INTRODUCTION
Pemphigus vulgaris, also called malignant pemphigus because of the evolution’s severity, is the most serious and most common of autoimmune bullous dermatoses. (1,2,3) In the etiopathogenesis of the disease, the responsibility goes to IgG autoantibodies that act on target antigens, desmoglein 3, desmoglein 1.
Aspergillosis is characterized by an invasion of blood vessels by hyphae, almost always limited to the lung tissue developed in immunosuppressed patients (5), with the occurrence of thrombosis, necrosis and hemorrhagic infarction. Massive inhalation of Aspergillus spores by healthy people may lead to diffuse, self-limited, acute pneumonia. All common species of Aspergillus that cause disease in humans are ubiquitous in the environment, growing on decaying vegetables. Inhalation of Aspergillus spores is extremely common, but aspergillosis is rare. Pulmonary aspergillosis is a possible complication of immunosuppressive therapy and it can cause complications such as allergic bronchopulmonary aspergillosis, chronic necrotizing pulmonary aspergillosis, bronchiectasis, respiratory failure, pulmonary fibrosis in severe cases (15,16,17), pulmonary aspergilloma and invasive aspergillosis. Other manifestations of the aspergillosis are sinusitis, endophthalmitis, encephalitis, Aspergillus endocarditis, abscesses in the myocardium, kidney, liver, spleen, soft tissue and bone. (13,14)

CLINICAL CASE
We report the case of a patient, 40 years old, from a rural area, who has been admitted to our clinic with a recent onset (of 2 months) of vesiculobullous lesions on the chest. The lesions had ulcerated and were covered with yellow-brown adherent crusts with expansion to the posterior thorax, upper limbs and the face. The Nikolsky phenomenon was positive in the periphery of the lesions. In the mouth, on the jugal mucosa, he presented multiple ulcerative lesions with irregular borders (figure no. 1).

Figure no. 1. Post bullous ulceration of the posterior torax

The histopathological exam revealed intraepidermal, intramalpighian bullae, with normal appearance of the dermo-epidermal junction; dermis with pericapillary reduced lymphocytic inflammatory infiltrate (figure no. 2). Direct immunofluorescence examination was positive for IgG, C3 with intraepidermal rete pattern. The corroboration of the clinical, histopathological and immunofluorescence (direct/indirect) established the diagnosis of pemphigus vulgaris.
Chest radiography showed no evidence of pleural and pulmonary changes at the moment of establishing a pemphigus vulgaris diagnosis.

**Figure no. 2. a, b. Intraepidermic bullae**

A systemic immunosuppressive treatment was initiated with corticosteroids (methylprednisolone 1.2 mg / kg) with a decrease of the dose depending on the clinical and biological response. We performed azathioprine therapy (100 mg / day) and administered short courses of antibiotic (Cefuroxime 2 g / day), antifungal (Fluconazole 150 mg / day), accompanied by a complementary therapy of topical drying, antiseptic and epithelising treatment. This led to a favourable evolution of the disease. After 6 weeks of initiating corticosteroid therapy, the patient developed a staphylococcal infection of the left index, left knee and pharyngitis with Enterobacter -for which he followed systemic antibiotic and topical treatment.

Approximately 4 months after the diagnosis had been established and immunosuppressive therapy was initiated, the patient was admitted to the clinic again. He presented weight loss (about 20 kg in 3 months), and a dry cough, accompanied by a stabbing sensation in the left hemitorax. Stetacustic slightly decreased the vesicular murmur in the pulmonary bases.

Relatively quickly afterwards, he developed a productive cough, initially with mucous sputum, then bloody and with a decreased vesicular murmur of the lungs in the left hemitorax, multiple foci of crackles in the apex and bases bilaterally. A chest x-ray revealed discrete inhomogeneous nodular opacities in the right subclavian area, the left parahilar area and the left lung base. Heart with stage I left ventricular hypertrophy, degree I. The costo-diaphragmatic sinuses were free of content (figure no. 3). CT of the chest revealed multiple bilateral pulmonary nodular and macronodular masses, most of them hollow (the largest SRL). The upper lobe of the left lung presented a condensation. Tissue mass with central necrosis lower left lobe. Low pericarditis (figure no. 4).

**Figure no. 3. Inhomogeneous nodular opacities**

**Figure no. 4. Nodular hollow bilateral pulmonary masses**

The appearance of a chest X-Ray, together with pneumology and infectious disease consultations, raised the suspicion of tuberculosis or staphylococcal pneumonia. Pulmonary tuberculosis was excluded for the following reasons: negative intradermal reaction to tuberculin, the sputum exam isolated pneumococci and Aspergillus, with negative cultures for Koch bacillus. Pneumococcal pneumonia was excluded because of the lack of typical radiologic appearance (“crumb” image), emphasizing the lack of Staphylococcus by Gram stain and by culture. Pulmonary aspergillosis was confirmed by isolation in culture of Aspergillus. Based on examination and pneumology advice, we established the following diagnosis: pneumococcal pneumonia and pulmonary aspergillosis.

We agreed on a systemic treatment with antibiotics and antifungals (Fluconazole initially 300 mg / day for a month, then itraconazole 200 mg / day for 3 months). This resulted in a complete remission of the pulmonary symptoms and the recovery of weight deficit. The complications of the long-term glucocorticoid therapy that occurred in our patient were: type II insulinonecessitant diabetes, hypercoagulable syndrome, cortisone myopathy, diffuse osteoporosis with compaction of T10 vertebral body, iatrogenic Cushing syndrome, stage II, hypertension, pyoderma-like lesions, pharyngitis with Enterobacter (figure no. 5,a,b).

**Figure no. 5. a. Postlesional hyperpigmentation; b. Cushingoid face**

**DISCUSSIONS**

Differential diagnosis was made with:

a) Staphylococcal pneumonia, which shows an insidious onset, fever, malaise, cyanosis, dyspnea, chest pain, cough with mucopurulent/ hemoptoic expectoration. The radiologic appearance showed: opaque multiple foci within them showed areas of hypertransparency, “crumb” aspect, with pleural damage. Examination of sputum by Gram stain and culture revealed Staphilococcus (7,8), unlike in our case where pneumococci and Aspergillus were isolated.

b) Primary pulmonary tuberculosis is usually located in the middle and lower lung fields. The lesion is usually peripheric and is associated with hilar or paratracheal lymphadenopathy. In most cases the lesion heals spontaneously and may be evidenced later as a small calcified nodule (lesion of Ghon). An examination of the sputum highlights acid- alcolo-resistant bacilli. The intradermal reaction to tuberculin has limited value in the diagnosis of active tuberculosis, due to its low sensitivity and specificity. False-negative reactions are common in immunosuppressed patients and those with aggressive tuberculosis.(9)

c) Nocardia pneumonia is typically subacute. Immunosuppressed patients may have a more acute onset with cough with small amounts of thick, purulent, odourless sputum. Fever, anorexia, weight loss are common; dyspnea, pleural pain and hemoptyse are less common. Radiographic appearance is variable. Infiltrates vary in size and have generally moderate or high densities. Nodules and formation of cavities are common.(6)
d) Eosinophilic pneumonia belongs to the group of eosinophilic syndrome of intrinsic origin. It is characterized by cough for at least 2 months, sputum eosinophils greater than 3%, and no evidence of airway obstruction. Eosinophils can often be observed in the bronchoalveolar lavage fluid. Radiologically, peripheral alveolar infiltrates, which can be migratory, can be observed and in a quarter of cases the appearance of pulmonary edema.(10,11)

It is known that the treatment of pemphigus vulgaris can lead to complications related to corticosteroids and immunosuppressive therapy.(12)

The treatment of aspergillosis can cause complications secondary to the antifungal therapy.(11)

Evolution of both pemphigus vulgaris and pulmonary aspergillosis is severe in the absence of treatment with exitus, but in the era of corticosteroid and immunosuppressant the pemphigus complications are related to the therapy, more than to the actual disease; pulmonary aspergillosis is evolving favourably with antifungal therapy.(1,2,3,5) Pemphigus vulgaris shows lasting remissions, the permanent cures being questionable; in most cases, pemphigus patients become corticoidependent for life. The healing prognosis for aspergillosis is good in immunocompetent patients.(1,2,3,5)

In medical literature, there exists an example of a case where a patient under polichimioterapic treatment for pemphigus vulgaris developed pulmonary aspergillosis and cerebral abscess and was diagnosed post-mortem.(18) In 1995, a group of Japanese dermatologists have reported the case of a 71-year old patient with pemphigus vulgaris who had been administered a treatment with steroids for seven months. He developed pulmonary invasive aspergillosis during therapy, with rapid progression to death, despite early diagnosis and treatment.(19)

The studies of M.S. Lionakis in 2003 and those of D.P. Kontoyiannis in 2011 on glucocorticoids and invasive fungal infections have shown that in vitro glucocorticoids can increase growth rate for Aspergillus flavus and Aspergillus fumigatus 67. A clinical study on respiratory function in patients with pemphigus vulgar showed that in the patients with pemphigus there was a slight reduction of CO diffusion capacity, with patients often developing respiratory tract infections that could be life-threatening.(20,21)

Medical literature reports more frequent cases of pulmonary nocardiosis secondary to immunosuppressive therapy of pemphigus.(22)

The particularity of our case consisted in the rapid development of a severe form of pulmonary aspergillosis, relatively shortly after the initiation of the immunosuppressive treatment (after 4 months), followed by infectious complications (pharyngitis with Enterobacter, staphilococcal infections) due to the high dose of corticosteroid therapy and secondary immunosuppression. This demonstrated the increased susceptibility to infection of the patient, who also developed other complications after the systemic corticosteroid therapy. Establishing a prompt diagnosis of pulmonary aspergillosis and setting a specific therapy has led to the healing of the patient’s lung infection, with a good performance and successful control of the bullous disease.

REFERENCES

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