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Review

15 years of the histopathological synovitis score, further development and review: A diagnostic score for rheumatology and orthopaedics

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ABSTRACT

The histopathological synovitis score evaluates the immunological and inflammatory changes of synovitis in a graduated manner generally customary for diagnostic histopathological scores. The score results from semiquantitative evaluation of the width of the synovial surface cell layer, the cell density of the stroma and the density of the inflammatory infiltration into 4 semiquantitative levels (normal 0, mild 1, moderate 2, severe 3). The addition of these values results in a final score of 0–9 out of 9. On the basis of this summation the condition is divided into low-grade synovitis and high-grade synovitis: A synovitis score of 1 to ≤ 4 is called low-grade synovitis (arthrosis-associated/OA synovitis, posttraumatic synovitis, meniscopathy-associated synovitis and synovitis with haemochromatosis). A synovitis score of ≥ 5 to 9 is called high-grade synovitis (rheumatoid arthritis, psoriatic arthritis, Lyme arthritis, postinfection/reactive arthritis and peripheral arthritis with Bechterew's disease). By means of the synovitis score it is therefore possible to distinguish between degenerative/posttraumatic diseases (low-grade synovitis) and inflammatory rheumatic diseases (high-grade synovitis) with a sensitivity of 61.7% and a specificity of 96.1%. The diagnostic accuracy according to ROC analysis (AUC: 0.8–0.9) is good. Since the first publication (2002) and an associated subsequent publication (2006), the synovitis score has nationally and internationally been accepted for histopathological assessment of the synovitis. In a PubMed data analysis (status: 14.02.2017), the following citation rates according to Cited by PubMed Central articles resulted for the two synovitis score publications: For DOI: 10.1078/0344-0338-5710261 there were 29 Cited by PubMed Central articles and for the second extended publication DOI:10.1111/j.1365-2559.2006.02508 there were 44 Cited by PubMed Central articles. Therefore a total of 73 PubMed citations are observed over a period of 15 years, which demonstrates an international acceptance of the score. This synovitis score provides for the first time a diagnostic, standardised and reproducible histopathological evaluation method enabling a contribution to the differential diagnosis of chronic inflammatory

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general joint diseases. This is particularly the case by incorporation into the joint pathology algorithm. To specify the synovitis score an immunohistochemical determination of various inflammation-relevant CD antigens is proposed to enable a risk stratification of high-grade synovitis (e.g.: progression risk and sensitivity for biologicals).

Contents

1. Pathogenesis of rheumatoid arthritis

Rheumatoid arthritis (RA) is the most frequent inflammatory systemic connective tissue disease with a predominantly symmetric manifestation at the peripheral, small joints of the upper extremities. Extraarticular manifestations exist in the bursa, synovial sheathes, in the subepidermal tissue, in the eyes, in the pleura and the internal organs [19]. Pathogenetically, the underlying cause of rheumatoid arthritis of RA lies in a chronic, destructive synovitis which is largely based on a dysregulation of the B lymphocyte and T lymphocyte response as well as fibroblast and macrophage activation [17,20,24]. Current data indicate an expansion of deregulated synovial T and B lymphocytes [17]. In RA, primary synovitis with secondary cartilage damage is observed, by contrast, in arthrosis (osteoarthrosis, OA) a secondary synovitis is present with primary cartilage damage [25,26].

2. Classification criteria of rheumatoid arthritis, histopathological synovitis diagnostics and differential diagnosis of synovial diseases

A synovial biopsy is not necessary for diagnosis and classification of RA according to the internationally applicable ACR criteria 2010 [15,19,23], this clinically weighted classification being based on clinical, seroimmunological, sonographic and radiological criteria.

In the event of incomplete classification of rheumatic joint disease or clinically unclear arthritis and arthritis-like diseases, a synovial biopsy can make a significant diagnostic contribution [4,13]. It is to be said generally that a histopathological differential diagnosis of “synovitis” is a comprehensive differential diagnosis and includes not only the differential diagnosis of inflammatory diseases [2,4,8,11,16,21,22]. This inflammatory, non-inflammatory, infectious, metabolic and neoplastic diagnosis spectrum is combined in the joint pathology algorithm (Diagram 1) [8], which illustrates the diagnostic position of the synovitis score.

2.1. Synovitis score as a standardised histopathological evaluation method

The fact that in inflammatory (e.g. Rheumatoid arthritis; RA) and non-inflammatory (e.g. osteoarthrosis; OA) joint diseases histopathological differences in the severity of the synovitis occur was regarded as knowledge based on histopathological diagnostic “everyday experience”. Histopathological scores in this regard have been developed since 1976 and focussed on evaluating the local activity diagnosis of the RA [12,16]. The synovitis score [6,7], however, provides for the first time a diagnostic, standardised and reproducible histopathological evaluation method which allows a contribution to the differential diagnosis of chronic inflammatory general joint diseases [8]. This is particularly the case by incorporation into the joint pathology algorithm [8] (Diagram 1).

2.2. Histopathological criteria of the synovitis score

The synovitis score evaluates the immunological and inflammatory tissue changes of synovitis in a graduated manner generally customary for diagnostic histopathological scores [6,7]. This score [6,7] represents a semiquantitative, additive evaluation method (additive score), which by specifying three compartments of synovitis (surface cell layer, stroma cells and inflammatory infiltration) is based on a graduated, semiquantitative evaluation of the width of the surface cell layer, the cell density of the stroma and the density of the inflammatory infiltration (absent, mildly, moderately and