Fusobacterium nucleatum causing a pyogenic liver abscess: a rare complication of periodontal disease that occurred during the COVID-19 pandemic

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SUMMARY
Fusobacterium nucleatum is a periodontal commensal and pathogen. In rare cases, these anaerobic gram-negative bacilli have been reported to cause pyogenic liver abscesses (PLAs). We describe a patient who developed a periodontal abscess during the COVID-19 pandemic and was unable to access the restricted General Dental Services at this time. She subsequently developed a F. nucleatum bacteraemia and liver abscess. The non-specific signs and symptoms experienced meant the patient self-isolated due to suspected COVID-19 infection and presentation to hospital was delayed. We also include the results of a literature search of other cases of PLAs attributed to F. nucleatum. PLAs often develop insidiously. They require percutaneous drainage and prolonged antimicrobial therapy. Clinicians should be aware of this rare complication of a dentoalveolar infection in a patient who is systemically unwell.

BACKGROUND
Fusobacterium nucleatum is an anaerobic gram-negative oral commensal and periodontal pathogen. Fusobacteria can undergo haematogenous spread and cause infection in multiple body systems. One rare process attributed to F. nucleatum is the formation of pyogenic liver abscesses (PLAs). Affected patients are usually immunocompromised. To the best of our knowledge, there are only 15 reported cases of F. nucleatum PLAs in immunocompetent individuals. The periodontium was the presumed source of infection in seven of these cases.

We report an immunocompetent patient with a F. nucleatum bacteraemia and PLA following a periodontal abscess during the COVID-19 pandemic when access to General Dental Services was limited.

CASE PRESENTATION
A 64-year-old woman presented to the Emergency Department with a 6-day history of lethargy, fever, shortness of breath and mild abdominal pain. Due to non-specific symptoms, the patient had self-isolated at home and underwent two COVID-19 PCR tests in the community. Both results were negative. It was noted that she had received oral antibiotics from her General Dental Practitioner (GDP) in preceding weeks for a troublesome periodontal abscess associated with an upper left posterior tooth. She had no relevant medical history and was an ex-smoker.

On admission, the patient was tachypnoeic with a respiratory rate of 30 breaths per minute and oxygen saturations were 99% on high flow nasal oxygen (60 L/min at 90%). She was tachycardic with a heart rate of 106 beats per minute and pyrexic at 38.3°C. Bilateral crepitations were noted on chest auscultation and abdominal examination showed mild generalised tenderness. No guarding or peritonism was noted. No facial swelling was observed.

Initial blood tests showed a marked inflammatory response, deranged liver function tests (LFTs) (table 1) and a metabolic acidosis, with a lactate of...
for culture and sensitivity testing. No growth was detected from this aspirate. Antibiotics were rationalised to intravenous Ceftriaxone and oral Metronidazole in accordance with Microbiology advice following the identification of *F. nucleatum* on blood culture analysis. While the differentials for a hepatic hypodensity may include primary or metastatic malignancy, no further tissue sampling in the form of biopsy or cytological assessment was undertaken in this case due to the clinical, microbiological and radiological indications that this was an infective process.

Further history was sought regarding the potential bacteraemia source. The patient had experienced ongoing pain from a mobile tooth in the upper left quadrant (ULQ). She was known to have generalised moderate periodontal disease with localised severe disease in the ULQ. An intraoral periapical radiograph demonstrates the severe bone loss in the ULQ, most notably interproximally between the UL7 and UL8. An area of periapical pathology can also be seen associated with the UL8 (figure 2). The UL8 was grade 2 mobile and symptomatic. Both UL7 and UL8 were of poor prognosis. The patient was aware of these findings and had previously received treatment for periodontal disease. She was keen to avoid extraction of these teeth. Due to her recent ULQ pain arising during the COVID-19 pandemic, the patient received advice, analgesia and antimicrobials from her GDP via phone consultation, as per guidelines at the time. Specifically, she received three separate courses of antibiotics in the form of Amoxicillin for 5 days, followed by a further course of Amoxicillin for 7 days and finally a course of Metronidazole for 5 days. At no time did she develop evidence of localised swelling or progression of symptoms and continued to decline to proceed with extraction(s) of either of these teeth.

Further investigations were performed to assess for any further complications in light of a confirmed *F. nucleatum* bacteraemia. A transthoracic echocardiogram excluded endocarditis and an ultrasound Doppler scan confirmed internal jugular vein (IJV) patency. This excluded Lemierre syndrome, an infectious thrombophlebitis of the IJVs secondary to *F. nucleatum* oropharyngeal infection. In the absence of signs, symptoms or evidence of any other pathology and with blood cultures positive for *F. nucleatum*, the periodontium was considered to be the source of infection in this case.

**OUTCOME AND FOLLOW-UP**

The patient responded well to percutaneous drainage and prolonged antibiotics for 6 weeks in total. An interval CT scan demonstrated significant improvement (figure 3). The patient attended her GDP for the necessary dental extractions and ongoing periodontal treatment.

**DISCUSSION**

PLAs are most often caused by intra-abdominal bowel leakage with subsequent spread to the liver via the portal circulation or via direct spread from biliary infections. Due to its rich blood supply, however, the liver may also be a site of haematogenous seeding from a bacteraemia originating from a more distant site. The periodontium is recognised as one such potential source. Significant risk factors include diabetes mellitus, liver transplant, intra-abdominal malignancy, biliary tract procedures and immunosuppression. It has been reported that individuals with diabetes are at 3.6 times greater risk for PLA and 43% of patients have underlying biliary disease. In the Western population, the most common bacterial pathogens in PLAs are *Streptococcus species* (29.5%) and *Escherichia coli* (18.1%). While in Asian populations *Klebsiella*...
Table 2  Reported cases of *Fusobacterium nucleatum* and pyogenic liver abscess

| Author          | Age | Sex | Immunocompetent? | Source | Treatment                                |
|-----------------|-----|-----|------------------|--------|------------------------------------------|
| Swaminathan and Aguilar⁵ | 76  | F   | Yes              | No source identified | Percutaneous drainage Intraoral antibiotics for 4 days Oral antibiotics for 4 weeks |
| Zafer et al⁶    | 51  | M   | Yes              | No source identified | Percutaneous drainage—unsuccessful Intraoral antibiotics for 6 weeks |
| Gohar et al⁷    | 54  | M   | Yes              | Periodontal disease considered a possible source | Tube thoracostomy for empyema Percutaneous drainage Intraoral antibiotics for 4 days Oral antibiotics for 6 weeks |
| Hammami et al⁸  | 63  | M   | Yes              | Periapical dental abscess | Percutaneous drainage Extraction of problematic tooth. Antibiotics (unspecified) |
| Jayasimhan et al⁹ | 51  | F   | Not commented    | Periapical dental abscess presumed source—nil evidence on examination (Prevotella pleuritidis also isolated) | Percutaneous drainage Intraoral antibiotics for 2 weeks Oral antibiotics for 4 weeks |
| Karantanos et al¹⁰ | 43  | M   | Yes              | No source identified | Percutaneous drainage Intraoral antibiotics for 6 weeks Oral antibiotics for 3 months |
| Wijomprecha et al¹¹ | 60  | M   | Yes              | Diverticulitis | Percutaneous drainage Intraoral antibiotics for 5 days Oral antibiotics for 4 weeks |
| Shigefuku et al¹² | 78  | M   | Not commented    | Colonic adenocarcinoma | Percutaneous drainage Intraoral antibiotics (duration not specified) |
| Kearney and Knoll¹³ | 23  | M   | Yes              | Myopericarditis | Percutaneous drainage Intraoral antibiotics for 6 weeks |
| Nagpal et al¹⁴  | 69  | F   | Diabetic         | Periapical dental abscess | Percutaneous drainage Dental extractions Intraoral antibiotics for 2 weeks Oral antibiotics for 4 weeks |
| Ahmed et al¹⁵   | 21  | M   | Yes              | Routine dental cleaning a possible cause | Percutaneous drainage Tuberculosis for associated pleural empyema Partial pleural decongestion with a VATS procedure Percutaneous drainage of abdominal and pelvic abscesses Intraoral antibiotics for 9 weeks |
| Houston et al¹⁶ | 66  | M   | Yes              | Diverticular perforation | Percutaneous drainage Intraoral antibiotics (duration not specified) Oral antibiotics for 6 weeks |
| Schütter and Götter¹⁷ | 58  | M   | Yes              | Perforated sigmoid diverticulitis and pyelonephritis | Percutaneous drainage of liver abscess Laparotomy and drainage of diverticular abscess+colostomy Intraoral antibiotics for 6 weeks |
| Ohyama et al¹⁸  | 59  | F   | Not commented    | Periapical dental abscess | Findings identified postmortem No treatment prior to death |
| Cigarran et al¹⁹ | 58  | M   | Immunocompromised | Recent dental extraction | Percutaneous drainage Intraoral antibiotics (duration not specified) Oral antibiotics for 4 weeks |
| Kajiya et al²⁰  | 59  | M   | Yes              | Periapical dental abscess | No percutaneous drainage—patient refused Intraoral antibiotics for 4 days Oral antibiotics for 4 weeks |
| Wells et al²¹   | 62  | M   | Ulcereative colitis | Colonoscopy and biopsies | Percutaneous drainage Intraoral antibiotics (duration not specified) |
| Ala et al²²     | 78  | F   | Polyarthritis (long-term steroid treatment) | Severe diverticulitis | Percutaneous drainage of subphrenic and intrahepatic collections Intraoral antibiotics for 6 weeks |
| Crippin and Wang²³ | 69  | M   | Yes              | Periapical periodontitis | Percutaneous drainage Antibiotics (unspecified) |
| Tweedy and White²⁴ | 29  | M   | Immunocompromised | Recent routine dental work (fillings and cleaning) 4 days prior to onset of symptoms | Percutaneous drainage initially and open surgical drainage after 10 days Intraoral antibiotics (duration not specified) Oral antibiotics for 4 weeks |

*pneumonia* has been shown to be the predominant pathogen.⁴ *Fusobacterium nucleatum* has been identified as a rare cause of PLAs in the literature. These patients are usually immunocompromised, however. It is very rare that this periodontal pathogen is found to be the causative microbe in an immunocompetent patient.¹

PLAs can be difficult to diagnose. History and examination are often non-specific. Peritonitis is identified in only 14% of patients and right upper quadrant abdominal tenderness in less than 40%.³ ⁸ The shortness of breath and tachypnoea in this case that were concerning for COVID-19 symptoms were likely due to diaphragmatic irritation or as a systemic response to underlying sepsis. Laboratory investigations may show hypoalbuminaemia, elevated gamma-glutamyl transferase, leukocytosis and an elevated alkaline phosphatase, which is known to be a sensitive marker of liver abscess.³ All these indicators were observed in our case. Early identification and appropriate drainage and antimicrobial therapy are the mainstays of treatment and necessary to prevent morbidity or mortality.

A literature search was performed using the PubMed database in the form of free text and medical subject headings searches. We used the search terms, ‘*Fusobacterium nucleatum*’ and “pyogenic liver abscess” (table 2).³ ⁴ ⁷ ⁹–²⁴ There were 20 cases of PLA where *F. nucleatum* was implicated as the causative pathogen in the English literature.

From these reports, 15 patients were described as either being immunocompetent or there were no specific comments regarding medical history to suggest anything to the contrary. From the immunocompetent or presumed immunocompetent patients, a dental or periodontal source for *F. nucleatum* PLA was suspected in seven cases.
Case report

This case demonstrates a very rare sequela of periodontal disease which occurred during the COVID-19 pandemic when General Dental Services were limited to emergencies that could not be managed at home. Conventional treatment for a likely periodontal abscess would usually entail drainage, either by instrumentation during subgingival debridement or by incision. Ultimately, if this is unsuccessful, the causative tooth may need to be extracted. In the absence of significant local or initial systemic features, however, this patient did not meet the criteria for face to face Dental treatment at the height of the pandemic. Extraction was ultimately offered due to the ongoing persistent symptoms and underlying poor prognosis of these teeth, but due to the mild localised symptoms the patient declined to proceed with this option.

In the absence of significant localised intraoral signs, and subsequent non-specific systemic symptoms, COVID-19 was suspected in this case by both the patient, and initially by health-care staff. Consequently, presentation to hospital was delayed. Fortunately, our patient responded to treatment and made a good recovery.

We believe Clinicians should be mindful of PLAs as a rare, but possible complication when managing patients with dentoalveolar infection who present atypically or are systemically unwell.

Learning points

1. The possibility of distant spread should be considered in the unwell or septic patient with dentoalveolar infection.
2. Patients with a confirmed *Fusobacterium nucleatum* bacteraemia or positive abscess aspirate should undergo a full dental assessment.
3. A full systematic review needs to be performed on all patients with presumed COVID-19 infection to exclude any other pathology.

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REFERENCES

1. Han YW. *Fusobacterium nucleatum*: a commensal-turned pathogen. *Curr Opin Microbiol* 2015;23:141–7.
2. Jayasimhan D, Wu L, Huggan P. *Fusobacterial* liver abscess: a case report and review of the literature. *BMC Infect Dis* 2017;17:440.
3. Vijayampeela K, Yukyava N, Somprong S, et al. *Fusobacterium nucleatum*: atypical organism of pyogenic liver abscess might be related to sigmoid diverticulitis. *Int J Med Sci* 2016;8:197.
4. Hammani MB, Noonan EM, Chhiparia A, et al. Denture-Associated oral microbiome and periodontal disease causing an anaerobic pyogenic liver abscess in an immunocompetent patient: a case report and review of the literature. *Gastroenterology* 2018;11:241–6.
5. Scottish Dental Clinical Effectiveness Programme. Acute Dental Problems - COVID-19 - SDCEP, 2020. Available: https://www.sdcep.org.uk/published-guidance/acute-dental-problems-covid-19/ [Accessed 28 Aug 2020].
6. Johnson King O, Sharma V. Lemiierre syndrome leading to Ankylosis of the temporomandibular joint. *Br J Oral Maxillofac Surg* 2019;57:1153–5.
7. Nagraj SJS, Mukhi J, Patel P. *Fusobacterium nucleatum*: a rare cause of pyogenic liver abscess. *Springerplus* 2015;4:283.
8. Pang TCY, Fung T, Samra J, et al. *Pyogenic* liver abscess: an audit of 10 years’ experience. *World J Gastroenterol* 2011;17:1622.
9. Swaminathan N, Aguilar F. Cryptogenic Pyogenic Liver Abscesses Due to *Fusobacterium nucleatum* in an Immunocompetent Patient. *Eur J Case Rep Intern Med* 2020;7:001741.
10. Zafar H, Rashid MU, Mandhaviya B, et al. Multiloculated liver abscess caused by *Fusobacterium*; role of Karius testing in diagnosis. *Cureus* 2020;12:e8823.
11. Gohar A, Jamous F, Abbadallah M. Concurrent *fusobacterium* pyogenic liver abscess and empyema. *BMJ Case Rep* 2019;12:e231994.
12. Karantanos T, Karanika S, Obisoye K, et al. *Pyogenic* liver abscess due to *Fusobacterium nucleatum* in a patient with liver hemangiomas. *Am J Med Sci* 2017;353:417–8.
13. Shigefuku R, Watanabe T, Kanno Y, et al. *Fusobacterium nucleatum* detected simultaneously in a pyogenic liver abscess and advanced sigmoid colon cancer. *Anaerobe* 2017;48:144–6.
14. Kearney A, Knoll B. Myopericarditis associated with *Fusobacterium nucleatum*-caused liver abscess. *Infect Dis* 2015;47:187–9.
15. Ahmed Z, Bansal SK, Dhillon S. Pyogenic liver abscess caused by *Fusobacterium* in a 21-year-old immunocompetent male. *World J Gastroenterol* 2015;21:3731.
16. Houston H, Kumar K, Sajid S. Asymptomatic pyogenic liver abscesses secondary to *Fusobacterium nucleatum* and Streptococcus vestibulans in an immunocompetent patient. *BMJ Case Rep* 2017;4:kbz2017-221476.
17. Schattnere A, Gotler J. Fever, night sweats, and abnormal liver enzymes. *Lancet* 2014;384:376.
18. Ohyama H, Nakasho K, Yamanegi K, et al. An unusual autopsy case of pyogenic liver abscess caused by periodontal bacteria. *AJP Infect Dis* 2009;62:381–3.
19. Cigarrán S, Neches C, Lamas JM, et al. A case report of a pyogenic liver abscess caused by *Fusobacterium nucleatum* in a patient with autosomal dominant polycystic kidney disease undergoing hemodialysis. *Ther Apher Dial* 2008;12:91–5.
20. Kajiya T, Uemura T, Kajiya M, et al. A case report of a pyogenic liver abscess caused by periodontal bacteria. *BMJ Case Rep* 2018;11:241–6.
21. Wells CD, Balan V, Smillie JD. Pyogenic liver abscess after colonoscopy in a patient with sigmoid diverticulitis. *Anaerobe* 2017;48:144–6.
22. Ala A, Safar- Aly H, Millar A. Metallic cough and pyogenic liver abscess. *Clinical Gastroenterology and Hepatology* 2005;3:424.
23. Alqarni A, Alaraby M, Alrashed A. Unrecognized etiology for pyogenic hepatic abscesses in normal host: dental disease. *Am J Gastroenterol* 1992;87:1740–3.
24. Tweedy CR, White WB. Multiple *Fusobacterium nucleatum* liver abscesses. *J Clin Gastroenterol* 1987;9:194–7.
25. British Society of Periodontology. 2020. Available: https://www.bsperio.org.uk/assets/downloads/good_practitioners_guide_2016.pdf [Accessed 7 Sep 2020].