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J. Delaloye · G. Merlani · C. Petignat · A. Wenger · K. Zaman · C. Monnerat · O. Matzinger · M. Beck Popovic · P. Vuichard · N. Ketterer · P. E. Tarr

Nosocomial nontyphoidal salmonellosis after antineoplastic chemotherapy: reactivation of asymptomatic colonization?

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Abstract An increased frequency of nontyphoidal salmonellosis is well established in cancer patients, but it is unclear whether this represents increased susceptibility to exogenous infection or opportunistic, endogenous reactivation of asymptomatic carriage. In a retrospective study, a simple case definition was used to identify the probable presence of reactivation salmonellosis in five cancer patients between 1996 and 2002. Reactivation salmonellosis was defined as the development of nosocomial diarrhea >72 h after admission and following the administration of antineoplastic chemotherapy in an HIV-seronegative cancer patient who was asymptomatic on admission, in the absence of epidemiological evidence of a nosocomial outbreak. Primary salmonellosis associated with unrecognized nosocomial transmission or community acquisition and an unusually prolonged incubation period could not entirely be ruled out. During the same time period, another opportunistic infection, *Pneumocystis* pneumonia, was diagnosed in six cancer patients. Presumably, asymptomatic intestinal *Salmonella* colonization was converted to invasive infection by chemotherapy-associated intestinal mucosal damage and altered innate immune mechanisms. According to published guidelines, stool specimens from patients hospitalized for longer than 72 h should be rejected unless the patient is neutropenic or ≧65 years old with significant comorbidity. However, in this study neutropenia was present in only one patient, and four patients were <65 years old. Guidelines should thus be revised in order not to reject stool culture specimens from such patients. In cancer patients, nosocomial salmonellosis can occur as a chemotherapy-triggered opportunistic reactivation infection that may be similar in frequency to *Pneumocystis* pneumonia.

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J. Delaloye · G. Merlani · C. Petignat · P. E. Tarr (✉)
Infectious Diseases Service, University Hospital, CHUV,
BH 07-865,
1011 Lausanne, Switzerland
e-mail: philiptarr@yahoo.com
Tel.: +41-21-3143020
Fax: +41-21-3141018

C. Petignat
Infection Control Division, CHUV,
1011 Lausanne, Switzerland

A. Wenger
Institute of Microbiology, University of Lausanne, CHUV,
1011 Lausanne, Switzerland

K. Zaman · C. Monnerat · O. Matzinger · N. Ketterer
Division of Hematology-Oncology, CHUV,
1011 Lausanne, Switzerland

M. Beck Popovic
Division of Pediatric Hematology-Oncology, Department of Pediatrics, CHUV,
1011 Lausanne, Switzerland

P. Vuichard
Oncology Service, Hôpital Sud Fribourgeois,
1632 Riaz, Switzerland

Introduction

In healthy persons, infection with nontyphoidal *Salmonella* (NTS) causes no symptoms or a self-limited gastroenteritis in >95% of cases. In the immunocompromised host, however, severe cases with bacteremia and metastatic infections may develop [1, 2]. Early diagnosis and treatment are important, because the infection may be life threatening [3]. It is well documented that NTS infections occur more frequently in cancer patients [4–12]. In a recent case-control study [13], prior cytotoxic chemotherapy or corticosteroid therapy was present more frequently in children with NTS bacteremia than in children with bacteremia caused by other Gram-negative rods. However, it is unclear whether the increased incidence of NTS infections in cancer patients is due to an increased susceptibility to de novo, exogenous infection, including hospital-acquired salmonellosis, or to

Table 1 Clinical and microbiological information on five patients with reactivation *Salmonella* enteritis associated with antineoplastic chemotherapy

Case no.	Age/sex	Underlying malignancy	Clinical information, chemotherapy regimen	Previous chemotherapy and/or radiotherapy	Neutropenia	Lymphopenia	*Salmonella enterica* serovar (body site of positive cultures)	Blood culture result	Antimicrobial treatment (duration)	Subsequent chemotherapy	Outcome, comments
1	28 years/F	Stage IIA diffuse large-B-cell lymphoma	Admission on 11/28/02; BEAM (during 1st course) started on 11/28, received autologous BMT; fever, abdominal pain, and diarrhea on 12/04	Yes, see text	Yes	Yes	Enteritidis[a] (stool)	Negative	Imipenem, ciprofloxacin (4 weeks)	No	Complete remission (11/2003)
2	5 mos./F	Stage III neuroblastoma	Admission on 03/04/2002; vincristine, cyclophosphamide (1st course) started on 03/09; fever, abdominal pain, and diarrhea on 03/11	No	No	No	Monschaui[a] (stool)	ND	Amoxicillin (7 days)	Yes, without relapse of salmonellosis	Complete remission (10/2003)
3	73 years/M	Colonic adenocarcinoma with liver metastases	Admission on 04/10/1999 with 1-month history of 2–3 semi-formed occasionally blood-tinged stools; oxalyplatine, 5-fluorouracil started on 04/12; abdominal pain, diarrhea on 04/24; no fever	No	No	ND	Enteritidis[a] (stool)	ND	Ciprofloxacin (11 days)	No	Palliative care
4	57 years/F	Stage IIIB multiple myeloma (IgG lambda)	Admission on 11/04/1998; VAD (doxorubicin, vincristine, dexamethasone), and high-dose cyclophosphamide (1st cycle) given on 11/04; diarrhea and vomiting on 11/07; no fever or abdominal pain	Melphalan, prednisone (1 cycle)	No	Yes	Enteritidis[b] (stool and urine)	Negative	Ciprofloxacin (7 days)	Yes, without relapse of salmonellosis	Follow up stool and urine cultures (11/17/98) sterile; oncologic relapse in 3/2003 (11/2003: in partial remission, thalidomide therapy)
5	27 years/F	Stage 1 Wilms tumor	Admission on 12/16/1997; cyclophosphamide, etoposide (1st cycle) started on 12/16; fever, watery diarrhea, abdominal pain on 12/20	No	No	Yes	Hadar[b] (stool)	Negative	Imipenem (at least 3 days[c])	Yes, without relapse of salmonellosis	Progressive cancer, died (2/1998)

BEAM, carmustine, cytarabine, etoposide, melphalan; BMT, bone marrow transplantation; ND, not determined
[a]Sensitive to ampicillin, amoxicillin/clavulanic acid, ceftriaxone, trimethoprim-sulfamethoxazole, ciprofloxacin
[b]Sensitive to ampicillin, amoxicillin/clavulanic acid, piperacillin/tazobactam, cefazolin, ceftriaxone, imipenem, trimethoprim-sulfamethoxazole, ciprofloxacin
[c]The patient was temporarily discharged on pass after 3 days of imipenem therapy, but it is unclear if oral antibiotics were continued as an out-patient

opportunistic reactivation of asymptomatic NTS stool carriage induced by antineoplastic chemotherapy.

The aim of this retrospective study was to identify a clinically useful method to differentiate between these possibilities. Nosocomial transmission of NTS is rare in Western countries [14, 15], and the typical incubation period for NTS infection is 6–48 h [1, 2]. Therefore, in a patient undergoing cancer chemotherapy, the onset of NTS diarrhea more than 3 days after admission to the hospital, in the absence of epidemiological evidence of nosocomial transmission, would suggest chemotherapy-triggered reactivation of asymptomatic NTS colonization. NTS stool colonization has been found in 0.15–0.5% of asymptomatic individuals [16, 17]. A low inoculum may cause colonization but no symptomatic infection, and <50% of stool carriers report a previous diarrheal episode [2, 18]. Even in asymptomatic cases, stool excretion of NTS continues for a median duration of 4–5 weeks in adults and 7 weeks in children <5 years of age [16, 17, 19]. In fact, 2–3% of convalescent adults and 15–32% of children still excrete salmonellae at 6 months post infection. Thus, a pool of asymptomatic carriers exists in the community at any time.

Here we report five cancer patients admitted to our medical center between 1996 and 2002 in whom chemotherapy-triggered reactivation seems the most likely explanation of nosocomial NTS enteritis. Reactivation salmonellosis in cancer patients has received no recent attention in textbooks of infectious diseases, and no review articles are available. However, we also found that the frequency of reactivation salmonellosis may be similar to that of another well-established opportunistic disease in cancer patients, *Pneumocystis carinii* pneumonia (PCP) [20].

Patients and methods

Medical records were reviewed for all patients who had at least one stool culture positive for NTS and who were hospitalized at the 814-bed University Hospital in Lausanne, Switzerland, during the period of January 1996 to December 2002. Nontyphoidal salmonellae were identified by standard microbiological criteria. Antimicrobial susceptibility testing was performed using the disk diffusion method.

Of the patients with nontyphoidal salmonellosis, the medical records of all cases with a concomitant diagnosis of a malignant tumor were reviewed. A case of reactivation salmonellosis was diagnosed if a patient fulfilled all four of the following criteria: (i) the patient was asymptomatic on admission; (ii) bacteremia or diarrhea (defined as ≥3 loose stools per day) due to NTS occurred more than 72 h after admission (thus, outpatient cases and cases occurring within 72 h of admission were excluded, since it would have been unclear if primary infection or reactivation disease was present); (iii) diarrhea or bacteremia occurred after initiation of antineoplastic chemotherapy; and (iv) there was no evidence of nosocomial acquisition of the infection. Potential nosocomial NTS transmission was investigated by the infection control service by review of culture results in the microbiology laboratory and by administration of a standardized questionnaire.

Documentation of asymptomatic NTS colonization prior to initiation of chemotherapy was not used in the case definition because routine stool cultures are not done at our hospital prior to chemotherapy. HIV-seropositive patients, patients infected with *Salmonella enterica* serovar Typhi or Paratyphi, and patients with insufficient documentation were also excluded. Neutropenia and lymphopenia were defined as an absolute neutrophil count and lymphocyte count of <1,000/mm^3 and 1,500/mm^3 (3,000 in children), respectively, at the time of the positive culture for NTS.

To assess the frequency of PCP in cancer patients during the same time period (1996–2002), we reviewed the medical records of all HIV-seronegative patients with morphological documentation of organisms in bronchoalveolar lavage fluid who had compatible clinical features, a concomitant diagnosis of a malignant tumor, and had received cancer chemotherapy or corticosteroids (in a dose equivalent to ≥20 mg prednisone for ≥4 weeks) during the 6 months preceding the diagnosis of PCP.

Illustrative case report

A 28-year old woman (case 1, Table 1) was diagnosed as having stage IIA diffuse large-B-cell lymphoma in January 2002. Complete remission was achieved after eight cycles of CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone). She relapsed in September 2002 and was treated with three cycles of rituximab-ESHAP (etoposide, cisplatine, cytarabine, methylprednisolone). During the second cycle (45 days before admission), while at home, the patient had an episode of watery diarrhea that resolved spontaneously and for which she did not seek medical attention. Peripheral stem cells were harvested, followed by a conditioning regimen (BEAM: carmustine, cytarabine, etoposide, melphalan) between 28 November 2002 and 3 December 2002.

On 4 December, 7 days after starting chemotherapy and 1 day before peripheral blood stem cell infusion, the patient developed severe diffuse crampy abdominal pain and watery diarrhea. Her medical history was otherwise unremarkable, and she was not taking any medications at home. From September 2002 until the time of admission, the patient received neither antibiotics nor antacids. There were no known contacts with patients with diarrhea, no exposure to animals, and no foreign travel, and the patient had not eaten food brought from outside the hospital. The patient's temperature was 38.2°C. There was grade 2 oral mucositis, and palpation of the right lower quadrant was tender, with guarding. The leukocyte count was 2.2×10 cells/l (90% neutrophils, 10% lymphocytes). Blood and urine cultures were sterile. Abdominal computed tomography scan demonstrated wall thickening of the entire colon.

A presumptive diagnosis of early neutropenic enterocolitis was made, and imipenem was started. Metronidazole was given until stool cultures and a cytotoxin assay for *Clostridium difficile* were negative on three occasions. The patient became overtly neutropenic (leukocytes, 2×10 cells/l) on 5 December. Stool cultures grew *Salmonella* serovar Enteritidis, which was sensitive to amoxicillin, trimethroprim/sulfamethoxazole, and ciprofloxacin. It was possible that this enterocolitis represented reactivation of intestinal carriage after primary (but undocumented) *Salmonella* infection 45 days before admission. Ciprofloxacin was added. During the next 6 days, the fever, abdominal pain, and diarrhea persisted and the absolute neutrophil count remained <500 cells/l, but the patient's condition remained stable. On 12 December, the patient became afebrile and the abdominal pain and diarrhea resolved concomitant with a rise in neutrophils to 1,100 cells/l. Imipenem was discontinued. Ciprofloxacin was switched to the oral formulation to complete a 4-week course of antibiotics. The patient recovered. At the most recent follow-up visit (November 2003), she was asymptomatic and in complete remission from her lymphoma.

Results

Between 1996 and 2002, 235 microbiological specimens from 214 patients were culture positive for NTS in our microbiology laboratory. The charts of ten patients with a concomitant diagnosis of a malignant neoplasm were reviewed. Of these, five patients were excluded because of diarrhea or bacteremia that was already present on admission to the hospital (n=3), HIV seropositivity (n=1), or insufficient documentation (n=1). During the same time period, *Salmonella* Typhi was recovered in culture from ten specimens (from 9 patients), *Salmonella* Paratyphi A from two specimens (2 patients), and *Salmonella* Paratyphi C from one patient. None of these patients had a concomitant diagnosis of a malignant cancer and were therefore excluded from the analysis.

Five of the ten cancer patients with nontyphoidal salmonellosis thus had an illness compatible with reactivation disease following the administration of antineoplastic chemotherapy. The clinical details of these five patients are summarized in Table 1. There were three women, one female infant, and one man, and the median age was 28 years (age range, 5 months to 73 years). Four patients were asymptomatic on admission to the hospital. On admission, patient 3 had a 1-month history of 2–3 semiformed stools per day, which was attributed to his colon cancer. He was included in the analysis because of the development of overt diarrhea (7–8 watery bowel movements) and severe abdominal pain after receiving chemotherapy. Overall, fever, abdominal pain, and diarrhea developed after chemotherapy in three, four, and five patients, respectively.

There were no other nosocomial cases of NTS infection during the hospital stay of any of the patients. NTS was recovered from the stool of all five patients and from the urine of one patient. Blood cultures were negative in three patients and were not performed in two patients. No definite metastatic infections were recorded. One patient was neutropenic and lymphopenic at the time of positive cultures, and two patients were lymphopenic only. No reliable information regarding antibiotic or antacid treatments in the past was available for four patients, but at the time of hospital admission and until the diagnosis of NTS enteritis, none of the patients received antibiotics. Salmonellosis occurred during induction chemotherapy in three patients and during intensification chemotherapy in two patients.

All NTS isolates were sensitive to all antibiotics tested (see footnote, Table 1). Nalidixic acid susceptibility testing was not performed on any of the isolates. All patients were successfully treated with antibiotics, with the treatment duration ranging from 3 days to 4 weeks. Antineoplastic therapy was continued in four patients after the recovery of the NTS, while in patient 3, chemotherapy was discontinued and palliative care initiated because of progressive colon cancer. No relapses of NTS infection occurred despite subsequent chemotherapy cycles in three patients. The duration of follow-up ranged from 3 weeks to 52 months.

No patient had a prior history of documented NTS infection, although an episode of diarrhea 45 days prior to admission in patient 1 may have represented primary NTS infection; stool cultures were not done at that time, however. Asymptomatic stool colonization prior to reactivation disease was recorded in one patient: Case 4 had asymptomatic salmonelluria on routine urine culture prior to chemotherapy (urine was collected for proteinuria quantitation). No antibiotic treatment was administered initially, and the patient developed enteritis following administration of cyclophosphamide.

During the same time period (1996–2002), six cases of PCP were diagnosed at our center in cancer patients without HIV infection who had received antineoplastic chemotherapy (n=4) or corticosteroids (n=2). None of these six patients was receiving prophylaxis against PCP at the time of PCP diagnosis.

Discussion

By use of a simple case definition, we identified the likely presence of reactivation disease, as opposed to primary infection, in five of ten cancer patients with nosocomial NTS enteritis over a 7-year period. Precise incidence estimates are not possible, given the unknown prevalence of asymptomatic *Salmonella* colonization in our cancer patients undergoing chemotherapy. Nonetheless, the frequency of reactivation disease was similar to that of PCP diagnosed during the same time period. *Pneumocystis* is an opportunistic pathogen that is a rare but well established cause of reactivated infection in cancer patients [20]. Reactivation salmonellosis has received little attention in the recent literature. It most likely represents the conversion of asymptomatic *Salmonella* stool colonization to

invasive disease, triggered by cancer chemotherapy, via damage to the gastrointestinal mucosa and alterations of innate immune mechanisms [21]. Cancer chemotherapy may thus "facilitate" the development of invasive salmonellosis. This term was used by Barza and Travers [22] in the context of prior antimicrobial therapy, which, by reducing the normal flora, decreases resistance to colonization and thus facilitates infection by pathogenic bacteria. On the other hand, it is also possible that antibiotics, e.g., PCP prophylaxis with trimethoprim/sulfamethoxazole (TMP/SMX), might be effective in treating unrecognized NTS colonization. Antibiotics might thereby prevent reactivation of salmonellosis, at least in settings such as ours, where TMP/SMX-susceptible strains predominate.

An increased occurrence of *Salmonella* infections in cancer patients was documented in several reports published between 1943 and 1969 [4–6, 8, 10, 11, 23]. None of these articles investigated, however, whether the patients had primary infection or reactivation disease. Nevertheless, in a report from 1994, 24 of 40 cancer patients with salmonellosis had received prior chemotherapy, and in 23 patients the infections were considered nosocomial [7]. There are, however, three additional cases of possible NTS reactivation in the literature [14, 24] in which nosocomial acquisition cannot be excluded. One of these patients [24] had reactivation bacteremia with negative stool cultures, which may suggest an extraintestinal site of *Salmonella* latency, such as the reticuloendothelial system [25]. Reactivation of salmonellosis that is latent in the reticuloendothelial system may also explain the higher frequency of salmonellosis in patients with hematological malignancies than in patients with other types of cancer [4–7].

Our experience suggests that reactivation salmonellosis, when recognized, can be successfully treated even while chemotherapy is continued. It has been reported previously that the continuation of antineoplastic therapy may not worsen the severity of salmonellosis in children [9]. None of the patients had complications of salmonellosis (such as bacteremia or metastatic infection), even though blood cultures were done in only three of the five patients. This is contrary to the notion that NTS infections may follow a more serious course in immunocompromised patients [1–3]. Potential explanations include the following: (i) three patients developed NTS reactivation while receiving induction chemotherapy and might be considered as only moderately immunosuppressed; (ii) the salmonellosis, by definition, became apparent after admission to the hospital in all patients, suggesting that early detection by stool cultures in the inpatient setting and timely administration of antibiotics could have prevented a complicated course; and (iii) there were no cases due to *Salmonella* Typhimurium, which, in some studies, has been identified as a serovar more likely to be associated with bacteremia [5, 8]. Whether neutropenia and lymphopenia are predictors of more severe or protracted illness, as in AIDS patients, is unclear.

Alternative explanations in these cases of nosocomial salmonellosis include the possibility of primary community-acquired *Salmonella* infection associated with an unusually long incubation period. While an incubation period for NTS enteritis of up to 72 h is consistently reported in the literature, there are occasional older reports of NTS outbreaks that have suggested incubation periods of more than a week in a minority of affected patients. However, such outbreaks either affected newborns [26] or, in some cases, the seemingly long incubation period may have been explained by secondary transmission or microbiologically undocumented diarrheal illness that was without a clear link to the outbreak in question [27, 28]

Nosocomial salmonellosis may also occur after eating contaminated food from outside sources that is brought to the hospital [29] or, with truly nosocomially acquired infection, for instance, in association with eating hospital food. No additional nosocomial cases of NTS infection were found in any of our five patients after careful epidemiological investigation. However, hospital-acquired salmonellosis, even though rarely reported nowadays [15, 16], cannot be completely excluded. Current nutrition guidelines at our hospital specify no food restrictions for chemotherapy patients until they are neutropenic, at which point no food containing raw eggs or raw meat is served. The fact that three of our patients had enteritis due to *Salmonella* Enteritidis is consistent with this being the most common serovar in cases of sporadic NTS infection in Switzerland and the serovar most consistently linked to consumption of undercooked eggs [30].

An additional consideration is that the positive stool cultures might incidentally have revealed a carrier state. A possible pathogenic role of NTS is difficult to disregard, however, in an immunocompromised patient with diarrhea and severe abdominal pain. In patient 1, the presence of bowel wall thickening on computed tomography scan and the clinical recovery of the patient concomitant with neutrophil recovery supported a diagnosis of neutropenic enterocolitis [31]. In fact, the pathogenesis of NTS reactivation enteritis may be similar to that of neutropenic enterocolitis: Injury to the bowel mucosa (due to the effects of chemotherapy, radiotherapy, or tumor infiltration) as well as impaired mucosal healing and altered neutrophil function due to neutropenia may provide a portal of entry for opportunistic invasion by endogenous gut microorganisms, including gram-negative bacteria, viridans streptococci, clostridia, or candida [32]. As in NTS carriers with reactivation disease after chemotherapy, unequivocal attribution of a pathogenic role of the organisms implicated in neutropenic enterocolitis is difficult since the same organisms can be found in the stools of asymptomatic patients.

The concept of NTS reactivation is not new and has been well documented in patients with conditions characterized by macrophage dysfunction (such as malaria, sickle cell disease, histoplasmosis, or bartonellosis [11]) and after renal transplantation [32]. In a report from Mexico [33], four of seven patients with systemic lupus erythematosus who developed NTS arthritis following treatment with cyclophosphamide and corticosteroids were

asymptomatic stool carriers. NTS reactivation has also been reported after major surgery [11, 13, 34]. Possible underlying mechanisms include the facilitating effects of prophylactic antibiotics, the immunosuppressive effect of "stress" associated with surgery, and gastrointestinal stress ulcers, which might permit invasive NTS infection. In anecdotal reports since 1930, it has been repeatedly observed that NTS may selectively infect tumor tissue [35, 36]. Presumably, necrotic cancer tissue may act as a fertile ground for *Salmonella* superinfection, in conjunction with defective immune surveillance at the site of the cancer. Such events might further facilitate the occurrence of NTS reactivation in cancer patients undergoing cancer chemotherapy. In order to take advantage of the apparent tropism for cancer tissue, the potential antitumor activity of an attenuated *Salmonella* Typhimurium strain is being investigated in animal models [37] and in patients with metastatic cancer in clinical trials [38, 39].

In contrast to NTS, the potential of *Salmonella* Typhi and Paratyphi to cause reactivation disease in cancer patients receiving chemotherapy is unclear. These organisms were not involved in any of our patients and have rarely been recovered from cancer patients, especially in Western countries [5, 7] but also in endemic areas such as Pakistan [40] or India [41]. The notion of chemotherapy-associated reactivation could be difficult to prove for *Salmonella* Typhi because of the longer incubation period and because nosocomial transmission of *Salmonella* Typhi is well documented in endemic areas [42, 43].

Nontyphoidal salmonellae are likely underreported as causative agents of chemotherapy-associated diarrhea. Stool cultures are infrequently obtained in chemotherapy patients because they frequently develop diarrhea and commonly are receiving or will soon receive antibiotics. Even when NTS enteritis is considered, it may be missed since three stool samples may be required to document intestinal carriage [16, 44]. Nonetheless, Yuen et al. [45] found NTS in the stools of five of 120 asymptomatic bone marrow transplantation (BMT) candidates in Hong Kong. Suppressive treatment with ciprofloxacin was successful in all patients. NTS enteritis also occurred in three of 60 allogeneic BMT patients from England [46]. In two of these three patients, salmonellosis occurred late, at the time of stable engraftment. Differentiation of NTS enteritis from the effects of intestinal graft-versus-host disease may be difficult in this setting, but it is crucial, as a fatal case has been reported [3]. Other studies of chemotherapy-associated diarrhea may not have identified any cases due to NTS because of the routine use of prophylactic antibiotics [23, 47–49] or because the study was limited to the period between days 20 and 150 after allogeneic BMT, i.e., several weeks after the administration of chemotherapy [49].

Bacterial stool cultures are expensive, and their yield in patients hospitalized for more than 3 days is <2%. Therefore, many hospitals reject stool culture specimens from such patients (the "3-day rule") [16, 44, 50]. Where strict rejection rules are in place, however, physicians should be aware that treatable cases of infectious diarrhea may be missed, particularly in tertiary care centers treating immunosuppressed patients [29]. In one prospective study [44], 14.4% (53 of 369) of all *Salmonella* isolates were cultured from stool specimens collected more than 3 days after admission. Regardless of whether the patients with nosocomial salmonellosis in this report ultimately had reactivation of asymptomatic carriage or nosocomially acquired disease, it is clear that the 3-day rule is problematic. Nosocomial salmonellosis cases that are missed due to the application of rules that require rejection of stool cultures [51] may be complicated by bacteremia and metastatic infection and may also lead to nosocomial transmission to other immunocompromised patients. It has been suggested that the 3-day rule be disregarded in patients >65 years of age with significant comorbidity, HIV infection, or neutropenia [16]. However, we show here that nosocomial salmonellosis in cancer patients can occur in the absence of neutropenia and in patients who are <65 years old. Thus, nosocomial stool culture guidelines should be modified to include cancer patients who develop significant diarrhea and abdominal pain after administration of chemotherapy.

As in patients with renal transplants [31] or systemic lupus erythematosus [32], physicians should be aware of the possibility of extended carriage with NTS in cancer patients, along with the possibility of chemotherapy-triggered reactivation. In medical centers such as ours, where physicians can request exceptions to the 3-day rejection rule, a high index of suspicion and close communication between the treating physician and the microbiology laboratory should facilitate identification of cases. The optimal duration of antimicrobial treatment for reactivation salmonellosis is unknown. Continuation of antibiotics for at least the duration of neutropenia and for a minimum of 10–14 days in bacteremic patients without endovascular or metastatic infection [1, 2] may be a prudent approach. Routine identification of the rare carriers prior to cancer chemotherapy is unlikely to be cost-effective. Further studies are required to determine the incidence of reactivation salmonellosis in relation to different chemotherapy regimens and to evaluate the best approach when a carrier is identified prior to chemotherapy (pre-chemotherapy eradication treatment versus pre-emptive antimicrobial therapy if diarrhea occurs after chemotherapy).

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