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# *Streptococcus gallolyticus ssp. pasteurianus* bacteremia during chemotherapy-induced neutropenia in a patient with malignant lymphoma

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## ABSTRACT

Background: *Streptococcus gallolyticus ssp. pasteurianus* is a commensal bacterium of the alimentary tract in humans and animals. This microorganism not only causes sepsis, endocarditis, and meningitis but is also associated with colorectal tumors. We report herein a rare case of *S. gallolyticus ssp. pasteurianus* bacteremia in a patient with concomitant colon cancer and aggressive malignant lymphoma during the neutropenic period after chemotherapy against lymphoma.

Case presentation: A 79-year-old man was found to have an adenoma in the ascending colon, and endoscopic mucosal resection (EMR) was planned to remove the lesion. However, he was diagnosed with diffuse large B-cell lymphoma during the pre-operation examination. The EMR was postponed, and he received rituximab, cyclophosphamide, etoposide, vincristine, and prednisolone (R-CEOP). He had a neutropenic fever with positive blood cultures for *S. gallolyticus ssp. pasteurianus* during the first course of R-CEOP. He improved as soon as cefepime was administered. Bacteremia did not recur thereafter, and he underwent EMR after completing six cycles of R-CEOP. The histological diagnosis of the colon tumor was well-differentiated adenocarcinoma in adenoma. *Streptococcus gallolyticus ssp. pasteurianus* was not detected in the culture of the resected tissue.

Conclusion: Although there have been few reports of bloodstream infection due to *S. gallolyticus ssp. pasteurianus* in patients with hematological malignancies undergoing cytotoxic chemotherapy, physicians should investigate the presence of coexisting colorectal tumors when this bacterium is isolated from blood cultures.

***Key words:*** *Streptococcus gallolyticus ssp. pasteurianus*, *febrile neutropenia*, *malignant lymphoma*

## INTRODUCTION

Febrile neutropenia (FN) is a common adverse event during chemotherapy for hematological malignancy, occurring in about 20% of patients with malignant lymphoma during chemotherapy. Bacterial pathogens are often detected in this condition. Among gram-positive organisms, *Staphylococcus aureus*, coagulase-negative *Staphylococcus*, *Enterococcus* spp., and viridans group streptococci are predominantly isolated. Among gram-negative bacilli, *Escherichia coli*, *Klebsiella* spp., and *Pseudomonas aeruginosa* are frequently detected[7)].

*Streptococcus gallolyticus* ssp. *pasteurianus* is a common commensal bacterium found in the alimentary tract of humans and animals. This pathogen is associated with colorectal tumors, and a 3.2% prevalence of *S. gallolyticus* infection was reported in an unselected cohort of colorectal cancer patients[1)]. Furthermore, this pathogen is associated with diabetes, sepsis, endocarditis, and meningitis[3,8,10–12)]. However, bacteremia caused by *S. gallolyticus* during FN caused by chemotherapy for malignant lymphoma has rarely been reported.

## CASE REPORT

A 79-year-old man showed an adenoma in the ascending colon and was planned to undergo endoscopic mucosal resection (EMR; Figure 1). However, computed tomography (CT) screening before EMR showed multiple lymphadenopathies. The EMR was postponed, and a thorough examination was performed for lymphadenopathies. Positron emission tomography (PET)-CT imaging showed involvement of subclavian and abdominal lymph nodes and spleen, visualized as areas of increased fluorodeoxyglucose uptake (Figure 2). The patient underwent biopsy of the left subclavian lymph node; histopathological findings showed diffuse prolifer-

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ation of large atypical lymphoid cells, which expressed CD20, CD79a, CD10, bcl-2, and bcl-6 but not MUM-1 (Figure 3a, b, c). His diagnosis was non-Hodgkin lymphoma (diffuse large B-cell lymphoma; germinal center B-cell subtype). The clinical stage was IV, and the International Prognostic Index score indicated high risk. He had atrial fibrillation and showed low ejection fraction in echocardiography. We considered that administration of anthracycline should be avoided; the patient received rituximab, cyclophosphamide, etoposide, vincristine, and prednisolone (R-CEOP). He had febrile neutropenia on day 13 during the first course of R-CEOP. Blood culture examination and VITEK2 system revealed the presence of *Streptococcus gallolyticus ssp. pasteurianus* at that time. Cefepime was administered according to the febrile neutropenia guidelines, before the results of antimicrobial susceptibility test were obtained. Subsequently, antibiotics were de-escalated to ampicillin, which has a low minimum inhibitory concentration (MIC). Sepsis caused by *S. gallolyticus ssp. pasteurianus* was not observed again during subsequent chemotherapies, and endocarditis did not develop. After six cycles of R-CEOP, the patient underwent EMR for colon polyp, which was diagnosed as well-differentiated adenocarcinoma in adenoma. *Streptococcus gallolyticus ssp. pasteurianus* was not detected in the culture of the resected adenoma tissue.

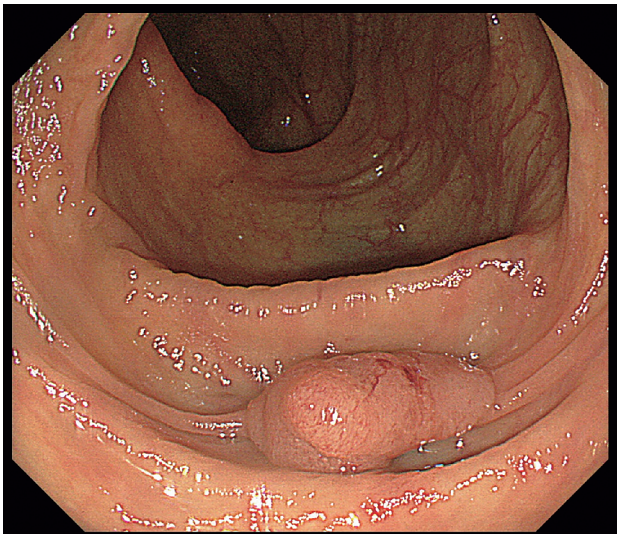

**Figure 1** Colon polyp in the ascending colon. The magnifying endoscopy image shows a raised lesion without stem and roundish and tubular pits ($III_L$).

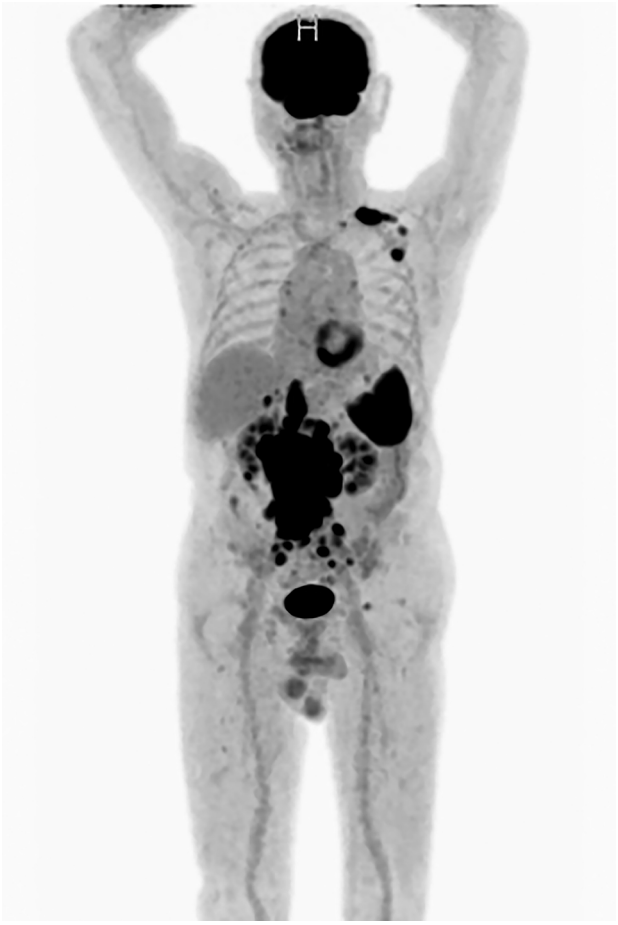


**Figure 2** Positron emission tomography-computed tomography image showing involvement of subclavian and large abdominal lymph nodes and spleen visualized as areas of increased fluorodeoxyglucose uptake.

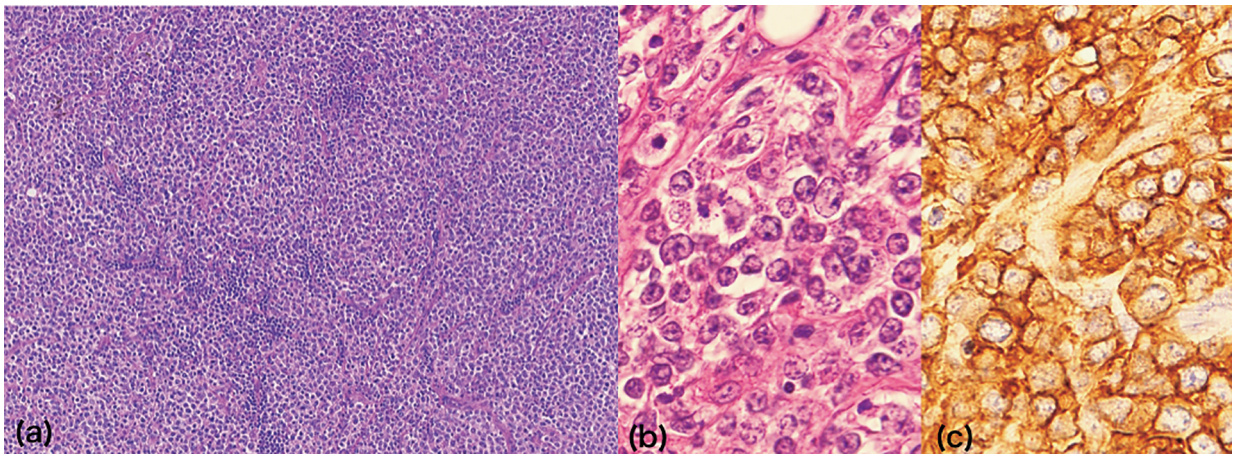


**Figure 3** (a) Biopsy specimen of the left subclavian lymph node. Diffuse proliferation of atypical lymphoid cells was observed (hematoxylin & eosin (H&E) stain; 100×). (b) These atypical cells show oval to round, vesicular nuclei and scanty cytoplasm (H&E; 400×). (c) Most lymphoma cells expressed CD20.

## DISCUSSION

*Streptococcus gallolyticus* was previously named *Streptococcus bovis*; three distinct *S. bovis* biotypes (I, II/1, and II/2) were identified. Based on the molecular characteristics, these subspecies were renamed *S. gallolyticus ssp. gallolyticus* (I), *S. gallolyticus ssp. infantarius* and *S. infantarius ssp. coli* (II/1), and *S. gallolyticus ssp. pasteurianus* (II/2), respectively[3,7]. *Streptococcus gallolyticus ssp. gallolyticus* and *S. gallolyticus ssp. pasteurianus* are associated with colon cancer development. Many studies have shown that bacteremia due to *S. gallolyticus ssp. gallolyticus* was significantly correlated with adenoma and carcinoma of the colon, compared with other *S. gallolyticus* subspecies[3]. However, Sheng et al. reported that *S. gallolyticus ssp. pasteurianus* bacteremia is more highly associated with digestive tract malignancies than *S. gallolyticus ssp. gallolyticus* bacteremia[9]. Blood invasion is believed to occur through bacterial translocation but not through macroscopic ulceration of the mucosa[4]. Boleij et al. reported that *S. gallolyticus ssp. gallolyticus* was an inefficient colonizer of a healthy intestinal tract because of its weak adhesion ability, but it could colonize adenomatous epithelial tissue with displaced collagen IV expression[2]. This species can more easily translocate the epithelium via a paracellular mechanism than other species with a stronger adhesion ability.

Febrile neutropenia is a common adverse event during cytotoxic chemotherapy such as CHOP and CHOP-like regimens. The incidence of *Staphylococcus spp.* is about 30% of gram-positive pathogens isolated from blood cultures of patients with cancer and febrile neutropenia[7]. *Streptococcus gallolyticus ssp*. bacteremia rarely occurs during chemotherapy for malignant lymphoma, and the frequency of bacteremia remains unknown. Corredoira et al. reported that the incidence of *S. gallolyticus ssp*. bacteremia with neutropenia was 3.1% of 257 cases[4].

However, in the present case, *S. gallolyticus ssp. pasteurianus* bacteremia developed during the first course of chemotherapy for malignant lymphoma. When continuing chemotherapy for patients with severe neutropenia who have experienced sepsis caused by this pathogen, it is important to consider the timing of tumor resection. Haimowitz et al. reported that *S. gallolyticus ssp. gallolyticus* was found in the blood of an apparently healthy blood donor who was subsequently diagnosed with a colon malignancy[6]. Some articles have reported the presence of *S. gallolyticus* in adenoma and colon cancer tissues, verified by western blot and quantitative PCR[1,5]. In the present case, the pathogen may be still colonized although it was not detected in the tissue culture of the adenoma tissue after completing six cycles of chemotherapy. The adenoma should have been removed as soon as possible before the next chemotherapy cycle to prevent recurrent bacteremia although the patient did not develop bacteremia again.

## CONCLUSION

Although bloodstream infection due to *S. gallolyticus ssp. pasteurianus* in patients with hematological malignancies undergoing cytotoxic chemotherapy is observed at a low frequency, physicians should investigate the presence of coexisting colorectal tumors when this bacterium is isolated from blood cultures.

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**Conflict of interest**

We have no conflict of interest.

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