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Case Report Open Access

Parainfluenza Virus Type 4b Infection in a Patient with Mixed Connective Tissue Disease

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Abstract

We describe the first reported case of bronchopneumonia by Parainfluenza Virus (PIV) type 4B without coinfection with any other respiratory virus in a patient with Mixed Connective Tissue Disease (MCTD) on chronic steroid therapy. The patient acquired an infection by PIV followed by a disease flare with development of bronchopneumonia. This report highlights the importance of considering rare microbiological diagnostics in patients on chronic corticosteroid treatment and autoimmune diseases. It also emphasizes the potential morbidity of this therapy in spite of its efficacy in patients with connective tissue diseases.

Keywords: Mixed connective tissue disease; Parainfluenza virus 4; Bronchopneumonia; Corticosteroid treatment

Introduction

The Mixed Connective Tissue Disease (MCTD) or overlap syndrome is a rare chronic disease, whose etiopathogenic mechanism is not completely understood. Treatment for moderate or severe forms is immunosuppression with corticosteroids, cyclophosfamide or azathioprine which determines a state of cellular immunosupresion that could facilitate infection.

Parainfluenza Virus (PIV) is a cause of respiratory tract infections and is included in the paramyxovirus family. Respiratory tract infections by PIV are characteristic of pediatric age and immunocompromised patients, they do not have a specific treatment and its clinical course is variable [1]. We describe the first case of bronchopneumonia by VPI4B in an adult with corticotherapy.

Case report

47 year old female with history of Mixed Connective Tissue Disease (MCTD) in treatment with 1 mg/kg/day of prednisone and 150 mg/day of azathioprine, who has received during his illness intravenous boluses of methylprednisolone and cyclophosphamide because of severe polyneuropathy. She has also presented episodes of oligoarthritis, livedo reticularis, Raynaud's phenomenon and ischemic hepatitis.

She was evaluated in the emergency department for fever and productive cough without dyspnea or chest pain, during the last five days. On physical examination she revealed a temperature of 38°C, lung auscultation with bilateral rhonchi and livedo reticularis, without any other relevant finding. The blood count showed normocytic anemia with elevation of acute phase reactants and lactate dehydrogenase (Table 1).

No legionella or pneumococcus antigens were detected in urine. Blood cultures were sterile.

Blood count	Results
Hemoglobin	12.6 g/dl
Hematocrit	38.90%
MCV	96.3 fl
MCH	31.3 pg
Leukocytes	4.7 × 103/uL
Neutrophils	4300
Lymphocytes	300
Monocytes	100
Platelet	422 × 103/uL
INR	0.8
Fibrinogeno	728 mg/dl
C-reactive protein	15.5 mg/dl
VSG	42 mm
ALT	26 U/L
AST	37 U/L
GGT	63 U/L
Total bilirubin	0.23 mg/dl
Urea	22 mg/dl
Creatinine	0.87 mg/dl
LDH	1058 U/L
Glucose	141 mg/dl

Table 1: Blood count at hospital admission.

A chest X-ray was performed with findings of bronchopneumonia (Figure 1) and an urgent bronchoscopy showed a morphologically normal larynx, trachea and bronchia with seromucous secretions.

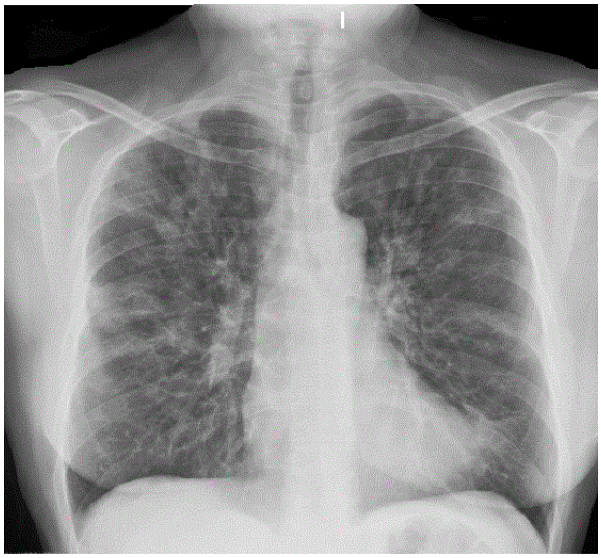

Figure 1: Chest X-ray. Multiple alveolar infiltrates predominantly peripheral without cavitation suggestive of bronchopneumonia.

Then empirical broad-spectrum antibiotic with meropenem, trimethoprim/sulfamethoxazole and clarithromycin was started. During her hospital admission, an immunological study was performed (Table 2) and serological analysis for respiratory viruses, such as, syncytial virus A and B, influenza A, B and C, parainfluenza 1, 2 and 3, adenovirus, enterovirus virus B, rhinovirus, metapneumovirus A and B, and coronavirus bocavirus, being all of them negative (Figure 2). Due to the persistance of her respiratory symptoms in spite of empirical ATB therapy, we decided to perform a bronchoscopy to expand the cytomicrobiological study, where we found positive results for PIV 4B.

Antibodies	Results
ANA (IFI)	Negative
Anti-B2 microglobuline IgG Anti-B2 microglobuline IgM	Negative Negative
Anti-mieloperoxidase	Negative
Anti-cardiolipin	Negative
Anti-proteinase 3	Negative
Anti-glomerular basement membrane	Negative
Anti-citrullinated peptide Anti-U1-ribonucleoprotein	Negative Positive
Complement C3 C4	118 mg/dl (normal) 16 mg/dl (normal)
Rheumatoid factor	15.3 U/ml (normal)
Cryoglobulins	Negative

Table 2: Immunological study.

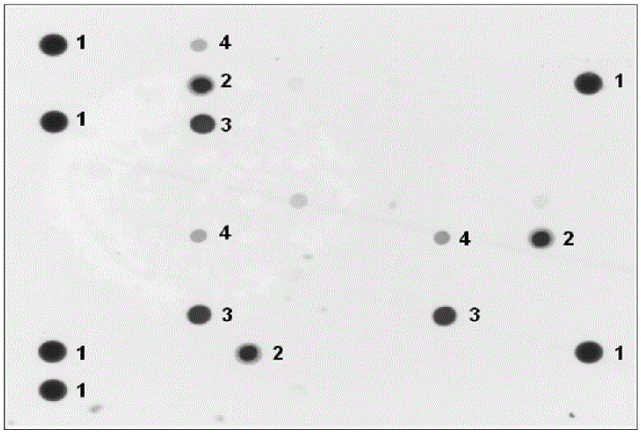

Figure 2: Microarray results for a bronchoalveolar lavage sample.

The study of respiratory viruses was performed using the kit commercial CLART® Entherpex assay, PneumoVir (Genomics, Coslada, Spain). (1) Position points with undiluted sample (2) An internal control is added in each amplification tube to control amplification efficiency. The assay is based on the amplification of a viral fragment by 2 multiplex reverse transcription-polymerase chain reaction test (RT-PCR) and subsequent hybridization a low density microarray (3) A microarray reader piloted by specific software performs the detection by colorimetric reaction and the interpretation of the results (4) bronchoalveolar lavage specimen of the reported patient was submitted for viral typing and a PIV4 was detected.

1: Position points; 2: Internal control, amplification and hybridization; 3: Commercial generic PIV4; 4: Bronchoalveolar lavage sample with PIV4 in the reported patient.

Finally, treatment was adjusted with rapid radiographic improvement, but without complete normalization of it, probably related to some degree of pulmonary interstitial disease by its connective tissue. Given the favorable clinical course of the patient, we decide her hospital discharge maintaining extended prophylaxis with trimethoprim/sulfamethoxazole for lymphopenia in relation to her cellular immunosuppression.

Discussion

We report the case of a woman of 47 years with MCTD treated with double immunosuppressive therapy who presented with a respiratory infection with a rare microbiological isolation that made us think about a broad differential diagnosis.

In the EMTC, certain disorders of the immune system with altered lymphocyte responses against autoantigens could be involved with high titles of antibodies anti-U1-ribonucleoprotein and anti-U1-70 in most patients [2-4]. The clinical manifestations involve a mixture of symptoms of other connective tissue diseases but without fulfilling the diagnostic criteria. Treatment for moderate or severe forms is immunosuppression with corticosteroids, cyclophosfamide or azathioprine, which determines a state of cellular immunosupresion

that can facilitate infection for any of them, being the pulmonary hypertension the main cause of death [5].

Parainfluenza Virus (PIV) is a cause of respiratory tract infections and is included in the paramyxovirus family. There can be four serotypes. The types 1 and 3 are part of the genus Respirovirus while types 2 and 4 are part of the genus Rubulavirus. There are two PIV4 serotypes, A and B, being the serotype 4B the most infrequent of all [1,6].

In general, The PIV is considered a causative agent of 10% of acute respiratory infections during the winter months, especially amongst children [7]. However, the PIV is objectively much less frequent in clinical practice, probably because of the technical difficulties in the virus isolation. In 2008, Hasman et al. performed a study using the technique of PCR. From 154 samples of respiratory secretions in adults with flu-like symptoms, a frequency of 5.8% of VPI was found [8].

The first presence of VPI 4 in Spain was communicated in a study made by Garcia et al. in 2002. 230 samples of nasopharyngeal secretions were analyzed, isolating VPI 4 in 9 patients: 8 of them where breastfed babies and an 8 years old boy. However, the VPI 4 can also affect adults immunocompromised by providing a broad spectrum of virulence [9].

Muscle weakness that affects some patients with MCTD may condition, a weakness of the smooth musculature of the airways that alters the production of an effective cough and therefore facilitates episodes of aspiration and respiratory infections [5].

The association of bronchopneumonia by VPI 4 MCTD in an adult with pharmacological immunosuppression is not yet described in our experience.

Conclusion

In the patients with EMTC moderate-severe treated with corticotherapy, due to the cellular immunosupression produced by them, and therefore facilitate viral infections, we emphasize the necessity of performing viral isolation test in the cases of respiratory infections, including VPI4.

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