PARANEOPLASTIC PEMPHIGUS CASE REPORT

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Abstract: *Paraneoplastic pemphigus is a rare autoimmune bullous dermatosis. It occurs more frequently around the age of 60 and is most commonly associated with lymphomas and leukaemia. This particular form of pemphigus has issues that are clinically, histopathologically and immunopathologically distinct from other forms of pemphigus. Severe mucosal erosions and a polymorph rash are the clinical manifestations. We report a case of paraneoplastic pemphigus diagnosed in the Clinical Hospital of Sibiu which allowed us to present a literature update of this subject.*

Keywords: *pemphigus, chronic lymphocytic leukaemia, paraneoplastic*

Rezumat: *Pemfigusul paraneoplazic este o dermatoză buloasă autoimună rar întâlnită. Apare mai frecvent în jurul vârstei de 60 de ani şi se asociază cel mai frecvent cu limfoame şi leucemii. Această formă particulară de pemfigus are aspecte clinice, histopatologice şi imunopatologice distincte de alte forme de pemfigus. Clinic se manifestă prin eroziuni severe ale mucoaselor şi o erupţie cutanată polimorfă. Pe marginea unui caz de pemfigus paraneoplazic diagnosticat în Clinica de Dermatologie Sibiu vom prezenta o actualizare a informaţilor existente în literatura de specialitate pe această temă.*

Cuvinte cheie: *pemfigus, leucemie limfocitară cronică, paraneoplazic*

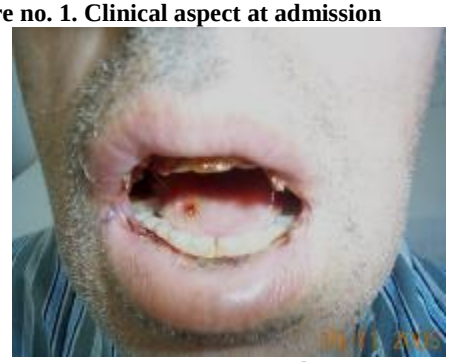
INTRODUCTION

We report a case of a 60 year old, male patient hospitalized in the Dermatology Department of the Clinical Hospital of Sibiu for the occurrence of the multiple erosions in the oral cavity. The ulcerations were infected and covered with haematic crusts and pseudomembranous deposits. These lesions were very painful with the limitation of feeding (picture no. 1).

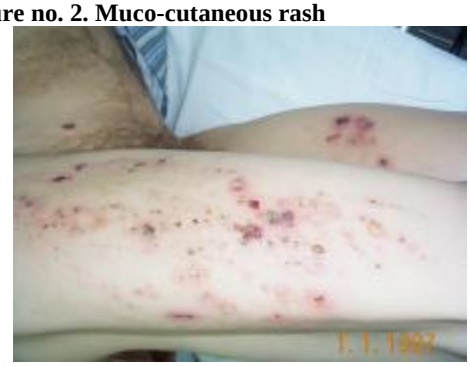
In the area of booth thighs and in the thorax area the patient presented a polymorphic rash (consisting of blisters and erosions covered by crusts) (picture no. 2).

The skin lesions were associated with massive and painful right underjaw lymph nodes (picture no. 3), purulent conjunctivitis (picture no. 4), asthenia, feeding problems and significant weight loss (5 kg / last month).

Picture no. 1. Clinical aspect at admission

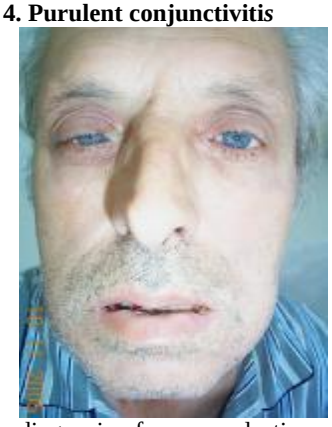


Picture no. 2. Muco-cutaneous rash



Picture no. 3. Massive and painful right

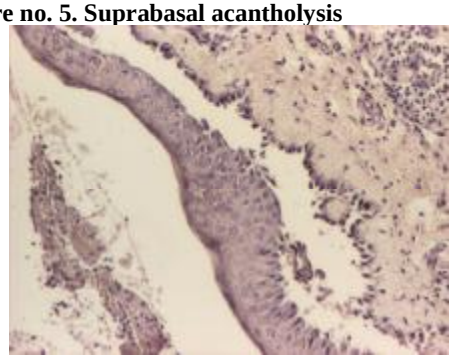
Picture no. 4. Purulent conjunctivitis



The diagnosis of paraneoplastic pemphigus was established by:

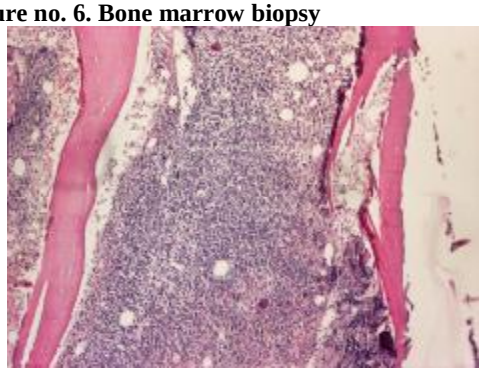
- The clinical aspect (oral erosions, polymorph cutaneous rash with blisters and erosions covered with crusts, Nicolsky sign - positive)
- The laboratory investigations: leucocytosis (L 114300-58800-53200/mm3) with lymphocytosis (LF = 80,6-83,5-84,4%)
- The Tzanck examination showed acantholytic cells
- Skin biopsy (intraepidermic acantholysis and chronic inflammatory infiltrate, mostly composed by lymphocytes) (picture no. 5).

Picture no. 5. Suprabasal acantholysis



- The bone marrow biopsy showed a bone marrow infiltration and a focal nodular process. This aspect was suggestive for chronic lymphocytic leukemia (picture no. 6).

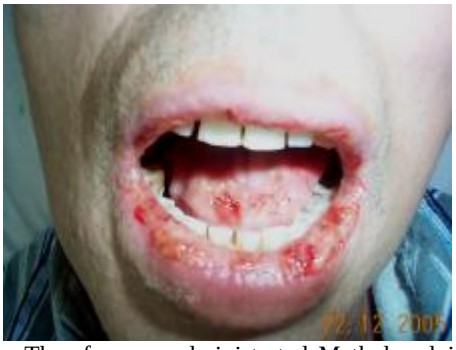
Picture no. 6. Bone marrow biopsy



The autoimmune process was controlled with corticotherapy (initially with 500 mg / day of intravenous Methylprednisolone followed by oral administration with a gradual decrease of the doses (4 mg / week).

At home the patient discontinued the treatment with a relapse of the muco-cutaneous lesions (fig. 7).

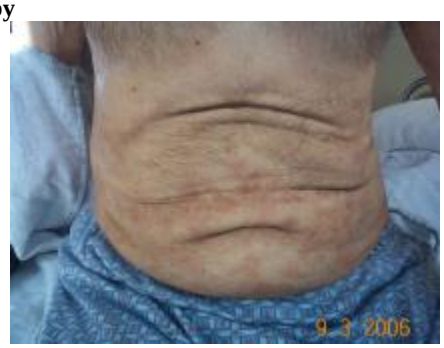
Picture no. 7. Multiple oral erosions after stopping the treatment

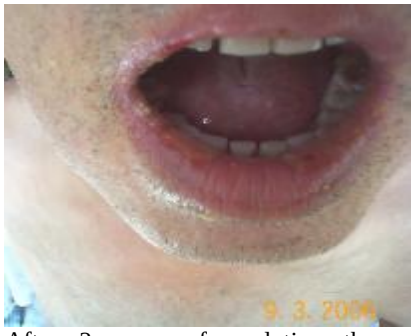


Therefore we administrated Methylprednisolone 1mg/kg in combination with 50mg / day of Cyclophosphamide. This treatment allowed us to obtain a good control of the muco-cutaneous lesions and a stabilization of leukaemia (leucocytes 10500/mm3 with lymphocytes 5100/mm3).

For the next 2 years from diagnosis the patient has shown recurrence of the muco-cutaneous lesions due to changeable treatment, but resolved with reinstating the corticoid therapy associated with Cyclophosphamide (picture 8 a, b).

Picture no. 8 a, b. Clinical aspect after reinstating the therapy

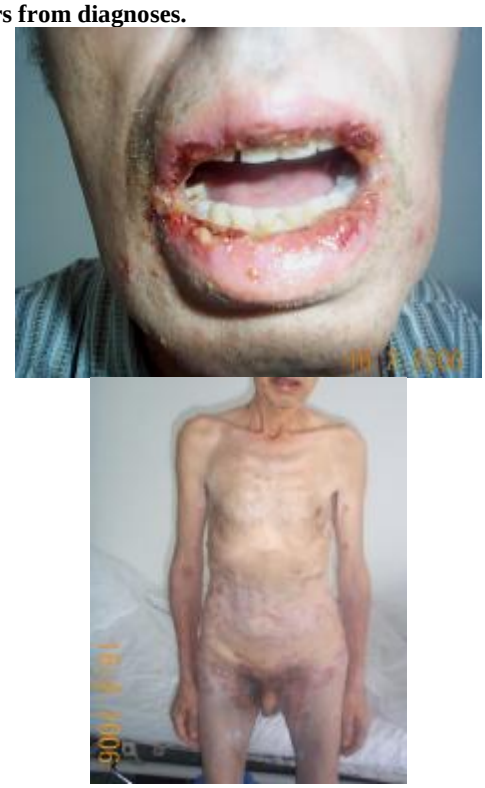




After 2 years of evolution the patient is hospitalized for a severe muco-cutaneous rash and

multiple blisters, with extensive oral erosions and emaciation (fig. 9).

Picture no. 9. Severe recurrence of the lesions after 2 years from diagnoses.



Enhancing lesions has been more difficult than the previous admission. A few months after the last admission the patient died.

DISCUSSIONS

Paraneoplastic pemphigus is an autoimmune disease characterized by the formation of antibodies against self epithelial antigens. It is a particular form of pemphigus which was first described by Anhalt in 1990. The initiation of the autoimmune process is most often due to lymphoproliferative neoplasias, the tumor antigens being able to trigger humoral and cellular immune responses. The immunoglobuline G type antibodies are directed against protein structures from the desmosomes. After the antigen-antibodies interaction, the desmosomes break, filaments of the cells retract and intercellular ties disappear with the occurrence of acantholysis.(5) Some authors consider that the autoimmune process is maintained by the excess production of cytokines, in particular interleukin 6.

Paraneoplastic pemphigus is a severe disease that often occurs after 60 years of age, with a slight predominance in women and with a high mortality (around 90%) due to associated neoplasia.

The diagnosis criteria in paraneoplastic pemphigus are:

- Severe and painful mucosal erosions associated with a cutaneous polymorph rash
- Histopathological changes are acantholysis, necrosis of keratinocyte, dermatitis of interface(8)
- Direct immunofluorescence shows a network of fluorescent intercells Ig G and C3 and linear or granular deposits of Ig G in the dermo-epidermic junction
- Indirect immunofluorescence reveals the presence of these specific antibodies (6)
- Immunoprecipitation and immunoblotting: highlights target antigens - desmoplakina I (250 kd), desmoplakina II (210 kd), bullous pemphigoid antigen (230 kd), envoplakina, periplakina (190Kd) plectina (500 kd) and an unidentified protein of 170 kd (1, 2, 10).
- Existence of neoplasia(3).

The polymorph aspect of the rash requires the knowledge of these criteria in order to exclude other bullous diseases (pemphigus vulgaris, polymorph erythema, epidermolysis bullosa, bullous pemphigoid, bullous drug eruptions, Stevens-Johnson syndrome, Lyell syndrome) and an early and accurate diagnosis of patients with this condition.

Paraneoplastic pemphigus is most often associated with non-Hodgkin lymphoma, chronic lymphocyte leukemia, Castleman disease, tymoma, sarcomas, Waldenstrom macroglobulinemia (4,7,9,11). Other rarely encountered malignancies are pancreatic adenocarcinoma, colon carcinoma, breast cancer, prostate and liver carcinoma.

In 1/3 of the cases the neoplasia is highlighted by the occurrence of the skin lesions. The neoplasia treatment associated with the immunosuppressive treatment reduces or stops the autoimmune process and allows a better control of both diseases.

In literature the association of pemphigus and chronic lymphocyte leukaemia is frequently encountered (18-29% of the cases) and it is an unfavorable prognosis factor. In this form of pemphigus the mucosal lesions are constantly present, dallying and painful. Because of the extensive erosions and the immunosuppressed status induced by neoplasia, the most frequent complication of paraneoplastic pemphigus is skin infection with possible sepsis.

Paraneoplastic pemphigus therapy can be done with coticoids or immunosuppressive agents in monotherapy or associated therapy. Other therapeutic options are plasmapheresis and human immunoglobulins IV but their utility is limited by the high costs and by the necessity of further studies. Supportive therapy and neoplasia therapy is necessary.

In our case the diagnosis of pemphigus leads us to chronic lymphocyte leukaemia. The associated therapy corticoids - cyclophosphamide allowed us to stop the autoimmune process with 2 years survival (mortality after 1 year is about 75%).

CONCLUSIONS

- Paraneoplastic pemphigus is a rare and particular form of pemphigus.

- Neoplasias most frequently associated with paraneoplastic pemphigus are lymphomas and leukaemia.
- Combined therapy corticoids – immunosuppressive agent's leads to a better control of the disease.
- Paraneoplastic pemphigus remains a severe disease with a high mortality caused by the disease itself, by the associated neoplasia and by the side effects of the long therapy.

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