were interpreted by one of two experienced radiologists, which may also limit generalizability to more general radiologists. We did not administer intravenous contrast medium, which may have reduced our ability to detect abscesses; however, because the MR imaging protocol was the same for both patient groups, this should not affect our overall conclusions. Nonetheless, it is possible that the absolute prevalence of abscesses in both immunocompetent patients and patients with hematologic malignancies was higher than what we report here.

In summary, patients with hematologic malignancies undergoing MR imaging for perianal symptoms have considerably greater local inflammatory signal change than immunocompetent patients with perianal sepsis. Fistula tracts are significantly less common in patients with hematologic malignancies, although rates of abscess formation are not significantly different. Perianal disease in patients with hematologic malignancies rarely required surgical treatment, either at the time of imaging or thereafter. Radiologists should recognize the potential for hematologic malignancies and associated neutropenia to alter the typical MR imaging features of perianal infection.

Disclosures of Conflicts of Interest: A.A.P.

Activities related to the present article: none to disclose. Activities not related to the present article: is on the speakers bureau of Warner Chilcott. Other relationships: none to disclose. S.H. Activities related to the present article: is a Senior Investigator for the National Institute of Health Research. Activities not related to the present article: has been an expert medical witness in multiple cases of anal fistula litigation. Other relationships: none to disclose. G.B. disclosed no relevant relationships. S.A.T. Activities related to the present article: is a Senior Investigator for the National Institute of Health Research. Activities not related to the present article: is a research consultant to Robarts. Other relationships: none to disclose.

References

- Howlander N, Noone AM, Krapcho M, et al, eds. SEER Cancer Statistics Review, 1975–2011, based on November 2013 SEER data submission. Bethesda, Md: National Cancer Institute, 2010. http://seer.cancer.gov/csr/1975_2011/. Published April 2014. Accessed July 2014.
- Swerdlow SH, Campo E, Harris NL, et al. WHO classification of tumours of haematopoietic and lymphoid tissues. 4th ed. Lyon, France: IARC, 2008.
- Safdar A, Armstrong D. Infections in patients with hematologic neoplasms and hematopoietic stem cell transplantation: neutropenia, humoral, and splenic defects. *Clin Infect Dis* 2011;53(8):798–806.
- Nicola P, Romani C, Cupelli L, et al. Mucositis in patients with hematologic malignancies: an overview. *Haematologica* 2007; 92(2):222–231.
- Vanhueverzwyn R, Delannoy A, Michaux JL, Dive C. Anal lesions in hematologic diseases. *Dis Colon Rectum* 1980;23(5):310–312.
- Barnes SG, Sattler FR, Ballard JO. Perirectal infections in acute leukemia: improved survival after incision and debridement. *Ann Intern Med* 1984;100(4):515–518.
- Bodey GP. Unusual presentations of infection in neutropenic patients. *Int J Antimicrob Agents* 2000;16(2):93–95.
- Chen CY, Cheng A, Huang SY, et al. Clinical and microbiological characteristics of perianal infections in adult patients with acute leukemia. *PLoS ONE* 2013;8(4):e60624.
- Slater DN. Perianal abscess: "Have I excluded leukaemia"? *Br Med J (Clin Res Ed)* 1984;289(6459):1682.
- Simpson JA, Banerjee A, Scholefield JH. Management of anal fistula. *BMJ* 2012; 345:e6705.

11. Büyükaşık Y, Özcebe OI, Sayinalp N, et al. Perianal infections in patients with leukemia: importance of the course of neutrophil count. *Dis Colon Rectum* 1998;41(1):81–85.
12. Freifeld AG, Bow EJ, Sepkowitz KA, et al. Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 Update by the Infectious Diseases Society of America. *Clin Infect Dis* 2011;52(4):427–431.
13. Buchanan G, Halligan S, Williams A, et al. Effect of MRI on clinical outcome of recurrent fistula-in-ano. *Lancet* 2002;360(9346):1661–1662.
14. R Core Team. R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing. <http://www.R-project.org/>. Accessed December 2014.
15. Parks AG, Gordon PH, Hardcastle JD. A classification of fistula-in-ano. *Br J Surg* 1976;63(1):1–12.
16. Halligan S, Stoker J. Imaging of fistula in ano. *Radiology* 2006;239(1):18–33.
17. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986;1(8476):307–310.
18. Robin X, Turck N, Hainard A, et al. pROC: an open-source package for R and S+ to analyze and compare ROC curves. *BMC Bioinformatics* 2011;12:77.
19. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. *Biometrics* 1988;44(3):837–845.
20. Boxer L, Dale DC. Neutropenia: causes and consequences. *Semin Hematol* 2002;39(2):75–81.
21. Lichtman MA. Battling the hematological malignancies: the 200 years' war. *Oncologist* 2008;13(2):126–138.
22. Boxer LA. How to approach neutropenia. *Hematology Am Soc Hematol Educ Program* 2012;2012:174–182.
23. Glenn J, Cotton D, Wesley R, Pizzo P. Ano-rectal infections in patients with malignant diseases. *Rev Infect Dis* 1988;10(1):42–52.