

A case of pulmonary infection with *Prevotella melanogenica* having the paving stone symptom

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ABSTRACT

Prevotella melanogenica is a typical organism present in the human oral cavity and female reproductive tract, which is responsible for causing periodontal disease and the inflammation of the female reproductive tract. The present report discusses the case of a young female patient who presented with cough and fever as the main clinical symptoms. Computed Tomography (CT) revealed multiple clusters of ground glass density shadows in both lungs, with network-like and paving stone-like changes. The alveolar lavage fluid was collected for next-generation sequencing, which revealed the presence of *Prevotella melanogenica*. The patient received treatments, CT revealed that the density of multiple flakes of ground glass density in both lungs was lower than the previously observed density. *Prevotella melanogenica* pneumonia is rare, and the paving stone symptom observed in CT is not specific. Therefore, the case reported here provides a novel perspective regarding the diagnosis of pneumonia.

CASE REPORT

CASE REPORT

A 16-year-old female patient was admitted to the Emergency Medicine Department with the complaint of coughing for one week and fever for three days. One week prior to admission, the patient had a cough with no evident inducement, accompanied by white sputum. While the amount of sputum was small, it was difficult to cough it out. In addition, dizziness and headache were present, which were not treated. Three days prior to admission, the patient had a fever, the cause of which was not evident. The highest body temperature reached was 39.0 °C, accompanied by chills, nasal congestion, runny nose, dizziness, headache, nausea, vomiting, abdominal pain, diarrhea, chest tightness, asthma, frequent urination, the urgency of urinating, painful urination, and back pain. The patient then visited the Emergency Medicine Department of our hospital, where routine blood tests were conducted. The blood

test results revealed the following: white blood cells, $22.51 \times 10^9/L$ ↑; red blood cells, $4.36 \times 10^{12}/L$; hemoglobin, 127 g/L; platelets, $320 \times 10^9/L$; the percentage of neutrophil cells, 86.9% ↑; the percentage of lymphocytes, 5.7% ↓; and the percentage of monocytes, 7.1%. The routine urine analysis revealed the following: white blood cells, 1+; protein, 2+; glucose, +-; occult blood, 2+; CRP, 246.87 mg/L. Pulmonary infection was considered, and the patient was admitted to the Emergency Medicine Department for further treatment. After admission, cefixime (2 g i.v. BID) was administered as an anti-infective treatment.

The examination conducted at admission revealed the following: body temperature, 38 °C; pulse, 118 bpm; breathing, 20 bpm; blood pressure, 113/69 mmHg. The patient was conscious at admission and in good spirits. Cyanosis of the lips and the swelling of the bulbar conjunctiva were not observed.

Breath sounds in both lungs were coarse, the dry and wet rales in both lungs were not evident, all heart sounds were well and regular, no pathological murmurs were detected, the abdomen was soft and with no tenderness, rebound pain, and muscle tension, and no edema was observed in either of the lower limbs. The blood gas analysis revealed the following: pH, 7.447; PaCO₂, 35.6 mmHg; PO₂, 79.7 mmHg; SO₂, 97.1%. The CT revealed multiple masses of ground-glass appearance in both lungs, with network-like and paving stone-like changes, and full lymph nodes in the mediastinum close to the right lower hilum (Figure 2A and 2B). These could be clinical considerations of pneumonia or pulmonary alveolar proteinosis (PAP).

A bronchoscopy was performed three days after admission. The color of the alveolar lavage fluid was clear and transparent, with no typical turbid fluid detection (Figure 1E) and no cloud flocculent or amorphous protein material detected under the bronchoscope (Figure 1A-1D). Excluding the possibility of alveolar proteinosis, the alveolar lavage fluid was collected for NGS, which revealed the presence of *Prevotella melanogenica*.

The patient continued to receive the anti-infective treatment with cefixime, which was supplemented with anti-cough, expectorant, immune-enhancement, and other treatments. After three days of this treatment, no further symptoms of fever were reported, along with significantly reduced coughing. Re-examination revealed significantly improved laboratory indicators. Therefore, the patient was discharged from the hospital after one week. After discharge from the hospital, a CT re-examination was performed within a month, which revealed that the multiple flaky masses with a ground-glass appearance in both lungs were lower than the previously observed ones, with only a slight ground-glass appearance along the two sides of the lungs. The distribution of the pulmonary bronchial vascular bundles suggested that the infectious disease had improved, although multiple small lymph nodes were visible in the mediastinum, a few of which were smaller than their previously observed sizes (Figure 2C and 2D). The relevant laboratory results during the patient's hospitalization are presented in Table 1.

DISCUSSION

Background

Prevotella melanogenica is a Gram-negative, non-spore-forming, free anaerobic microbial species belonging to the genus *Prevotella*. *Prevotella melanogenica* typically exists in the oral cavity and female reproductive tract in humans, and is responsible for causing periodontal disease and the inflammation of the female reproductive tract. *Prevotella melanogenica* is capable of adhering to and invading macrophages, and activating the NF- κ B signaling pathway by binding to TLR2 (1), which enhances the expressions of IL-1 β , IL-6, and TNF- α in macrophages (2). *Prevotella melanogenica* secretes the T6SS protease, which destroys epithelial cells (2) and further damages the host tissue through the production of collagenase and lipase (1). In addition, the ability of *Prevotella melanogenica* to induce abscesses was reported to be correlated

to the presence of a mucopolysaccharide capsule. The presence of capsular material suppresses phagocytosis (3). Recent studies have demonstrated that *Prevotella melanogenica* may also cause systemic diseases such as aspiration pneumonia. The cases of lung infection reported for the bacteria are, however, relatively rare, and the clinical symptoms lack specificity, which often leads to misdiagnosis.

Etiology & Demographics:

Prevotella melanogenica is a conditionally pathogenic anaerobic bacteria, which is mainly responsible for oral infections and inflammation of the female reproductive tract. In addition, under the conditions of low immunity and invasive surgical procedures, this bacterial species may cause invasive pneumonia (4), skin and soft tissue infections, intracranial infections (5), joint infections (6), etc.

Clinical & Imaging findings:

Paving stone symptom is a special imaging feature that is reported in only 76 relevant publications. If the duplicate cases, cases not confirmed in pathological diagnosis, and cases with an unclear clinical diagnosis are excluded, only a total of 342 cases with imaging manifestations of the paving stone symptom are reported in the literature. Among these, 149 cases (43.57%) are of alveolar proteinosis, 78 cases (22.8%) are of viral pneumonia, 23 cases (6.7%) are of bacterial pneumonia, and 92 cases (26.9%) are of other conditions. Paving stones are common in alveolar proteinosis, with typical HRCT manifestations of ground-glass density shadow changes in both lungs, thickening of the interlobular septum, and a distinct boundary with the surrounding normal tissues (7, 8). The paving stone imaging feature may also be detected in diseases such as pulmonary edema, pulmonary hemorrhage, nodules, non-specific interstitial pneumonia, viral infection, peripheral T-cell lymphoma, and erosive mucinous adenocarcinoma (9–13). However, in the above diseases, no cases of pneumonia caused due to infection with *Prevotella melanogenica* are reported so far. Anaerobic pneumonia usually leads to lung abscesses, with the CT manifestations of single or multiple cavities in the posterior wall of the bilateral lung lobes. Gas and liquid may be observed in the cavity, with the typical gas–liquid level (14). The above-mentioned characteristic manifestations were not detected in the case considered in the present study. In view of the lack of typicality in the clinical and imaging manifestations of the concerned patient, metagenomic second-generation sequencing technology was finally adopted in the present study to identify the bacteria, and the patient was finally diagnosed with lung infection due to *Prevotella melanogenica*.

Treatment & Prognosis:

Prevotella melanogenica is a Gram-negative, non-spore-forming, anaerobic bacterial species belonging to the genus *Prevotella*. Cefixime is a third-generation cephalosporin drug belonging to the class of β -lactam antibiotics used against bacteria, mainly the Gram-positive cocci and Gram-negative bacilli. Considering the evident relief achieved in the symptoms of fever, cough, and sputum in patients with pre-treatment, a re-examination was performed, which revealed that the levels of white blood cells and related infection indicators were lower than the previously observed values. After the cause was

determined, the use of cefixime as the anti-infective treatment was continued. The follow-up CT re-examination revealed that the lesion was significantly absorbed compared to the previous status, which confirmed that the anti-infective treatment was effective.

Differential Diagnoses:

Pulmonary alveolar proteinosis: Pulmonary alveolar proteinosis (PAP) is a rare disease characterized by the alveolar accumulation of a surfactant composed of proteins and lipids due to impaired surfactant clearance by alveolar macrophages. The diagnosis of PAP is initiated by the results of computed tomography (CT) and confirmed based on the bronchoalveolar lavage fluid (BALF) staining results. CT reveals the paving stone symptom, and the patient's bronchoalveolar lavage fluid is milky white (7, 15).

Summary:

The present report discusses a case of the rare imaging manifestation of pneumonia caused due to a rare bacterial infection. Considering the diagnosis and treatment experience with the case reported here, it is recommended, despite it not being a typical treatment modality, to add *Prevotella melanogenica* pneumonia to the list of identification signs of pulmonary diseases with the paving stone symptom. In addition, early NGS detection through alveolar lavage is recommended in the diagnosis and treatment of the disease. This would assist in the early identification of the cause of the disease, thereby enabling an effective prediction of disease progress and formulation of an effective treatment plan.

TEACHING POINT

Although the paving stone symptom is rarely detected in the infection with *Prevotella melanogenica*, its identification based on alveolar sedimentation is nonetheless important. Through the study of this case, when the pavement sign appeared in CT, we could not help thinking whether it was *Prevotella* infection.

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FIGURES

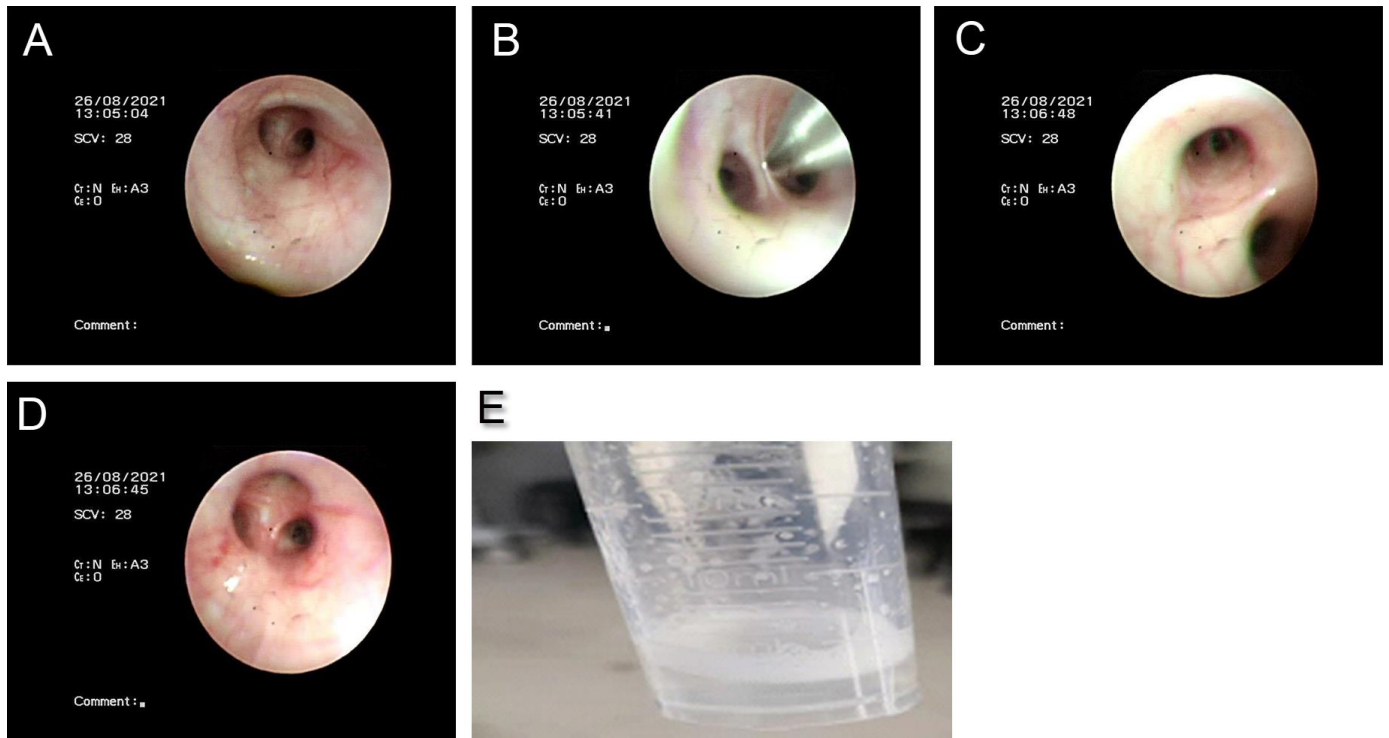


Figure 1: 16-year-old female patient with pulmonary infection with *Prevotella melanogenica*.

Findings: The bronchoscopy analysis revealed no cloudy or amorphous protein substances (1A-1D). The color of the bronchoalveolar lavage fluid is clear and transparent (1E).

Technique: Bronchoscopy

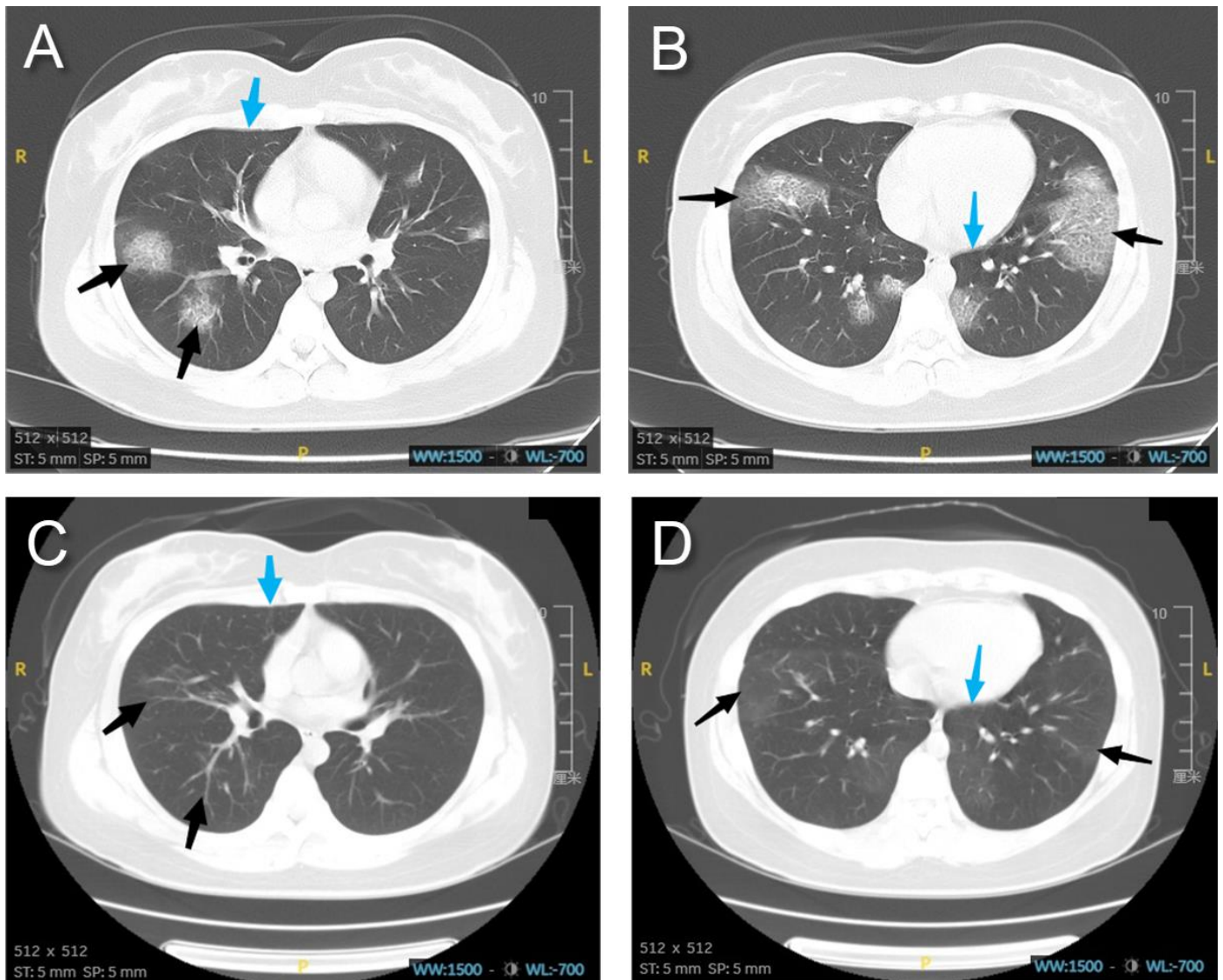


Figure 2: 16-year-old female patient with pulmonary infection with *Prevotella melanogenica*.

Findings: There are multiple masses of ground-glass opacity in both lungs, with network-like and paving stone-like changes (Figure 2A and 2B, black arrows); the pleura is visibly thickened (Figure 2A and 2B, blue arrows).

After treatment, the ground-glass opacities are noticeably less (Figure 2C and 2D, black arrows), and the thickening of the pleura in both lungs has improved compared to the previous observations (Figure 2C and 2D, blue arrows).

Technique: CT chest without contrast, lung window

Variable	Before Admission	On Admission	After discharge	Reference range, Adult
White cell count (x10 ⁹ /L)	22.51 ↑	12.15 ↑	7.69	3.50–9.50
Red cell count (x10 ¹² /L)	4.36	3.62	4.00	3.80–5.10
Hemoglobin (g/L)	127	105	116	115–150
Platelets (x10 ⁹ /L)	320	421 ↑	601 ↑	125–350
PCT (ng/mL)	0.19	0.06	<0.04	0.04–0.50
CRP (mg/L)	50.61 ↑	66.27 ↑	2.26 ↑	<0.80
IL-6 (pg/mL)	246.87 ↑	103.59 ↑	9.28	0.00–10.00
ESR (mm/h)	65 ↑		32 ↑	0–20
Antinuclear antibody	negative		negative	<1:80
T-SPOT (SFCs/2.5 × 10 ⁵ PBMC)	0	0	0	<6
KL-6 (U/mL)	202			<500

Table 1: Laboratory Examination Data of the patient with pulmonary infection with *Prevotella melanogenica*.

Etiology	<i>Prevotella melanogenica</i>
Risk factors	Immunocompromised, aspiration, invasive operation
Treatment	Cefixime
Prognosis	Can be completely healed, leaving no sequelae to the lungs
Findings in the imaging analysis	Chest CT showed multiple masses of ground-glass density shadows in both lungs, which showed network-like and paving stone-like changes, full lymph nodes in the mediastinum near the right lower hilum
Laboratory examination	Leukocytes were elevated, mainly neutrophils. Urine white blood cells are elevated, urine occult blood is positive
Clinical symptoms	Fever, cough, phlegm, headache, dizziness

Table 2: Summary table of pulmonary infection with *Prevotella melanogenica*.

Pulmonary alveolar proteinosis (PAP)	PAP is a rare disease characterized by the alveolar accumulation of a surfactant composed of proteins and lipids due to impaired surfactant clearance by alveolar macrophages. The diagnosis of PAP is initiated by a CT scan and confirmed based on bronchoalveolar lavage fluid (BALF) staining results. CT reveals the paving stone symptom. The patient's bronchoalveolar lavage fluid is milky white.
Diffuse alveolar hemorrhage (DAH)	Diffuse or focal pulmonary hemorrhage may present with a paving stone symptom, particularly in the subacute phase. It is represented by the accumulation of hemosiderin-containing macrophages in the interstitium. Coexistence with consolidation and a history of hemoptysis assist in establishing the diagnosis.
Exogenous lipoid pneumonia (ELP)	ELP has the typical features of consolidation, with ground-glass opacities surrounded by a thickening of the interlobular septa on CT, representing the paving stone symptom. Transbronchial biopsy and bronchoalveolar lavage assist in the diagnosis of ELP.

Table 3: Differential diagnosis table for pulmonary infection with *Prevotella melanogenica*.

ABBREVIATIONS

BID = bis in die
bpm = beats per minute
CRP = C-reactive protein
ESR = erythrocyte sedimentation rate
HRCT = High-resolution computed tomography
IL-1 β =Interleukin 1 beta
IL-6 = Interleukin- 6
iv = Intravenous
KL-6 = Krebs Von den Lungen-6
NF- κ B =Nuclear factor-kapa B
NGS = next-generation sequencing
PAP = pulmonary alveolar proteinosis
PBMC = peripheral blood mononuclear cell
PCT = procalcitonin
SFCs = spot-forming cells
TLR2 = Toll-like receptor 2
TNF- α =tumor necrosis factor-alpha
T-SPOT = T cell spot detection
U = unit

KEYWORDS

Prevotella pneumonia; Prevotella; Lung; Paving stone symptom; Case report

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