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

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Accepted 13 December 2020

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.[1] *Fusobacteriae* can undergo haematogenous spread and cause infection in multiple body systems.[1 2]

One rare process attributed to *F. nucleatum* is the formation of pyogenic liver abscesses (PLAs). Affected patients are usually immunocompromised.[3] 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.[4]

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

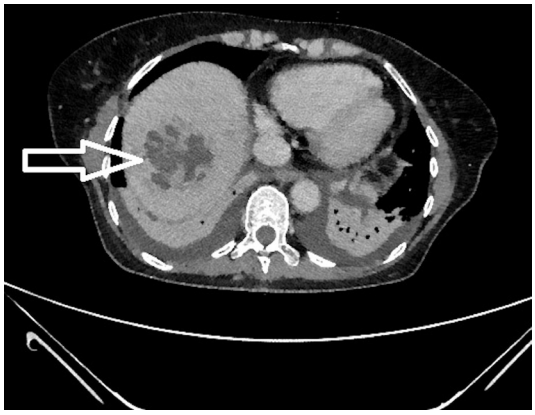

Figure 1 CT scan demonstrating a 5.5×4.8 x 3.7 cm multilobulated cystic lesion in the right lobe of liver consistent with a liver abscess. Bilateral lower lung consolidation and small pleural effusions were also noted.

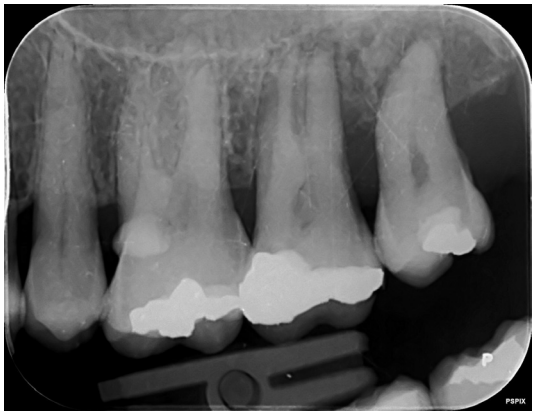

Figure 2 An intraoral periapical radiograph demonstrating severe periodontal disease affecting the upper left quadrant.

To cite: Collins L, Diamond T. *BMJ Case Rep* 2021;**14**:e240080. doi:10.1136/bcr-2020-240080

Table 1 Initial blood test results highlighting inflammatory markers and liver function tests

Blood test	Normal range	Result on presentation
WCC	4.0–10.0×10^9/L	25.3
CRP	<5 mg/L	216
Total bilirubin	<21 umol/L	9
GGT	6–42 U/L	110
AST	<32 U/L	84
ALP	30–130 U/L	200
Albumin	35–50 g/L	31

ALP, alkaline phosphatase; AST, aspartate aminotransferase; CRP, C-reactive protein; GGT, gamma-glutamyl transferase; WCC, white cell count.

7.1. An initial chest radiograph was unremarkable. Urine screen was clear. Initial blood cultures were obtained.

Provisional diagnoses after assessment in the Emergency Department were given as either COVID-19 or sepsis of unknown origin. The patient was resuscitated, and broad-spectrum intravenous antibiotics were commenced in line with local trust Policy. In our case, this was Tazocin and Gentamicin.

INVESTIGATIONS

An ultrasound scan of the abdomen was performed due to ongoing mild abdominal tenderness and deranged LFTs on day 2 of admission. An ill-defined lesion within the right lobe of the liver was identified containing both solid and cystic components measuring 4.3×3.5×3.4 cm. A CT scan was recommended.

The subsequent CT scan was completed to further characterise these ultrasound findings. A 5.5×4.8×3.7 cm multilobulated cystic lesion consistent with a right hepatic lobe abscess was identified (figure 1). No other intra-abdominal pathology was demonstrated.

Blood cultures obtained in the Emergency Department identified a *F. nucleatum* bacteraemia. Serological assessment for HIV was negative.

TREATMENT

Once identified, percutaneous drainage of the PLA was performed by an Interventional Radiologist under CT guidance and a drain was placed. Purulent abscess fluid was drained, and this was sent 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.[5] 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.[1 6]

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.[7] Significant risk factors include diabetes mellitus, liver transplant, intra-abdominal malignancy, biliary tract procedures and immunosuppression.[3] 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.[4]

In the Western population, the most common bacterial pathogens in PLAs are *Streptococcus species* (29.5%) *and Escherichia coli* (18.1%).[4] While in Asian populations *Klebsiella*

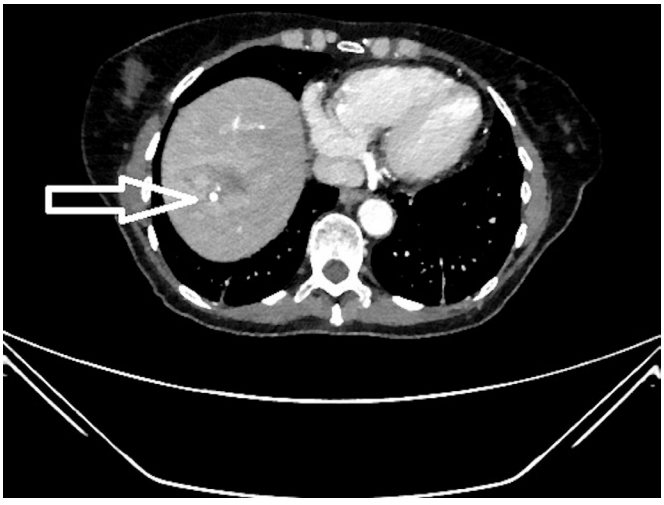

Figure 3 Repeat CT scan showing improvement to liver abscess following percutaneous drainage and antimicrobial therapy. Previously seen consolidation and effusions have resolved.

Table 2 Reported cases of *Fusobacterium nucleatum* and pyogenic liver abscess

Author	Age	Sex	Immunocompetent?	Source	Treatment
Swaminathan and Aguilar[9]	76	F	Yes	No source identified	Percutaneous drainage Intravenous antibiotics for 4 days oral antibiotics for 4 weeks
Zafar *et al*[10]	51	M	Yes	No source identified	Percutaneous drainage—unsuccessful Intravenous antibiotics for 6 weeks
Gohar *et al*[11]	54	M	Yes	Periodontal disease considered a possible source	Tube thoracostomy for empyema Percutaneous drainage Intravenous antibiotics for 4 days Oral antibiotics for 6 weeks
Hammami *et al*[4]	63	M	Yes	Periapical dental abscess	Percutaneous drainage Extraction of problematic tooth. Antibiotics (unspecified)
Jayasimhan *et al*[2]	51	F	Not commented	Periodontal disease presumed source—nil evidence on examination (*Prevotella pleuritidis* also isolated)	Percutaneous drainage Intravenous antibiotics for 2 weeks Oral antibiotics for 4 weeks
Karantanos *et al*[12]	43	M	Yes	No source identified	Percutaneous drainage Intravenous antibiotics for 6 weeks Oral antibiotics for 3 months
Wijarnpreecha *et al*[3]	60	M	Yes	Diverticulitis	Percutaneous drainage Intravenous antibiotics for 5 days Oral antibiotics for 4 weeks
Shigefuku *et al*[13]	78	M	Not commented	Colonic adenocarcinoma	Percutaneous drainage Intravenous antibiotics (duration not specified)
Kearney and Knoll[14]	23	M	Yes	Myopericarditis	Percutaneous drainage Intravenous antibiotics for 6 weeks
Nagpal *et al*[7]	69	F	Diabetic	Periodontal disease	Percutaneous drainage Dental extractions Intravenous antibiotics for 2 weeks Oral antibiotics for 4 weeks
Ahmed *et al*[15]	21	M	Yes	Routine dental cleaning a possible cause	Percutaneous drainage Tube thoracostomy for associated pleural empyema Partial pleural decortication with a VATs procedure Percutaneous drainage of abdominal and pelvic abscesses Intravenous antibiotics for 9 weeks
Houston *et al*[16]	66	M	Yes	Diverticular perforation	Percutaneous drainage Intravenous antibiotics (duration not specified) Oral antibiotic for 6 weeks
Schattner and Gotler[17]	58	M	Yes	Perforated sigmoid diverticultis and pylephlebitis	Percutaneous drainage of liver abscess Laparotomy and drainage of diverticular abscess+colostomy Intravenous antibiotics for 6 weeks
Ohyama *et al*[18]	59	F	Not commented	Periodontal disease	Findings identified postmortem No treatment prior to death
Cigarran *et al*[19]	58	M	Immunocompromised	Recent dental extraction	Percutaneous drainage Intravenous antibiotics (duration not specified) Oral antibiotics for 3 weeks
Kajiya *et al*[20]	59	M	Yes	Periodontal disease+dental caries	No percutaneous drainage—patient refused Intravenous antibiotics for 4 days Oral antibiotics for 4 weeks
Wells *et al*[21]	62	M	Ulcerative colitis	Colonoscopy and biopsies	Percutaneous drainage Intravenous antibiotics (duration not specified)
Ala *et al*[22]	78	F	*Polymyalgia Rheumatica* (long-term steroid treatment)	Severe diverticular disease	Percutaneous drainage of subphrenic and intrahepatic collections Intravenous antibiotics for 6 weeks
Crippin and Wang[23]	69	M	Yes	Periapical periodontitis	Percutaneous drainage Antibiotics (unspecified)
Tweedy and White[24]	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. Intravenous 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.[3]

PLAs can be difficult to diagnose. History and examination are often non-specific. Peritonism 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).[2–4 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.

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.[6] Conventional treatment for a likely periodontal abscess would usually entail drainage, either by instrumentation during subgingival debridement or by incision.[25] 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 healthcare 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.

Acknowledgements Clinical information and dental periapical radiograph provided by Dr David McKee (General Dental Practitioner).

Contributors LC wrote the text. The report was reviewed and edited by TD.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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