Pulmonary and thoracic infection by *Fusobacterium nucleatum*

**Infección pulmonar y torácica por Fusobacterium nucleatum**

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<td>Pneumonias involving the pleura and posterior chest wall invasion, which may reach the skin forming a fistula, are very infrequent.</td>
<td>Fusobacterium nucleatum is an anaerobic bacterium that is part of the oral microbiota and dental plaque. It can be a source of local infections, such as caries, gingivitis, periodontitis, and, potentially, distant-site or extra-oral infections, so we present an illustrative case of this condition.</td>
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**Abstract**

*Fusobacterium nucleatum* is an anaerobic bacillus that is part of the oral microbiota and dental plaque. This can cause local and potentially remote infections, which are exceptional in pediatrics. **Objective:** To present the case of a patient with lung injury with chest wall invasion by *Fusobacterium nucleatum*. **Clinical Case:** An 11-year-old female immunocompetent patient who consulted due to a two-week history of cough, night sweats, without fever or weight loss, and increased volume at the left spleen thoracic level. There was no history of chest wall trauma or travel outside the country. Two weeks before the onset of symptoms, she was treated for dental caries. Imaging studies and CT scan showed left spleen pneumonia, which invades the pleura and the chest wall. A minimal thoracotomy was performed, releasing a thick, foul-smelling liquid. The studies for common germs and tuberculosis were negative. Hematology ruled out tumor lesions. The anaerobic study reported the development of *Fusobacterium nucleatum*. The patient was treated with penicillin followed by amoxicillin presenting good clinical and radiological responses. The dental procedure was suspected as the cause of infection. **Conclusions:** *Fusobacterium nucleatum* can occasionally cause remote or extra-oral infections in immunocompetent patients, such as pneumonia with chest wall invasion, therefore it is necessary to bear it in mind.

**Keywords:**  
Fusobacterium  
Nucleatum;  
Fusobacterium Theory;  
Pneumonia;  
Empyema

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**Clinical Case**

Healthy 11 year and 9 months old schoolgirl, who consulted due to a two-week history of left dorsalgia, associated with cough, night sweats, no fever, no weight loss, and progressive increase in chest wall volume in the left dorsal region, at the T9 level. Chest X-ray (Figure 1) was suggestive of left basal pneumonia, and chest CT scan (Figure 2) showed left pulmonary consolidation without signs of abscesses and periostal reaction in the 9th, 10th, and 11th ribs adjacent to the process.

It was observed that the inflammatory involvement went beyond the pleura to the soft tissues of the left posterior chest wall, with increased fat density and thickening of the musculature due to edema. These findings suggested pneumonia due to an unusual germ. *Actinomyces* infection, tuberculosis, mycobacteria, or a neoplastic lesion was suspected.

The dental clinical record was reviewed, finding reports from the age of 8, with 9 procedures due to caries, mostly due to dentin, three extractions of primary teeth, and one extraction of a marginal periodontal abscess a year earlier. There was no report of gingivitis or periodontitis. Two weeks before the onset of symptoms, she was treated for dentin caries by a pediatric dentist. She had no history of chest trauma or travel outside the country.

The following laboratory tests were performed: blood count with normal WBC count and platelets, hemoglobin and hematocrit with mild hypochromic anemia, erythrocyte sedimentation rate and C-reactive protein moderately increased, liver tests, alphafetoprotein, and immunoglobulins within normal ranges.

A minimally invasive thoracotomy was performed at the level of the 7th left intercostal space; dissection by planes released a thick, viscous, yellowish, and foul-smelling content. Samples were taken for biopsy, culture for aerobes, anaerobes, smear microscopy, and culture for mycobacteria.

Current aerobic cultures were negative at the 7th and 15th day of incubation. Bacilloscopies were negative and Lowenstein-Jensen medium cultures were negative at 60 days. Mycobacteria cultures were negative at 40 days.

The anatomopathological record reported the presence of a fibro-adipose vascular tissue, with lymphocytic and macrophage inflammatory infiltration, with areas of necrosis and hemorrhagic infiltration. PAS was negative.

Samples of secretion in BACT/ALERT FN PLUS® blood culture bottles were sent to the Public Health Institute of Chile (ISP) for anaerobes culture, according to the protocol for the transfer of biological samples, resulting in *Fusobacterium nucleatum* development.

Complementary tests were performed to rule out dissemination to another parenchyma which were normal (abdominal and pelvic ultrasound). Delayed bone scintigraphy showed improvement of rib lesions and ruled out other lesions.

She was treated with intravenous sodium penicillin for 3 weeks, changing to oral therapy with amoxicillin,

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**Introduction**

*Fusobacterium nucleatum* is an anaerobic, Gram-negative, non-sporogenous bacterium. Its name is due to its elongated rod-like shape of different dimensions. It is part of the oropharyngeal, gastrointestinal, and genitourinary microbiota. In the oropharynx, it is important in forming bacterial plaque, where it plays comprehensive and beneficial roles in biofilms, contributing to both periodontal health and disease.

Depending on clinical circumstances, it can have pathogenic activity, thus, in periodontal lesions, such as gingivitis, periodontitis, or in dental procedures, it is identified as a possible source of bacteremia and invasive infections. In adult patients, there are reports of pleuropulmonary infections associated with dental problems when occurring bronchoaspiration associated with poor oral health, and in clinical reports of different bacterial isolates including brain and hepatic abscess, spondylodiscitis, and endocarditis.

In children, infections due to this microorganism are infrequent. There is a case of endobronchial lesion due to pulmonary infection by *Fusobacterium nucleatum* in a healthy child; a study of 41 cases of necrotizing pneumonia which only one of them was due to *Fusobacterium nucleatum*; and there is also a reference of osteomyelitis of the knee, all in previously healthy children, and osteomyelitis of the femur.

On the other hand, it has been associated with adverse pregnancy events such as chorioamnionitis and stillbirth; there is scientific interest in the digestive tract due to associations related to colorectal cancer, although experimental investigations are still in progress. *Fusobacterium necrophorum* is another species considered pathogenic, which is associated with ear, nose and throat (ENT) infections that may be complicated due to septic thrombophlebitis of the jugular vein, and may present septic emboli in the lung, joints, muscles, soft tissues, liver, spleen, kidneys, and central nervous system. It is also known as Lemierre’s disease or necrobacillosis, which was highly mortal before the antibiotic era.

The objective of this report is to present a case of a pulmonary lesion with chest wall invasion by *Fusobacterium nucleatum*. 

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She was treated with intravenous sodium penicillin for 3 weeks, changing to oral therapy with amoxicillin,
completing 4 months of treatment, evolving favorably. In the last follow-up visit at 9 months post-treatment, the patient was asymptomatic, with complete resolution of pulmonary and thoracic lesions.

Discussion

The genus *Fusobacterium* are Gram-negative anaerobic bacilli, composed of numerous subspecies, among them *Fusobacterium nucleatum* and *Fusobacterium necrophorum*, which are the most identified as pathogens. *Fusobacterium necrophorum* is the main etiological agent of Lemierre’s syndrome or necrobacillosis, which is a rare pathology due to oropharyngeal infection that can be complicated by internal or external jugular vein septic thrombophlebitis, usually in young people and previously healthy adults, although there are reports in younger children. Septic emboli are one of the complications, where the lung is the most affected organ, and other locations such as joints, skin, bones, and meninges have been described.

*Fusobacterium nucleatum* is part of the oropharyngeal, gastrointestinal, and genitourinary microbiota, and is the most frequently isolated species in the oral cavity, capable of coexisting with different microbial species and adhere to epithelial cells, playing an important role in the formation of bacterial plaque, and in diseases such as dental caries, gingivitis, periodontitis, which can be a source of extraoral infections. Adhesins and lipopolysaccharides of the cell membrane provide its adhesion capacity. The gene encoding the adhesin is FadA, which is also a virulence factor and is a potent stimulator of inflammatory cytokines, IL-6, IL-8, and TNF.

*Fusobacterium nucleatum* has also been detected as a predominant species in amniotic fluid and fetal membrane associated with preterm delivery and in cord blood associated with neonatal sepsis. According to the results of preclinical studies in pregnant mice, it has been suggested that *Fusobacterium nucleatum* is transferred from the maternal oral cavity to the intrauterine cavity through hematogenous transmission. Periodontal disease has therefore been associated as one of the risk factors for adverse pregnancy events such as chorioamnionitis, preeclampsia, prematurity, neonatal sepsis, and stillbirth. *Fusobacterium nucleatum* has been associated with...
gastrointestinal disorders; 10-100 times higher levels of FadA and *Fusobacterium nucleatum* have been reported in patients with adenomas and colorectal cancer compared with healthy controls. Therefore, FadA, which is a unique gene of this microorganism, would be a marker to identify individuals at risk of developing cancer. Other studies have observed that a high abundance of *Fusobacterium nucleatum* is associated with a worse patient prognosis and cancer recurrence because, in part, it may promote resistance to chemotherapy.

Infections by anaerobic microorganisms in pediatrics present low incidence but can be serious and mortal. They are associated in newborns with prolonged labor, premature rupture of membranes, maternal chorioamnionitis, prematurity, fetal distress, and necrotizing enterocolitis, and in older children with appendicitis, abdominal trauma with ruptured viscer, in soft tissues with skin abscesses of the buttocks, perirectal areas, vulvovaginal, head, and fingers. Predisposing conditions include chronic disorders such as neoplasms, hematologic diseases, immunodeficiencies, chronic kidney failure, and decubitus ulcers.

In a study of anaerobic infections over 18 months in children under 1 month and over 5 years of age, 3,898 positive cultures were obtained, of which only 2.9% developed anaerobic agents, mainly from cultures obtained from abdominal fluids, soft tissue, and blood cultures. The most frequent agents included Bacteroides (38.4%), Propionibacterium (15.8%), Clostridiodes (14.4%) and Fusobacterium (4.8%).

Clinical reports of pulmonary infections due to *Fusobacterium nucleatum* in the pediatric age group are rare. There is a report of a previously healthy child with pneumonia and endobronchial lesion. In a French tertiary pediatric care hospital, during 5 years, 41 necrobiotic arthritis of the knees and a case of osteomyelitis of the femoral epiphysis due to *Fusobacterium nucleatum*, which was initially suspected as a bone tumor.

A Canadian study of bacteremia incidence, which included 95% of all blood cultures collected from both inpatients and outpatients over 10 years, processed and centralized by a single laboratory, concluded that the overall annual incidence of *Fusobacterium bacteremia* was 0.55 per 100,000 population. *Fusobacterium nucleatum* cases had a median age of 53.5 years, while *Fusobacterium necrophorum* cases had a median age of 21 years.

In 72 cases of *Fusobacterium spp.* reported, 61% corresponded to *Fusobacterium nucleatum* and 25% to *Fusobacterium necrophorum*. The latter was identified in a younger population with no comorbidity or associated mortality, while *Fusobacterium nucleatum* patients were older with comorbidities such as cancer or on dialysis, with mortality of 10%.

Bacteremia due to *Fusobacterium nucleatum* has been observed in patients with hematopoietic diseases such as lymphomas or leukemia, and the predisposing factors are severe neutropenia due to immunotherapy and oral mucositis.

Other diagnoses that can be considered in cases of pleuropulmonary and thoracic symptoms or empyema necessitans, once a tumor lesion has been ruled out, are infection by *Mycobacterium tuberculosis* or Actinomycyes, which is identified in most cases. Other agents identified are aerobic agents such as *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas spp.*, and fungi such as *Aspergillus*. Foreign body aspiration, such as grass inflorescences, can cause complex pulmonary lesions, and inhalation of fungal spores can cause pulmonary lesions such as histoplasmosis. In Chile, there are reports of infections by *Aspergillus* of young people who went hiking in the Ecuadorian jungle, and a geologist who explored subway mines in Central America and Peru.

Regarding the treatment of our patient, it was decided to continue with penicillin, initiated at the hospital of origin, while awaiting the results of the bacteriological studies. Only the samples for isolation of anaerobic microorganisms sent to the ISP, according to the transfer protocol, reported development of *Fusobacterium nucleatum*. Another way to identify microorganisms that are difficult to culture is by broad-range PCR followed by 16S rDNA sequencing.

The patient evolved favorably, with no complications after surgical emptying and treatment with penicillin and later with amoxicillin. In infections by *Fusobacterium spp.*, there are reports that 95% are sensitive to penicillin, clindamycin, metronidazole, amoxicillin with clavulanic acid, and imipenem. Some strains produce beta-lactamase and are resistant to macrolide antibiotics. Prolonged treatment is recommended depending on the evolution and clinical response.

Regarding the possible odontogenic etiology, although the patient did not report infections such as gingivitis or periodontitis, numerous studies report that asymptomatic and transitory bacteremia occurs during dental procedures such as scaling, dental extractions, and periodontal surgery, and, in people with poor dental hygiene, common activities such as brushing teeth with bleeding or chewing can also be a risk factor. In healthy individuals, these transient bacteremias have no clinical significance and are eliminated, unlike in patients with affected immune system.

Our patient did not have immunological involvement. Only a dental procedure could be confirmed as...
a possible source of thoracopulmonary infection, however, we have not yet clarified how this germ reached the respiratory tract, either via the oral or hematogenous route.

Conclusions

Fusobacterium nucleatum can occasionally cause distant-site or extra-oral infections in immunocompetent patients, such as pneumonia with chest wall invasion, so it is necessary to bear it in mind.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

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