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CASE REPORT

# Hepatic Granuloma Mimicking Tuberculosis: *Achromobacter Xylosoxidans* in a Patient with Familial Mediterranean Fever

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ABSTRACT

Achromobacter xylosoxidans is an aerobic, gram-negative bacillus that is rarely isolated. The most common infections caused by it are hospital-acquired infections. Bacteremia, catheter-associated infections, and pneumonia are common clinical presentations and they are seen especially in immuncompromised patients or in patients with predisposing factors such as hematological and solid malignancies, chronic renal failure, diabetes mellitus, cardiac disorders and steroid treatment. Community acquired infections are very rare in healthy individuals. Here we present a patient with Familial Mediterranean Fever who developed hepatic abscess caused by Achromobacter xylosoxidans. To our knowledge, this is the first case reported with Familial Mediterranean Fever and hepatic granuloma caused by Achromobacter xylosoxidans. In countries where tuberculosis is endemic, granulomatous diseases such as tuberculosis should be excluded when there is a hepatic granuloma and clinicians should keep in mind other infectious diseases such as Achromobacter xylosoxidans that can easily be misdiagnosed as tuberculosis.

Key words: Achromobacter xylosoxidans, hepatic granuloma, familial mediterranean fever, liver abscess, tuberculosis

## INTRODUCTION

Achromobacter xylosoxidans formerly called Alcaligens xylosoxidance is an aerobic, non- fermentative, gram-negative bacillus that is rarely isolated. It was first characterized by Holmes et al. and then named by Yabuuchi and Ohyama [1]. This bacterium normally lives in aquatic sources in the environment and hospital as well as in the human gut. It may cause both community-acquired and nosocomial infections. The most common infections caused by the bacterium are hospital-acquired infections. Bacteremia, catheter-associated infections, and pneumonia are common clinical presentations. Post-operative infections of the eye, meningitis, endocarditis, hepatobiliary infections, peritonitis, urinary tract infections /and otitis were also reported [2, 3]. The pathogen is commonly isolated from immunocompromised patients or in patients with predisposing factors such as hematological and solid malignancies, chronic renal failure, diabetes mellitus, cardiac disorders and steroid treatment. Mortality is high in immunocompromised patients with invasive infections [1]. We present a patient with Familial Mediterranean Fever (FMF) who developed hepatic abscess in which Achromobacter xylosoxidans was identified as the causative agent.

## CASE

A sixty-one year old woman who had a diagnosis of FMF for thirty years was admitted to Hacettepe University Hospital with abdominal pain. She had abdominal pain for 6 months that had increased and localized to right upper quadrant in the last few days. She had no nausea, vomiting, weight loss or fever. She was on 3x0.5 mg colchicine treatment for FMF. She had a history of cholecystectomy 10 years ago. On her physical examination, tenderness was detected in the epigastric region with no organomegaly, mass or ascites. Laboratory investigations revealed a normal hemogram, liver and renal function tests other than elevated erythrocyte

Table. Laboratory values of the patient

| Parameter | Value | Range |
|---|---|---|
| Alanine Aminotransferase | 9 U/L | < 35 |
| Aspartate Aminotransferase | 21 U/L | < 35 |
| Alkaline Phosphatase | 125 U/L | 30 - 120 |
| Gamma-Glutamyl Transferase | 47 U/L | < 38 |
| Direct Bilirubin | 0.164 mg/dL | 0 - 0.2 |
| Indirect Bilirubin | 0.32 mg/dL | 0 - 1.2 |
| Total Protein | 6.69 g/dL | 6.4 - 8.3 |
| Albumin | 3.65 g/dL | 3.5 - 5.2 |
| Blood Urea Nitrogen | 18.17 mg/dL | 8 - 23 |
| Creatinine | 0.77 mg/dL | 0.51 - 0.95 |
| Calcium | 9.09 mg/dL | 8.8 - 10.6 |
| CRP | 2,9 mg/dL | 0 - 0.8 |
| Erythrocyte Sedimentation Rate | 61 mm/hour | 0 - 25 |
| Hemoglobin | 11.9 gr/dL | 11.7 - 15.5 |
| Leukocyte Count | 5.1 x10^3/µL | 4.1 - 11.2 |
| Lymphocyte % | 18 % | 18.8 - 50.8 |
| Monocyte % | 4 % | 4.1 - 12.2 |
| Neutrophil % | 77 % | 39.9 - 73 |
| Eosinophil % | 0.7 % | 0.8 - 6 |
| Platelet Count | 202 x10^3/µL | 159 - 388 |
| Anti-HIV antibody | negative | negative |
| Brucella Agglutination | negative | negative |
| VDRL | negative | negative |
| ANA (Antinuclear antibody) | negative | negative |
| p-ANCA | negative | negative |
| c-ANCA | negative | negative |

p-ANCA: Perinuclear antineutrophil cytoplasmic autoantibody
c-ANCA: cytoplasmic antineutrophil cytoplasmic autoantibody
VDRL: Venereal Disease Research Laboratory

sedimentation rate (61 mm/hour) and C-reactive protein (CRP): 2,9 mg/dL. The purified protein derivative (PPD) skin test was positive with 15 mm diameter. The laboratory values of the patient are listed in table 1. Abdominal ultrasonography showed a liver abscess (2.5 cm) in the parenchyma, and a dense extra-parenchymal collection (6x4 cm) at the surrounding region and milimetric calcifications in the spleen that were more likely to represent tuberculosis. Her abdominal magnetic resonance imaging (MRI) revealed a liver abscess with extra-parenchymal extension with calcifications, which was suggestive of a granulomatous state (Figure). In addition, there were lesions in the spleen that was suggestive of tuberculosis. On her chest computer tomography (CT) scan there were a group of multiple lymph nodes greater than 10 mm at the right hilar region, a 24x16 mm of parenchymal opacity at the posterior region of inferior lobe of right the lung, minimal pleural effusion at the right side and parenchymal nodules at the left side (the largest 4mm in size). A CT-guided tru-cut biopsy of the lesion that was located posterior region of inferior lobe of the right lung showed a granulomatous inflammation and necrosis. Tuberculosis polymerase chain reaction (PCR) and culture were found to be negative. The liver biopsy also showed a granulomatous inflammation with necrosis. Specific microorganisms such as fungi and Mycobacteria were not detected with Grocott' s methenamine silver stain, Periodic acid-Schiff Stain and acid-fast stain in both of the specimens. The possible granulomatous diseases including sarcoidosis, infections (including HIV, CMV, EBV, brucellosis, syphilis, toxoplasmosis and fungal infections) and vasculitis were excluded as differential diagnosis: HIV, CMV, EBV, brucellosis, syphilis and toxoplasmosis were excluded with specific serological tests. Autoimmune antibodies were also negative. (Table ) Vasculitis were excluded by clinical, laboratory findings and histological findings of the biopsy. Blood cultures did not yielded any pathogens. The culture of the liver biopsy specimen yielded Achromobacter xylosoxidans. The PCR and the culture of the specimen from the hepatic abscess that was drained were negative for tuberculosis. After the biopsy was performed we empirically started intravenous ampicillin-sulbactam treatment. As the microorganism was sensitive to ampicillin-sulbactam we continued antibiotic treatment. After four weeks of antibiotic treatment, the abdominal ultrasonography revealed regression of the hepatic abscess.

## DISCUSSION

Achromobacter xylosoxidans usually causes hospital-acquired infections including bacteremia, catheter-associated infections, pneumonia, post-operative infections of the eye, meningitis, endocarditis, hepatobiliary infections, peritonitis, urinary tract infections and otitis [2, 3]. They are seen especially in immunocompromised patients or in patients with predisposing factors such as hematological and solid malignancies, chronic renal failure, diabetes mellitus, cardiac disorders and

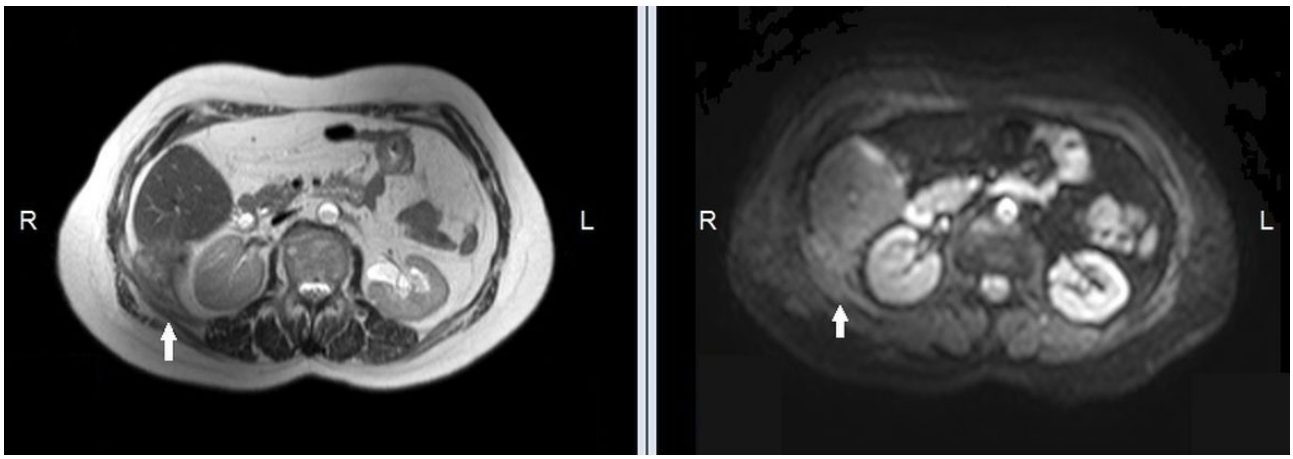


Figure. Abdominal magnetic resonance image illustrating the liver abscess with extra-parenchymal extension with calcifications (arrow)

steroid treatment [1]. Community acquired infections are very rare in healthy individuals. Community-acquired Achromobacter xylosoxidans infections are seen as pneumonia occasionally in patients who have underlying diseases of the lung such as tuberculosis [4]. Nevertheless, it has never shown to cause hepatic abscess in patients with tuberculosis. To our knowledge, this is the first case reported with Familial Mediterranean Fever and hepatic granuloma caused by Achromobacter xylosoxidans. Our aim is to emphasize the importance of rare microorganisms such as Achromobacter xylosoxidans in the etiology of granulomatous diseases beside careful exclusion of tuberculosis especially in endemic countries. Achromobacter is reported in hepatobiliary and abdominal infections in the form of liver abscesses, dialysis-associated peritonitis, or severe intra-abdominal infections and pseudocyst [5]. Asano, K., et al previously reported three patients with hepatic granulomas caused by Achromobacter xylosoxidans [3]. The important common characteristic of these patients and our patient was a history of cholecystectomy with no underlying disease other than diabetes mellitus. The longest time interval from cholecystectomy until liver abscess was 38 months, but in our patient, it was 10 years. Two of the patients' autopsy revealed systemic secondary amyloidosis due to chronic infection. As our patient has FMF, a possible secondary amyloidosis may be a predisposing factor for Achromobacter xylosoxidans granuloma. FMF is not a disease that causes immunosupression and there is not any evidence in the literature showing that Achromobacter xylosoxidans infections are more common in FMF patients. In 2009, the FDA approved colchicine as a monotherapy for the treatment of FMF and gout flares. Side effects include gastrointestinal upset and neutropenia. High doses can also damage bone marrow leading to anemia and cause hair loss. All of these side effects can result from hyper inhibition of mitosis. However, there is no evidence showing a predisposition for abscess or granuloma formation. Hepatic granulomas (HGs) are multiple, discrete, sharply defined, nodular infiltrates, consisting of aggregates of epithelioid cells or macrophages, surrounded by a rim of mononuclear cells, predominantly lymphocytes [6]. The association between this pathologic finding and a specific disease entity is not clear. The etiology of HG includes infections, neoplasms, drugs, and autoimmune diseases. The frequency of HGs may change according to the geographical area and diagnostic experience of the health center [6]. According to the literature it is found in 2.4–10% of the liver tissue specimens. In a study from our country, the prevalence of HGs was found to be 1.6 %. Sarcoidosis and tuberculosis was the most common etiologic factor [7]. In another study from our country hepatic granulomas were detected in 6.05 % of liver specimens and primary biliary cirrhosis (PBC) was the most common cause of them [8]. The prevalence of hepatic granulomas was reported to be 2.2 % in our center and PBC, sarcoidosis, and miliary tuberculosis were the most commonly encountered causes [6]. In a more recent study from our country, HGs were detected in 1.31% of the specimens and the leading cause of HGs was PBC, followed by sarcoidosis [9]. In these present studies, the cases of tuberculosis were rarely diagnosed. Indeed, these results are not expected for Turkey where tuberculosis is endemic. This can be attributed to the fact that these studies were held in tertiary centers and such tuberculosis patients might be treated in primary

health care centers without referral. In our patient tuberculosis PCR and culture were found to be negative. The positivity of PPD skin test in our patient may be due to BCG vaccination because the diameter of tuberculin skin test might be higher in vaccinated individual [10].

## CONCLUSION

To our knowledge, this is the first case reported with FMF and hepatic granuloma caused by Achromobacter xylosoxidans in the literature. As a developing country in Turkey, where the tuberculosis is endemic, granulomatous disease such as tuberculosis should be excluded when there is a hepatic granuloma and keep in mind other infectious diseases such as Achromobacter xylosoxidans that can easily be misdiagnosed as tuberculosis.

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