

Identifying of the Best Sites for the Hystopathologic Study of Tarsitis in Patients With Spondyloarthropathies

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Background: Foot involvement in patients with spondyloarthropathies (SpA) includes a peculiar clinical spectrum ranging from tarsal swelling to bone ankylosis similar to axial disease in patients with ankylosing spondylitis. Hypothetically, the study of these lesions could help to explain phenomena that occur in the vertebral column.

Objective: To identify the best site for sampling foot tissues in cadavers with a view to implementing the procedure in patients with SpA.

Material and methods: Six sites including foot tendons and entheses from the cadavers of individuals <50 years with no musculoskeletal disease were selected by consensus. Tissue samples included >1 cm of tendon and synovial sheath and 0.2 mm of periosteum, which were fixed in 5-formaldehyde solution, 70% alcohol, and paraffin. Paraffin blocks were then cut into 3 µ slices and stained with hematoxylin, eosin, and Masson trichromic.

Results: There were 31 pieces of tendon, 8 pieces of entheses, and 5 pieces of periosteum, but no synovial membrane was identified. Tendons were identified in more than a half of the sites biopsied and entheses in 50% of samples from the upper segment of the tendon and synovial sheath of the *tibialis posterior* and the *peroneus brevis* insertion on the 5th metatarsal head. Tendon tissues consisted of fusiform cells in an undulated pattern separated by fine bands of loose and dense connective tissue. Enteses included tendon, epitendon, and endotendon attachments to bone through a small fragment of non-calcified fibrocartilage.

Conclusion: Slightly more than 50% of the sites selected for study contained tendon tissues useful for histologic examination. The same results were obtained for entheses in only one site. Overall, these sites appear suitable for study in patients with SpA.

Key words: Spondyloarthropathies. Ankylosing spondylitis. Ankylosing tarsitis. Enthesis. Enthesopathy. Tendon.

Identificación de sitios ideales para el estudio histopatológico de la tarsitis en pacientes con espondiloartropatías

Antecedentes: La afección del pie en pacientes con espondiloartropatías (SpA) incluye un espectro de la clínica peculiar, que va desde la inflamación hasta la anquilosis del tarso similar a la que ocurre en el esqueleto axial de pacientes con espondilitis anquilosante. Hipotéticamente, el estudio de dicha lesión podría ayudar a explicar los fenómenos que ocurren en la columna vertebral.

Objetivo: Identificar en cadáveres el sitio ideal para la toma de biopsias con el propósito de implementar el procedimiento en pacientes con SpA.

Material y métodos: Por consenso, se escogieron 6 sitios en el tarso que incluían tendones y entesis en 6 cadáveres humanos < 50 años sin enfermedad osteomuscular. Se tomaron muestras > 1 cm de tendón y vaina sinovial y 0,2 mm de periostio que se fijaron en una solución de 5-formaldehído, alcohol etílico al 70% y parafina. Los bloques de parafina se cortaron en porciones de 3 de espesor que fueron teñidos con hematoxilina, eosina y tricrómico de Masson.

Resultados: Se identificaron 31 tendones, 8 entesis y 5 periostios, pero no membrana sinovial. En más de la mitad de los sitios biopsiados se identificó tendón y entesis en el 50% de las inserciones de la parte superior

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Manuscript received August 23, 2005; accepted for publication March 21, 2006.

del tendón y la vaina sinovial del tibial posterior, y en la inserción del peroneo corto en la cara externa de la cabeza del quinto metatarsiano.

Los tendones estuvieron constituidos por haces ondulados de células fusiformes con arreglo longitudinal separados por finos septos de tejido conectivo y tejido conectivo denso alrededor. En las entesis se identificó la unión del tendón, endotendón y epitendón al hueso a través de un fragmento de fibrocartilago no calcificado.

Conclusión: En un poco más de la mitad de los sitios seleccionados se pudieron obtener muestras de tendones para estudio histológico; el mismo resultado se obtuvo con respecto a las entesis de uno sólo de los sitios estudiados. Estos sitios parecen ser ideales para el estudio de pacientes con SpA.

Palabras clave: Espondiloartropatías. Espondilitis anquilosante. Tarsitis anquilosante. Entesis. Entesopatía. Tendón.

Introduction

Spondyloarthropathies (SpA) constitute a family of entities that share clinical and immunogenetic aspects. The most important clinical alterations result in inflammation and bone proliferation evident in joints (synovitis) and entheses (enthesitis) of the vertebral spine and other extremities, and, in a minority of cases, in the affection of other tissues or organs. The SpA group includes ankylosing spondylitis (AS), reactive arthritis, psoriatic arthritis, arthropathies associated to Crohns' disease or ulcerative colitis, and a growing group of undifferentiated forms. In the past few years, the morphologic study of SpA has been concentrated on the entheses and neighboring structures such as bursae and synovial sheaths.¹⁻⁵ The enthesopathy that characterizes SpA involves several processes: inflammation, proliferation and endochondral bone metaplasia, bone proliferation, and the formation of osteophytes and bony spurs.⁶⁻⁹ From a clinical standpoint, the acute phase of enthesitis is characterized by hypersensitivity and pain when pressure is applied to the affected sites, and frequently by increased volume, especially when bursae and synovial tendon sheaths are involved. In the chronic phase, enthesophytes, interosseous bridging and bone ankylosis can be found.^{10,11} Enthesopathy affects axial and peripheral entheses. In the peripheral sites, the entheses most frequently affected are those on the lower extremities, specially on the calcaneus (plantar fascia entheses and Achilles tendon), on the bones that

form the tarsus, on the heads of the first and fifth metatarsals, on the anterior tibial tuberosity and on the greater trochanter. On the axial skeleton, the most frequently affected entheses are the ones located on the ischium, the iliac crests and spines, the sacroiliac, interapophyseal and costosternal joints, and the vertebral bodies.

In Mexican patients with SpA, tarsal affection is an episode that frequently is accompanied by acute phase inflammation and, sometimes, by chronic phase ankylosis.^{12,13} The combination of inflammatory and structural tarsal alterations is known as ankylosing tarsitis. As a first stage in the study of the definition of tarsal affection in patients with SpA, it is important to identify the ideal site for biopsy sampling on the feet of cadavers with the purpose of implementing the procedure in patients with SpA.

Material and Methods

The study was done on tissues obtained from 6 human cadavers with an age less than 50, which died of different causes, none related with illness that could interfere with the present study. The sites selected and chosen by consensus were: *a)* superior extensor retinaculum tendon and sheath; *b)* inferior extensor retinaculum tendon and sheath; *c)* posterior tibialis tendon and sheath at the site of insertion to the internal side and periosteum of the first metatarsal; *d)* superior posterior tibialis tendon and sheath; *e)* peroneal brevis tendon and sheath on the site of insertion to the external side and periosteum of the fifth metatarsal; and *f)* superior portion of the peroneal longus and brevis tendon and sheath (Figure 1). Samples were obtained by both authors, AUV, a plastic surgeon, and RRG, rheumatologist.

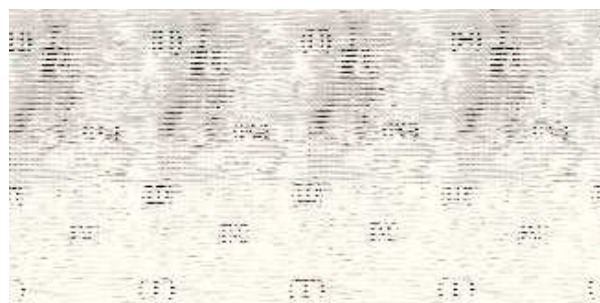


Figure 1. Tibialis posterior entheses. The image shows the tendon (T), non calcified fibrocartilage (FNC), calcified fibrocartilage (FC), a bone spur (EO), and bone (H) (10).

Sample Preparation

Samples were carefully dried with the purpose of including at least 1 cm of tendon and synovial sheath and 0.2 mm of periosteum. Afterwards they were fixed in a 5-formaldehyde, 70% ethylic alcohol, and paraffin. Finally, 3 μ deep fragments were cut and stained with hematoxylin and eosyn (HE) and with Massons' trichromic.

Results

Thirty-one portions of tendons, 8 entheses, and 5 periosteum were identified in biopsied tissues (Table). In none of the cases was synovial membrane identified. In more than half of any of the sites biopsied, tendon was identified—including endo and epitendon—but no tendon synovial membrane. In at least 50% of the samples taken in 2 of the biopsied sites, specifically on the posterior tibialis superior tendon and synovial sheath and on the insertion of the peroneal brevis to the external side of the fifth metatarsal head, entheses were identified. The tendons were formed by undulated bands of fusiform cells with a longitudinal arrangement (tendon in itself) separated by fine septa of connective tissue (endotendon) (Figures 1 y 2). Some of the tendons were surrounded by dense connective tissue or epitendon (Figure 3). Findings on the entheses included the site of union of tendon, epitendon, and endotendon to the bone through a fragment of non calcified fibrocartilage.

Discussion

The results of this study confirm the presence of tendon, endotendon and epitendon in approximately two-thirds of the samples taken, and entheses in 2 of them. With respect



Figure 2. In this image the entheses of the peroneal brevis tendon is shown. While the tendon (T) and the calcified (FC) and non calcified fibrocartilage FNC—are easily observed, in this site it was not possible to identify the articular, chondral or enthesal fibrocartilage or cartilage (2.5).

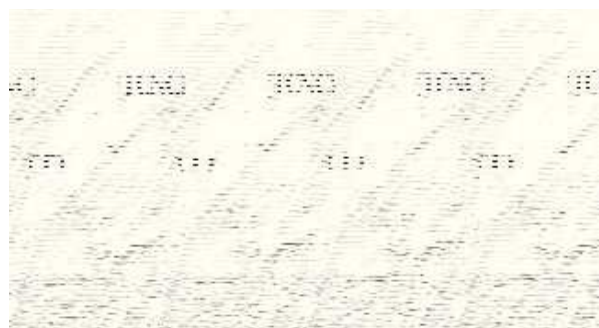


Figure 3. Peroneal brevis common sheath. The tendon with endo and epitendon, separated by a fragment of non calcified connective tissue (10).

TABLE. Structures Identified in Each of the Studied Sites

| Site | Structure Identified | | |
|--|----------------------|----------|------------|
| | Tendon | Enthesis | Periosteum |
| Superior extensor retinaculum tendon and sheath | 4 | 0 | 0 |
| Inferior extensor retinaculum tendon and sheath | 6 | 0 | 0 |
| Tendon, synovial sheath, and insertion of the posterior tibialis on the head of the first metatarsal | 6 | 0 | 0 |
| Superior posterior tibialis tendon and sheath | 6 | 4 | 4 |
| Peroneal brevis tendon on its insertion to the external side and periosteum of the fifth metatarsal head | 4 | 3 | 1 |
| Superior part of the peroneus longus and brevis tendon and sheath | 5 | 1 | 0 |

to tendons, this work shows the sites in which there is a larger probability of obtaining the best samples for hystopathologic study. With respect to the entheses only two sites were appropriate, specifically the insertions of the superior part of the posterior tibialis and the peroneal brevis. The application of the results of this study concerns the histopathologic study of foot affection in patients with SpA and specifically ankylosing tarsitis, with the goal of obtaining information that permits the establishment of theoretical bases for the pathogenesis of said process.¹⁴ In an indirect manner, the information obtained could explain some of the episodes that occur in the vertebral spine and sacroiliac joints of patients with SA. In detail, foot affection, especially in patients with juvenile SpA, produces pain and an increase in volume of the mid-foot as well as pain in the insertions of the Achilles' tendon and the plantar fascia on the calcaneus. In the phase of most notable inflammation, some alterations can be found by magnetic resonance imaging which indicates the presence of inflammation in some of the affected zones, for example, zones of hyperintensity on the abovementioned entheses or through the width of the tarsal bones. In chronic phases it is possible to find structural alterations of a diverse nature that ultimately determine the degree of limitation of the patient. Such alterations are constituted by a progressive reduction of the joint space, bone proliferation on the entheses (enthesophytosis), bone bridging between the tarsal bones and, in more advanced cases, partial or total tarsal ankylosis. These types of alterations appear similar to the ones that are found on the vertebral spine in patients with AS and

probable represent the same kind of mechanism and pathogenic alterations.

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