Thiamazole-Induced Agranulocytosis Leading to Abscessus Pneumonia—Rare, But Challenging

Agranulocytosis induced por tiamazol que lleva a absceso pumonar. Un reto infrecuente

Dear Editor,

The antithyroid agents (carbimazole, methimazole, thiamazole, propylthiouracil and benzylthiouracil) are the drug class that is associated with a high risk of agranulocytosis. Isolated severe neutropenia or agranulocytosis, defined as an absolute neutrophil count of less than 0.5 × 10^9/L occurring in a subject treated with antithyroid agents should be considered as a drug-induced agranulocytosis, until proven otherwise. Agranulocytosis is rare and may develop in 0.2–0.5% patients using antithyroid drug therapy.¹ The clinical evidence of infectious complications associated with antithyroid-drug-induced (ATD) agranulocytosis is usually symptomatology in fever (92%) and sore throat (85%), pharyngitis (46%), acute tonsillitis (38%), pneumonia (15%) and urinary tract infection (8%).²

A 61-year-old, Caucasian female was admitted to the emergency department with complaints with fever up to 39°C, chills and cough and general weaknesses which started a day after discharge from other hospital (hematology department) where she was treated for gastric pain and neutropenia (leukocyte was 1.2 × 10^9/L, neutrophils 0.03 × 10^9/L) induced by thiamazole. She was afebrile. Chest X ray was normal. She recovered successfully after 10th days with granulocyte colony-stimulating factor and discharged from hospital. Previously, she has been with hyperthyroidism for 21 years, six month ago before hospital admission her therapy was changed to thiamazole.

On admission to our hospital, her vital signs were within normal limits, except for a temperature of 38.8°C and respiratory rate 22/min. Physical examination revealed atonic bilateral equal air entry with no added rhonchi or wheezing. Cardiovascular and neurological examinations revealed no abnormalities. The abdomen was soft and non-tender, without palpable visceromegaly.

Fig. 1. Chest X ray showing abscessus pneumonia (A); HRCT demonstrated extensive pulmonary abscess over both the lungs (B).
Her initial chest X-ray showed a multifocal abscessing pneumonia (Fig. 1A). CT was immediately performed which confirmed multifocal abscessus in lungs (Fig. 1B). Admission labs revealed hemoglobin 12.5 g/dL, white count 8.8 × 10^3/L, neutrophil 5.99 × 10^3, platelets count 197 × 10^3/L. Her serum sodium levels were 138 mEq/L, and the blood urea nitrogen (BUN) and creatinine values were 20 mg/dL and 0.9 mg/dL respectively. C reactive protein (CRP) was 252 ng/ml, while procalcitonin was 78.7 μg/L. Arterial blood gas showed a pH of 7.30 and PO₂ of 60 mmHg, PCO₂ 46 mmHg, SO₂ 90%.

Initially, the patient was started empirically with broad-spectrum antibiotics: Vancomycin 1 g/12 h, Amikacin 1 g/12 g and Orvagyl 500 mg/8 h. Blood culture, throat culture, blood fungal culture, acid-fast bacillus blood culture, and urine culture were all negative. Despite antibiotics therapy, patient was febrile up to 38 °C, and in the absence of adequate laboratory as well as radiologically answer, therapy was changed into Meropenem 1 g/12 h and Orvagyl 500 mg/8 h. On third day, patient was afebrile and feeling better. Her CRP was 9.7 ng/ml, white count 11.2 × 10^3/L, platelets 210 × 10^3/L. During the following days, the patient’s condition, and laboratory parameters improved in parallel with the neutrophil count. She received above mentioned therapy for fourteen days after she was discharged in good condition and radiological finding. She was released from the hospital with recommended Propylthioracil 50 mg twice daily. She was regularly checked up by endocrinologist and pulmonologist with no relapse of disease.

Antithyroid drugs, especially thioamides—including propylthioracil, methimazole and carbimazole—have adverse hematological effects, ranging from mild leukopenia to agranulocytosis and aplastic anemia. Agranulocytosis, defined as a marked decrease in the number of granulocytes, frequently <500/µL, is a rare complication. Fever and sore throat are common symptoms of antithyroid drug induced agranulocytosis. Patients with an absolute neutrophil count <100/µL tend to have a greater risk of infectious and fatal complications than do patients with a neutrophil count >100/µL. The mortality rate is greater in patients aged ≥65 years than in those aged <65 years.

The lungs are the most common organ to be infected in febrile neutropenic patients. The chest radiograph is the standard initial investigation to look for pulmonary changes, but its sensitivity has been shown to be very low. High resolution computed tomography (HRCT) chest can detect the abnormality with a high degree of accuracy, as well as differentiate between different types of infections. It is extremely useful in early detection or exclusion of a focus of infection and characterization of the focus. Exact etiological diagnosis is not possible in most of the cases, but identification of broad category of infective causes itself is very important for the appropriate therapy. Previous studies have proven that the most common cause of febrile condition is Pseudomonas aeruginosa. Our case was different from previous described in literature, in its beginning, but similar in good prognosis after granulocyte colony-stimulating factor and empirical antibiotic therapy. However, the recovery time in our cases was slightly longer than in previous cases (14 vs. 6.8 days). Nowadays, more people are undergoing surgical treatment as a permanent solution.

In conclusion, ATD-induced agranulocytosis is rare, but the severity of this possibly life-threatening condition means its management is essential to a good prognosis. Our case suggests that patients with antithyroid drug-induced agranulocytosis who present with severe infections should be treated empirically with broad-spectrum antibiotics with antipseudomonal activity.

Alternative way in patients with hyperthyroidisms is surgery or radioactive iodine which seem to be effective options to restore an euthyroid state. In fact, radioactive iodine was demonstrated as a successful option, with 88.8% of patients experiencing euthyroidism after treatment.

References


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PD-L1 Expression in a Non-Small Cell Lung Cancer Specimen Obtained by EBUS-TBNA

Expresión de PD-L1 en muestras de cáncer pulmonar no microcítico obtenidas por EBUS-TBNA

To the Editor,

Lung cancer is the leading cause of cancer death worldwide among both men and women, accounting for 1.6 million deaths annually. In Chile, it is the second leading cause of death due to cancer. Non-small cell lung cancer (NSCLC) accounts for 85% of lung cancers; unfortunately, up to 80% of cases are diagnosed in advanced stages, requiring systemic therapy. In recent decades, significant advances have been made in the treatment of these patients, with the development of therapies aimed at specific mutations of the tumor cells (targeted therapies) and more recently with immunotherapy.

Among the most widely used immunotherapies are monoclonal antibodies against PD-1 or PD-L1. Their action is based on the ability of some tumors to evade the immune system through the expression of PD-L1, a ligand for a protein called PD-1 (programmed cell death protein 1). When PD-1 and PD-L1 bind, T cell activation is inhibited, thus blocking the normal immune response to tumor

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