The study of synovities with articular inflammatory liquid, through clinical-statistical, histological and immunohistochemical methods

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Abstract
Introduction: The examination of the synovial is very useful in the positive and differential diagnostic of many articular diseases and especially in the conditions of acute monoarthritis. Materials and Methods: The study focused on the establishment of clinical-statistical, histopathological and immunohistochemical correlations on a group of cases anatomo-pathologic diagnosed with synovity with articular inflammatory liquid. The group was divided in five subgroups: rheumatoid polyarthritis, uric arthropathy (gout), TBC arthritis, sarcoidosis and villo-nodular synovity. Results and Discussion: During the clinical-statistical study the number of arthritis with articular inflammatory infiltration was pursued, the specific location of them and the correlation of the clinical dates with paraclinical ones. In the histopathological and immunohistochemical analysis was pursued the presence of the inflammatory infiltration through the implication of both types of B- and T-lymphocytes in different proportions taking into consideration the cause of the synovity. Conclusions: The synovial biopsy is indicated at patients at whom the diagnostic is not established after the clinical evaluation. The examination of the synovial tissue can be the only way of establishing a definitive diagnostic in inflammatory arthropathies.

Keywords: synovities, lymphocytes, synovial biopsy.

Introduction
The synovial membrane covers all intra-articular structures excepting the articular cartilage and it is responsible of the molding of the synovial liquid.

The synovial membrane is a particular serous, responsible for the production of the synovial liquid and represents a characteristic structure of the diarthrosis. It is rich innerved and has the structure of a membrane made up of two layers [1]: the lining layer that limits the articular cavity; the subsynovial layer made up of lax conjunctive tissue is rich in sanguine vessels and lymphatic vessels, poor in cells(macrophages, fibroblasts) that explains the extreme reactivity at inflammation of the synovial [2].

The lining layer is made up of synoviocytes and synovioiblasts ordered in mono or bi cell layers compact but discontinuous [3, 4].

The synoviocytes are not layered on basal membrane existing o continuity between the intercellular spaces of the conjunctive tissue and the articular cavity.

The synovial membrane has a rich vascularization with the formation of a dense capillary network with anses that reach the free surface of the synovial.

These elements (the lack of the basal membrane and the vascularization type) have the aim to encourage the filtration of the plasma that after the elaboration of synoviocytes of the hyaluronic acid, proteoglycans it will make up the synovia, which is responsible for the cartilage’s nutrition and the lubrication of the articulation.

The basic functions of the synovial membrane are:
• macrophage capacity of relief of the articular cavity;
• the filtration of the serum for the partial formation of the synovial fluid;
• the secretion of some elements of the matrix and of the synovial liquid;
• the immunological reactivity of the cellular components.

In the articular pathology, the examination of the synovial liquid can be the only way of making a final diagnostic. The synovial biopsy is indicated at patients at whom the diagnostic is not established after the clinical examination.

Rheumatoid arthritis is the most frequent of human systemic autoimmune diseases. It is characterized by the formation, in synovial membranes, of an inflammatory
and invasive tissue, the rheumatoid pannus, capable of eroding adjacent cartilage and bone, subsequently leading to joint destruction. Both cellular and humoral autoimmune mechanisms have been implicated in the still poorly understood initiating and perpetuating events of RA pathogenesis. Reflecting the humoral autoimmune processes occurring during RA is the presence of auto-antibodies of diverse specificities in the serum of patients. The initial change in the joints is an inflammatory reaction in the synovial tissues, with hyperemia and an accumulation of inflammatory cells [5]. Most the cells are lymphocytes and plasma cells, but also neutrophils and macrophages are found [6]. Investigation by electron microscopy and immunofluorescence has shown that both type B-lymphocytes and type T-lymphocytes participate in the rheumatoid synovial reaction [7, 8].

Gout is a disorder of purine metabolism in which sodium urate is deposited in a variety of tissues, and particularly in the tissues of the joints. About 90% of affected individuals are men. The symptoms of gout usually develop after middle age. The joint lesions of gout are usually slowly progressive [6]. The tophus is the pathognomonic lesion of gout—a mass of urates, crystalline or amorphous, surrounded by an intense inflammatory reaction, composed of macrophages, lymphocytes, fibroblasts and foreign body giant cells [9].

Tuberculous arthritis may originate in synovial membrane [10] or it may be consequent on an adjacent focus of tuberculous osteomyelitis. In either case, the disease is usually secondary to a primary focus in the lungs [11, 12]. The knees are the joints most commonly affected by tuberculosis.

During our study 19 cases of synovitis were diagnosed with articular inflammation process from these cases four cases were rheumatoid polyarthritis, four cases were urate arthropathy, six cases of villonodular synovitis and one case of sarcoidosis.

Materials and Methods

We achieved a descriptive study on a period of three years (2007–2010) following up the cases of synovitis with an inflammatory source diagnosed in the Pathology Anatomy Laboratory of the Oradea County Hospital. In the study were included cases of macroscopy confirmed histological and that have an articular inflammatory process as source.

As in the specialty literature, as well in our cases the beginning location is at the synovial of the knee with hypertrophy and articular source. The lesions primary or secondary evolve rapidly with the destruction of the articular cartilage leading to characteristic aspects of the disease. Being a superficial articulation the diagnostic is easy and can be set even in the beginning stage of the disease. The knee is hypertrophied through articular source the muscle hypertrophy accompanies this signs. The synovial biopsy establishes the tuberculosis diagnostic.

The tuberculous tibio-tarsian osteoarthritis and medio-tarsian osteoarthritis is rare (4% of the tuberculous osteoarthritis), but in our study it reached 50% from the cases diagnosed with TBC arthritis.

The immunohistochemical markers used in this study are the antibodies of the T- and B-cellular lines, which recognize antigen expressed mainly by the T- and B-cells. Because they have different specifications, their usage is vital in association.

CD20 antigen is a membrane antigen. It marks especially the B cells and the cells of the germination centers and the cells of the mantel zone. It does not mark the histiocytes or the plasmocytes.

It does not present crossed reactivity with the nonhematopoetic tumors. It is useful together with the LCA for the distinction of the lymphomas from the nonlymphomas tumors. Moreover, some lymphomas that are not marked with LCA (or are marked very little) are marked very well with CD 20.

CD45RO antigen recognizes a LCA alternative limited at the T-cells. It marks the T-cells, the granulocytes and some histiocytes. A cytoplasm mark can often be observed at different types of tissue. There are marked approximately 70% of the lymphomas with T-cells.

Results

At all these patients a synovial biopsy was realized, and the biological material taken was analyzed and studied immunohistochemical and histopathological. The studied cases were divided in five subgroups, taking into consideration the source of the synovitis (Table 1, Figure 1).

Table 1 – The repartition of the cases taking into consideration the source of the synovitis

<table>
<thead>
<tr>
<th>Synovitis</th>
<th>No. of cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuberculous osteoarthritis</td>
<td>4</td>
<td>21.05</td>
</tr>
<tr>
<td>Rheumatoid polyarthritis</td>
<td>4</td>
<td>21.05</td>
</tr>
<tr>
<td>Uric arthropathy</td>
<td>4</td>
<td>21.05</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>1</td>
<td>5.26</td>
</tr>
<tr>
<td>Villonodular synovities</td>
<td>6</td>
<td>31.57</td>
</tr>
<tr>
<td>Total</td>
<td>19</td>
<td>100</td>
</tr>
</tbody>
</table>

From the 19 cases studied, 12 cases (63.15%) are men and seven cases (36.84%) are women (Table 2).

Table 2 – The repartition of the studied cases taking into consideration the sex

<table>
<thead>
<tr>
<th>Gender</th>
<th>No. of cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>12</td>
<td>63.15</td>
</tr>
<tr>
<td>Female</td>
<td>7</td>
<td>36.84</td>
</tr>
<tr>
<td>Total</td>
<td>19</td>
<td>100</td>
</tr>
</tbody>
</table>

From the total of the 19 inflammatory synovities, four cases were uric arthropathy. All these cases were at men patients. The location of the uric arthropathy is at the level of the foot in three cases and in one case at the level of the knee (Figures 2–4).

During our study, at patients diagnosed with rheumatoid polyarthritis, as well as in the specialty literature, the majority affected are women with a ratio women/men of 3/1 (Figure 5).

Concerning the age, we can tell that after the age of 20 years, the number of cases increases until the age of 60 years and after this age, it decreases. As well as in our study from the four cases studied two cases belong
to the decade of age 51–60 years, one case belongs to
the decade of age 31–40 years, and one case belongs to
the decade of age of 71–80 years.

In our study too, at patients diagnosed with
rheumatoid polyarthritis, the affectation was mono-
articular at the level of the knee, in the specialty
literature are quoted under 5% of cases with mono-
articular beginning (Figure 6).

Figure 1 – Chronic synovity with inflammatory source
and follicular disposal and dilated (HE stain, ob. ×10).

Figure 2 – Chronic synovity with inflammatory
lympho-plasmocytary infiltration with follicular
disposal (HE stain, ob. ×40).

Figure 3 – Chronic synovity at a 46-year-old man with
a rich inflammatory infiltration and with numerous
capillaries of neoinstallation (CD20 immunostaining,
ob. ×20) with positive immunomarking at the level of
perivascular disposed B-lymphocytes.

Figure 4 – Chronic synovity at a 40-year-old man with
diffuse and nodular inflammatory infiltration (CD45RO
immunostaining, ob. ×10) with T-lymphocytes with po-
sitive immunomarking (brown), diffuse and with a trend
to architectural nodularity, and with B-lymphocytes
with negative immunomarking and diffuse disposal.

Figure 5 – Rheumatoid polyarthritis at a 57-year-old
woman (CD20 immunostaining, ob. ×20) with inflam-
matory infiltration with B-lymphocytes, with positive
imunomarking with nodular disposal, and with inflamatory infiltration diffuse with T-lymphocytes
non-marked.

Figure 6 – Rheumatoid polyarthritis at a 57-year-old
woman (CD45RO immunostaining, ob. ×20), with inflammatoy infiltration with T-lymphocytes, with
positive immunomarking with diffuse disposal and
dilated capillaries.
In our group at the patients diagnosed with TBC arthropathy, three patients are men and one patient is a woman. At patients diagnosed with TBC arthropathy, a number of two cases (50%) were diagnosed through the affection at the knee’s articulation and a number of two cases (50%) were diagnosed with through the affection of the small articulations from the level of the foot, too (Figures 7 and 8).

During our study, we found a case of sarcoidosis with arthritis situated at the level of the ell and six cases of villo-nodular synovity, four cases were men and two cases women. Regarding the articulation affected by villo-nodular synovity, three cases were found at the level of the knee and three cases at the level of the hand’s articulations (Figures 9–11).

**Discussion**

The synovities are inflammatory diseases with a complex and diverse etiopathogeny, in which the synovial biopsy is indicated at patients at which the diagnostic is not well determined after the clinical evaluation or after the present symptomatology, it cannot be fitted specifically into a diagnostic [2].

Rheumatoid polyarthritis, inflammatory, systemic and chronic disease with unknown etiology and autoimmune pathogeny it is characterized through an arthropathy with destructive and deform evaluation [12]. As well as in the specialty literature, in our study rheumatoid polyarthritis is one of the many inflammatory chronic diseases, which is currently present at feminine patients [5].

TBC arthritis is a chronic arthritis, destructive, determined by *Mycobacterium tuberculosis* [10]. As well as in the specialty literature our study showed a 50% affectionation of the knee articulation, the rest of 50%
being diagnosed at the level of the foot’s small articulations. In the specialty literature are quoted below 4% cases of TBC synovitis with the affection of the foot’s small articulations [8].

The uric arthropathy is a metabolic disease defined through the tissular presence of crystalline deposits of monosodic urate. The biologic marker and the prior condition for the advent of gout is hyperuricemia with the two suppositions: the increase of the uric acid production and the decrease of the elimination of the uric acid (chronic renal insufficiency; diabetes; high blood pressure; the use of diuretics) [2]. As well as in the specialty literature, at the patients from our study, the disease’s etiology was through the decrease in the elimination of the uric acid [13–21].

The macroscopic and microscopic aspects in the diagnostic of synovitis are essential offering the elements for positive diagnostic.

In the rheumatoid polyarthritis, the combination of villous hypertrophy, proliferation of the synovioocytes, lymphoplasmocytary infiltration with the trend of lymphoid nodules, fibrin deposits and focal necrosis is typical. In PR at the beginning, the mentioned modifications can be absent and can predominate the vascular occlusions or a slight vasculitis [2].

In the uric arthritis, the synovial membrane presents typical uric granulomas. In the acute phase predominates a synovial infiltration with granulocytes meanwhile in the chronic form the infiltration is lymphoplasmocytary.

The villo-nodular synovitis, inflammatory chronic lesion formed by histiocytaire elements, granules of hemosiderin, big multinuclear cells, fibroblasts, the proliferation is villous or nodular with zones of lymphocytes and plasmocytes.

During our study, as well as in the specialty literature the immunohistochemical study of the inflammatory infiltration demonstrated the implication of both types of B- and T-lymphocytes in the pathology of PR because of the activation of the two types of lymphocytes [13].

Conclusions

The group studied by us was formed of 19 patients diagnosed with synovitis with an articular inflammatory source. From these, 21.05% were cases diagnosed anatomo-pathologic of rheumatoid polyarthritis, 21.05% were diagnosed with TBC arthritis, 21.05% were uric arthropathy and 31.57% villo-nodular synovitis.

The subgroup of TBC arthritis presented a ratio men/women of 3/1 as in the specialty literature. Taking into consideration the location disposal of the cases 50% were disposed at the level of the knee’s articulation and 50% were disposed at the level of the small articulations of the foot. In the specialty literature are quoted under 4% cases of TBC synovitis with affection of the small articulation of the foot.

The subgroup of synovitis diagnosed with rheumatoid polyarthritis presented a ratio men/women of 1/3, the real reason of this difference is not entirely known but it is considered that it is due to the effect of hormonal factors on the immune function. From these cases, 50% are situated in the decade of age of 51–60 years.

The cases diagnosed with uric arthropathy were observed in our study only at men, confirming other studies that establish a ratio men/women of 5–7/1.

In this study, at the studied case of rheumatoid polyarthritis, CD20 immunoreaction was present at all cases as well as CD45 RO immunoreaction, the marker being membranar and cytoplasmatic too. The immuno-histochemical study of the inflammatory infiltration proved the implication of both types of B- and T-lymphocytes in the pathology of rheumatoid poly-arthritis, the lesions that appear are considered a result of the intensification and interrelations of those two types of lymphocytes.

References


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