

## PATIENTS WITH ASSOCIATED ENT PATHOLOGY IN AUTOIMMUNE CUTANEOUS DISEASE - CLINICAL STUDY

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**SUMMARY: Introduction:** Because of the complex pathology found in autoimmune diseases and big scale of diseases placed in this category, we tried to cast down our attention in the study, regarding pathology from the Oto-Rhino-Laryngology sphere.

**Premises and goals:** We proposed ourselves to analyze the information resulted from the study, from the point of view of the ENT symptomatology's prevalence. Those symptoms may appear constantly in the clinical picture of the cutaneous autoimmune diseases or very rare.

**Material and methods:** The study group was made out of in-patients in the ENT, Dermato-Venerology and Nephrology University Clinics between October 2006 – July 2009. **Results:** From the autoimmune pathological entities, the study group was portioned in the following way: Pemfigus vulgar – 14 cases, Systemic lupus erythematosus – 8 cases, Scleroderma – 3 cases, Conjunctive tissue mixed disease – 3 cases, Dermatomiozistis– 3 cases, Behchet disease – 2 cases, Bullous Pemphigoid – 1 case, Sjögren syndrome – 1 case, Wegener granulomatosis– 1 case, Henoch-Schölein purpura – 1 case. A high prevalence has been noticed of the fungi and microbial infections, respectively 10 determinations of oral candida and 9 of Nasal Staphylococcus.

**Conclusions:** It can be observed the frequency of opportunistic microbial and fungal infections on the host's dropping immunity system. The lack of a distinct anatomical barrier between the superior respiratory ducts segments, allows the propagation of the infection through continuity. As result we have noticed the inter penetration of the clinical symptoms and frequent complications, by damaging the middle ear, the mouth pocket and larynx.

**Key Words:** autoimmune diseases, ENT.

### STUDIU ASUPRA UNUI GRUP DE PACIENȚI CARE PREZINTĂ DETERMINĂRI DIN SFERA O.R.L. ÎN BOLILE CUTANATE AUTOIMUNE

**Rezumat: Introducere:** Datorită patologiei complexe prezente în cadrul bolilor cutanate autoimune și a numărului mare de boli ce fac parte din această categorie, am încercat să ne aplecăm în studiul nostru, asupra patologiei din sfera Oto-Rino-Laringologiei.

**Premise și obiective:** Ne-am propus să analizăm datele rezultate din studiu, din punct de vedere al prevalenței simptomatologiei O.R.L. din cadrul tabloului clinic al bolilor cutanate autoimune, precum și simptomatologia O.R.L. asociată în mod excepțional.

**Cazuistică și metodă:** Grupul de studiu a fost format din pacienți internați în Clinicile Universitare de O.R.L., Dermato-Venerologie și Nefrologie, în perioada octombrie 2006 – iulie 2009. **Rezultate:** Din punct de vedere al entităților patologice autoimune, grupul a fost împărțit astfel: Pemfigus vulgar - 14 cazuri, Lupus eritematos sistemic - 8 cazuri, Sclerodermie - 3 cazuri, Boală mixtă de țesut conjunctiv - 3 cazuri, Dermatomiozită - 3 cazuri, Boală Behchet - 2 cazuri, Pemfigoid bulos - 1 caz, Sindrom Sjögren - 1 caz, Granulomatoză Wegener - 1 caz, Purpură Henoch-Schönlein - 1 caz. S-a constatat o prevalență mărită a infecțiilor fungice și microbiene, respectiv 10 determinări de candidoză orală și 9 de stafilococie nazală.

**Concluzii:** Se observă frecvența prezenței a infecțiilor oportuniste microbiene și fungice pe fondul scăderii imunității gazdei. Lipsa barierelor anatomice distincte între segmentele căilor respiratorii superioare, permite propagarea infecției prin continuitate, având drept urmare întrepătrunderea simptomatologiei clinice și frecvente complicații prin afectarea urechii medii, a cavității bucale și a laringelui.

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## INTRODUCTION

Immunology is one of the most dynamic biological sciences. The immunitary function is essential for the human and animal body; therefore the severe immunitary dysfunctions are incompatible with survival. Then again the inadequate activation of the immunitary function brings as a consequence the initiation or progression of the pathological conditions of hypersensitiveness and autoimmune diseases, amplifying the interest for Immunology studies.

Developing knowledge in fundamental immunology for the past 20 years has been associated with new aspects regarding pathogenetic mechanisms resulting from immune implication diseases, especially the autoimmune diseases.

Natural anti – body are Ig's, secreted by a special B cells set meaning CD5 attaching themselves with low affinity to the antigens found on various bacteria. They activate the complement and their physiological role is to remove rapidly the bacteria from the region of infection. The natural anti-body reacts in a crossed way with A and B erythrocyte antigens. They can tight themselves to a series of normal cells components (e.g. nucleus proteins), explaining why some of the normal appearing subjects have anti-nuclear antibodies. Auto antibodies can be divided in two categories:

- With organ or tissue specificity, where the antigen target is limited to an organ (e.g. thyroid gland );
- Without organ - specificity where the antigen presents a large distribution confronted by nucleus structures or cells cytoplasm.

Specific organ antibodies are frequently being manifested in autoimmune diseases affecting one or more organs.

Nonspecific organ antibodies, antinuclear and anti – cytoplasmatic are being described in certain systemic rheumatic diseases, called collagenases for which they are considered as disease markers (systemic lupus eritemateous, rheumatoid poliarthritis, conjunctive tissue mixed disease, Sjögren syndrome, scleroderma, polimiozitis/ dermatomiozitis). Auto antibodies anti-Sm is found exclusively in patients with LES. Auto antibodies associated with scleroderma and overlap scleroderma syndromes, are being often produced against the nucleoli components. Nevertheless nonspecific organ antibodies can be associated with a single organ injury (e.g. primitive billiary cirrhosis, whit the targeted antigen mitochondria, largely distributed though the disease is exclusively limited to the liver). Antinuclear anti bodies

and anti-muscles sleek (low titre) have been present in patients with chronic B and C viral hepatitis.

In LES has been identified various auto antibodies, important for the diagnosis and fiziopathology elucidation, because some of them participate in building the mobile or fixed tissue immune complexes, even though it isn't clear which one is pathogenic. Presently, it is known, that auto antibodies can, in certain circumstances, penetrate the intact cellular membrane. These auto antibodies can attach the complement, mediate citotoxicity complement - dependent. Anti-endothelial cell antibodies correlate with the disease activity in: Wegener's Granulomatosis, Behchet disease, LES, rheumatoid poliarthritis and vasculities.

Anti-DNA antibodies can contribute to lupus nephritis apparition because of the crossed reactivity with the renal antigen. Immune thrombocytopenic purpura is an autoimmune disease, where auto platlets auto-antibodies are attaching the antigens found on the platlets surface and megacariocytes. This leads to platlets production diminution either by interfering with proliferation/maturation of the megacariocyte, or by destroying the intramedullar plaquettes.

In the last years the study of the auto-antibodies and auto-antigens, autoimmune diseases and phenomenon, in connection with autoimmunity, attracts more and more researches. Numerous techniques (immuno-chemistry, molecular biology) are used for detecting the auto-antibodies. These can be ELISA, immunodot, Western-blot, which are being made with purified or recombinated antigens, or with peptide synthesis. Still, it is very important, that, in the autoimmune serology, the study of the new auto-antibodies with new technologies and the new reagents to be continuously correlated with clinical manifestation.

Because of the complex pathology found in autoimmune diseases and big scale of diseases placed in this category, we tried to focus our attention in the study, regarding pathology from the Oto-Rhino-Laryngology sphere.

We included in the auto-immune cutaneous diseases the dermatoses and autoimmune bubbly disease like vasculopathies with autoimmune pathogeny.

## PREMISES AND GOALS

We proposed ourselves to analyze the information resulted from the study, from the point of view of the ENT simptomatology's prevalence. Those symptoms may

appear constantly in the clinical picture of the cutaneous autoimmune diseases, or very rare.

## MATERIAL AND METHODS

The study group was made out of in-patients of University Clinics ENT and Dermato-Venerology, at the Municipal Emergency Hospital Timișoara, as well as in the Clinic of Nephrology from the Emergency County Hospital Timișoara, between October 2006 - July 2009.

The criteria of the study that includes 37 patients were:

- Typical ENT damage at patients with cutaneous autoimmune disease;
- The presence of ENT damage which do not have a connection with the background disease;
- The appearance of ENT damage in the context of autoimmune disease complications or after a therapy.

We also tried to keep the equal representation principle between distinct types of patients, accounting for the gender, age, social environment and disease.

Finally we've analyzed the patients group concerning the presence of ENT simptomatology.

Clinical exam, Tzanck citodiagnosis, histopathological exam and the direct and indirect immunofluorescence, have been the basic investigation for a positive diagnosis.

In order to identify the pathogen agents, we used the following paraclinical investigations:

1. Pharyngeal exudates culture which confirmed us the presence of:

- a. Hemolytic  $\beta$  streptococcus;
- b. Staphylococcus aureus in association only with the Hemolytic  $\beta$  streptococcus;
- c. Arcanobacterium haemolyticum;
- d. Candida spp.

2. Culture of the nasal secretion that can confirm the presence of:

- a. Staphylococcus aureus – part, with local treatment recommendation depending on the clinical and epidemiological context;
- b. Haemophilus influenza, Streptococcus pneumoniae, Neisseria meningitides, depending on the patient's age;

3. Auricular secretion culture:

- a. When external otitis occurs, the microscopy is holding back because of the numerous contaminants in this area. The existence on the smear, of an inflammatory reaction with germs presence, especially intraleucocitary ones, guiding the microbiologist towards the pathogen germ incriminated in the affection;

b. Internal otitis where the pathological product was gathered through tympanocentesis is usually, monobacterial and the identification for the antibiogram are much easier;

c. The necessity of isolating in pure culture, followed by the identification at a species level and making the antibiogram, is imposed by the growth, recently, of the microbial agents number that produce beta-lactamase.

4. Fungi identification and culture that confirms the presence of:

- a. Candida spp., Saccharomyces at the superior respiratory tract level;
- b. At the gastro - intestinal tract level concerning the immunodeprimated patients: Candida spp., Aspergillus spp., Zygomycetes;
- c. Aspergillus spp., at the ear level;
- d. Aspergillus spp., Fusarium at the nasal sinus level.

5. Microscopic exam of the pharyngeal exudates for fusospiril can confirm the presence of :

- a. Fusiformis bacillus (fusiformis fusiformis – bacillus Gram negative) and spirochetes (Borrelia vincentii) at the pharyngeal level.

From the socioeconomical point of view, the 37 patients group, involved:

- 27 women and 10 men (73% and 27%);
- 13 patients from the country side and 24 from the urban environment;
- 17 patients with ages between 20-39 years, 13 with ages between 40-59 years and 7 over 60 years (46%, 35% and 19%).

From the autoimmune pathological entities point of view, the group was split in the following way:

1. Pemfigus vulgar (PV) – 14 cases;
2. Systemic lupus erythematosus (LES) – 8 cases;
3. Scleroderma (SD) – 3 cases;
4. Conjunctive tissue mixed disease (BMT) – 3 cases;
5. Dermatomiozistis (DM) – 3 cases;
6. Behchet disease (BB) – 2 cases;
7. Bullous Pemphigoid (BP) – 1 case;
8. Sjögren syndrome (SSj) – 1 case;
9. Wegener granulomatosis (WG) – 1 case;
10. Henoch-Schölein purpura (HSP) – 1 case.

The study group was then divided regarding the laboratory and paraclinical investigations and the principal diagnosis (autoimmune disease), secondary presence or the lack of ENT symptoms from the main diagnostics found through ENT specialty consultations, disease: table 1.

**Table 1**

Principal Dg.	I. Secondary O.R.L. diagnosis	II. Secondary O.R.L. diagnosis -2	Typical symptoms in the main disease
BB	-	-	Oropharingian ulcerations
BB	-	-	Oropharingian ulcerations
BMTC	Bilateral neurosensorial deafness		None
BMTC	Chronic maxillary sinusitis	Acute rhinitis	None
BMTC	Oral candida	Acute eritametos angina	Dysphagia
DM	Nasal Staphylococcus	Oral candida	None
DM	Oral candida	-	None
DM	Bilateral chronic parotids	-	Dysphonia and dysphagia
HSP	Hypertrophic chronic angina	Nasal septal perforation	Gastrointestinal symptoms
LES	Nasal staphylococcus	-	None
LES	Acute rhino-pharingo-laryngeal catarrh	Left maxillary mucocel	Bleeding bubbles, erosions, buccal ulcerations
LES	Hypertrophic chronic angina	-	Bleeding bubbles, erosions, buccal ulcerations
LES	Chronic maxillary sinusitis	-	None
LES	Oral candida	-	None
LES	Nasal staphylococcus	-	None
LES	Nasal staphylococcus	-	Bleeding bubbles, erosions, buccal ulcerations
LES	Oral candida	-	None
PB	Oral candida	-	Bleeding bubbles, erosions, buccal ulcerations
PV	-	-	Bladder, bleeding bubbles, erosions, buccal ulcerations
PV	Nasal staphylococcus	Oral candida	Bladder, bleeding bubbles, erosions, buccal ulcerations
PV	Oral candida	-	Bladder, bleeding bubbles, erosions, buccal ulcerations
PV	Hypertrophic chronic angina	-	Bladder, bleeding bubbles, erosions, buccal ulcerations
PV	Oral candida	Bilateral fibros adhesive otitis	Bladder, bleeding bubbles, erosions, buccal ulcerations
PV	Oral candida	-	Bladder, bleeding bubbles, erosions, buccal ulcerations
PV	Nasal staphylococcus	-	Bladder, bleeding bubbles, erosions, buccal ulcerations
PV	Nasal staphylococcus	Chronic rhinitis	Bladder, bleeding bubbles, erosions, buccal ulcerations
PV	Nasal staphylococcus	Bilateral cerumen plug	Bladder, bleeding bubbles, erosions, buccal ulcerations
PV	-	-	Bladder, bleeding bubbles, erosions, buccal ulcerations
PV	-	-	Bladder, bleeding bubbles, erosions, buccal ulcerations
PV	-	-	Bladder, bleeding bubbles, erosions, buccal ulcerations

**Table1** (continued)

PV	-	-	Bladder, bleeding bubbles, erosions, buccal ulcerations
PV	-	-	Bladder, bleeding bubbles, erosions, buccal ulcerations
SD	Bilateral neurosensorial deafness	-	Eating difficulty, dysphagia
SD	Allergic rhinopharyngitis	-	None
SD	Nasal staphylococcus		none
SSJ	Nasal staphylococcus	-	Xerostomy
WG	subglottic tracheal stenosis	tracheotomy	Hemorrhagic rinorea, nasal mucosal ulcerations, sinusitis, deafness

## DISCUSSIONS

1. It can be observed the frequent presence of opportunistic microbial and fungal infections on the host's dropping immunity system.
2. The lack of the distinct anatomical barrier between the superior respiratory ducts segments, allows the propagation of the infection through continuity; as a result we have noticed the inter penetration of the clinical symptoms and frequent complications, by damaging the middle ear, the mouth pocket and larynx.
3. Pharyngitis, the acute inflammation of the pharynx, has usually viral origins, but it can be the result of group "A" beta - hemolytic streptococcus, *Mycoplasma pneumonia*, *Chlamydia pneumonia* or other bacteria. Differencing the viral pharyngitis from those bacterial ones, only with the clinical exam is very difficult. In both cases, the pharyngeal mucosa may have a slight congestion or be severely inflamed and could be covered by a membrane and by the exudates, together with swallowing pain. Fever, cervical adenopathy and leukocytosis are present as much as in the viral pharyngitis as well as in the streptococcus one, being more obvious in the second one.
4. Tonsillitis, the acute inflammation of the palatine tonsils, usually caused by the streptococcus infection, rarely because of a viral infection, is clinically characterized by pain at swallowing which goes to the ears. High fever, alteration of the general state, headache and vomiting are frequent. The tonsils have edema and arhyperemic. There could be an purulent exudates present at the crypts level and a white, thin, non-confluent membrane, limited at the tonsils level, which is removed without bleeding. Angina Vincent, characterized by superficial and painful ulcer, with eritematous edges, is produced by a spindle – shaped bacillus and a spirochaete, which can be seen on the smear.
5. Rhinitis is often caused by viruses (rhinoviruses, adenoviruses, flu viruses, Coxsackie A) and rarely by bacteria. Microbiological examination of the nasal and pharyngeal exudates is indicated for screening pathogenic germs in the superior respiratory duct (it is solicited and indicated in epidemiological purpose – e.g. establishing the infection source, quarantining the healthy carriers, workers from the food industry).
6. An important role in the appearance of the otitis, has the rhinopharynx. The congestion and the edema of Eustachio's oviduct, that blocks the normal cavity drainage and the elimination of the occasional and local contamination determine the inflammation. Tonsillitis and pharyngitis can determine the appearance of the middle otitis by spreading inflammation and infection. Adenoidal vegetation determines the appearance of the otitis by mechanical path – through their volume, as well as by the inflammatory path, through the infections they maintain.
7. More than a half of the patients studied, (26) presented the basic symptomatology.
8. Only 8 patients did not present other signs of ENT. sphere, besides those already present in the basic disease context.
9. The highlight was the particularity of the Wegener case, representing a medical challenge, especially because although the female patient was young she didn't positively react to the systemic and local applied treatment.

## CONCLUSIONS

1. Most of the cutaneous autoimmune diseases have ENT. sphere determinations.
2. The diagnosis of autoimmune diseases can be established with delay because of these symptoms leading at a long period of a false diagnostic.
3. Treating ENT. manifestations in these autoimmune diseases is important, but their outcome necessitates the autoimmune disease diagnosis and its treatment.
4. Fast diagnose of these diseases avoids complications and deteriorations that could lead to big social implications, work incapacity days even to young subjects (the patient that had the Wegener had to be maintained for a long time and could be healed only with autoimmune disease treatment).
5. Late diagnosis can lead to deterioration of major organs (kidney, lungs), leading to major problems and exitus.

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