Fusobacterium nucleatum bacteremia with liver abscess following administration of anti-COVID-19 vector-based vaccine

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Abstract

Immunization of the population through vaccination against COVID-19 is recognized as a public health priority. The most difficult scientific challenge for vaccines is the clinical safety and efficacy. We report a patient presenting with Fusobacterium nucleatum bacteremia and liver abscess formation following administration of anti-COVID-19 viral-vectored vaccine.

Introduction

Fusobacterium species are anaerobic, Gram-negative, rod-shaped, adherent, non-motile and non-spore-forming bacteria.*Fusobacterium nucleatum* is an oral bacterium, commensal to the human oral cavity, that plays a role in periodontal disease and colorectal neoplasm[1,2].*F. nucleatum* is a rare cause of bacteremia; the annual reported incidence is 0.22–0.76 cases/100,000 population[3,4]. Risk factors for *F. nucleatum* bacteremia include malignancy, older age, alcohol abuse, immunosuppression, and dialysis; infection is often hospital-acquired[3].

Immunization of the population through vaccination is recognized as a public health priority against COVID-19. The clinical efficacy and safety for vaccines against the novel coronavirus is the most difficult scientific challenge at present. We report the case of a 67-year-old man, an immunocompetent patient with *F. nucleatum* bacteremia and liver abscess formation following administration of the first dose of anti-COVID-19 viral-vectored vaccine during the COVID-19 pandemic.

Case history

A 67-year-old physician with a past history of hypertension, allergic rhinitis and hepatic hemagioma for 10 years received the first dose of ChAdOx1nCov-19 vaccine on 2021/3/22. Three days later, he presented with fever, up to 39°C, combined with general soreness. He took an acetaminophen tablet and his fever subsided completely. However, fever up 39.3 with chills occurred on 3/31, and he was admitted for detailed evaluation. Blood culture was done. Neither leukocytosis nor a higher C-reactive protein (CRP) level was noted, and the Covid-19 PCR was negative. The next day, his fever subsided and he was discharged.

However, he developed a fever, up to 38.5, 2 days after discharge. Owing to persistent fever for 3 days, he subsequently visited the infectious disease outpatient department and was admitted for further evaluation. On admission, he had a temperature of 37.6, blood pressure of 127/71 mmHg, and heart rate of 80 beats per minute. On physical examination, he did not have a toxic appearance, but his tonsils had erythematous enlargement. No neck lymphadenopathy was found. His chest examination revealed clear breathing sounds, and a regular heart rhythm without murmur. His abdominal examination revealed a soft abdomen without rigidity or rebound, and no tenderness to palpation. There was no lower extremity edema. His skin was intact without rashes. His white blood cell count was $20.14\times10^3/\mu L$ (reference range $3.8–10.8\times10^3/\mu L$)

with 86.8% neutrophils, hemoglobin was 12.9 g/dL (reference range 12–15.5 g/dL), and platelet count was 246×10^3/μL (reference range 150–450×10^3/μL). His liver chemistries revealed aspartate aminotransferase of 50 U/L, alanine aminotransferase of 60 U/L, and total bilirubin of 0.64 mg/dL. Meanwhile, a CRP level of 148.56 mg/L (reference range <5 mg/L) and procalcitonin C of 3.1 ng/ml (reference range <0.5 ng/mL) were found, which revealed his inflammatory markers were significantly more elevated than during the previous admission. His COVID-19 nasopharyngeal swab test was still negative. Both abdominal echography and computed tomography of the abdomen showed 4.5-cm abscesses at left lateral segment of the liver (Figure 1). Blood cultures were obtained and he was given empiric antibiotic treatment. The liver abscess was drained with a pigtail catheter on the next day. The pus smear revealed Gram-negative bacilli. Later, his blood cultures, which had been collected during the previous admission, yielded*Fusobacterium nucleatum* (*F. nucleatum*). He then underwent a colonoscopy examination, which revealed diverticulosis at the cecum and ascending colon. A dentist was consulted and asymptomatic periodontitis was found.

The patient then received antibiotics with metronidazole and underwent liver abscess drainage. His fever subsided completely and he was discharged under a stable status. After 4 weeks of metronidazole treatment, the patient was able to return to his normal daily life.

Discussion:

Fusobacterium species are Gram-negative anaerobic bacilli which are normally a constituent of the oropharynx, gastrointestinal tract, and female genital flora. Overall, *Fusobacterium* species are a rare cause of bacteremia, accounting for $< 0.001\%$ of all bacteremia and $< 1\%$ of anaerobic bacteremia cases among adults[5]. *Fusobacterium* bacteremia generally affects males more than females[6,7], with the primary infection source typically being the respiratory tract, abdomen, or pelvis[6,8]. With respect to the hepatic abscesses associated with *Fusobacterium* species, oropharyngeal disease or intestinal sources of infections including diverticulitis have been postulated as the potential initial portal of entry[7]. Our patient had periodontal disease, but no evidence of oropharyngeal infections was noted.

Was this bacteremia event a coincidence or a complication related to vaccination? *F. nucleatum* is an adhesive bacterium. It can co-aggregate with various microbial species in the oral cavity, and plays a key role in dental plaque formation[7,9]. In healthy individuals, there is an established homeostasis between immunity and oral cavity microorganisms that do not cause diseases. Once disseminated outside the oral cavity and under dysbiosis, *F. nucleatum* induces exacerbated inflammation, thus turning into a pathogen[10,11]. Regulatory T cells (Tregs) have been known to act on the balance of immunopathogenesis of periodontal lesions. When Tregs function was inhibited, it increased alveolar bone loss and inflammatory cell migration, and as such, the tissue damage associated with periodontitis was noted[12]. Furthermore, *F. nucleatum* stimulates Toll-like receptor 4 (TLR4)-mediated inflammatory responses in the placentas of pregnant mice, causing fetal demise. Suppression of inflammation protects the fetuses, even in the presence of bacterial colonization[13]. However, the exact molecular immunological pathway against *F. nucleatum* is not fully understood. Therefore, we supposed that our patient experienced both wanted and unwanted immunogenicity and the disruption of symbiont status after vaccination, which led to *F. nucleatum* bacteremia.

Fever developed off and on in our patient about 1 week after vaccination. All laboratory data initially showed no abnormality, and he was treated as having an adverse effect post-vaccination. Then, on day 3 of his second admission, the blood culture that was obtained during his first hospitalization grew *F. nucleatum* . The Oxford AstraZeneca chimpanzee adenovirus-vectored vaccine, ChAdOx1 nCoV-19, has appeared to be effective and safe for SARS-CoV-2 immunization[14]. The incidence of objectively measured fever was low in the 18–55 years standard-dose group (12 [24%] of 49), and no fevers were recorded in either the 56–69 years or older standard-dose groups within 7 days after the prime vaccination with ChAdOx1 nCoV-19[14]. Therefore, the diagnosis of systemic adverse reactions post-vaccination should be determined carefully by a clinical physician, especially fever occurrence during an unexpected period among the elderly patient group.

During the COVID-19 pandemic, the normal processes of clinical inference and diagnosis were disrupted and delayed treatment of bacteremia has been noted[15]. Although *F. nucleatum* bacteremia associated with

coronavirus disease was reported recently during the COVID-19 pandemic[16], to the best of our knowledge, this is the first case report of *F. nucleatum* bacteremia with hepatic abscess in an immunocompetent patient post-anti-COVID-19 vaccine administration. The exact relationship between host immunological reaction and the pathogenesis of bacteremia is difficult to identify at present, so further research is needed to elucidate this interaction.

Authorship

AUTHOR CONTRIBUTIONS

Jiun-Ting Wu:contributed to the literature search, and wrote the manuscript

Yung-Fa Lai:provided the concept and design of this report

Chien-Tung Chiu: qualified the patient's image

All authors approved the final version of the manuscript.

Ethical approval

The patient gave permission and informed consent for the publication of this case report.

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Conflict of Interest Statement

The authors have no conflicts of interest to disclose.

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