Original article

Villonodular synovitis of the ankle. Analysis of the risk of recurrence

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A B S T R A C T

Introduction: Villonodular synovitis (VNS) is a rare disease with an incidence of 1.8 per 1,000,000 inhabitants. VNS of the ankle has seldom been described and evaluated given its extreme rarity (2.5% of VNS cases). It presents an 11% recurrence rate. We report a continuous retrospective series with the main objective of clinically and radiologically evaluating these ankles searching for any risk factors of recurrence. At revision the study’s main endpoint was the existence of local recurrence (radiological and clinical) and the secondary endpoint was the existence of tibial talar osteoarthritis. The working hypothesis was that recurrence could be subclinical, warranting systematic imaging studies during follow-up.

Material and methods: The study was retrospective, conducted on seven patients (six males) whose mean age was 42 years treated over a period of 9 years (two diffuse forms and five localized forms). The initial treatment consisted in synovectomy via the conventional approach. Four patients also received adjuvant isotopic synoviothrosis treatment. The revision was clinical (MMTS, AOFAS, and OMAS scores) and radiological (standard and MRI) to evaluate the joint after-effects and search for recurrence.

Results: Six patients were seen at a mean 6.5 years of follow-up. One case of early recurrence (4 years) was noted, with a major clinical manifestation because it was associated with joint destruction requiring arthrodesis, and one case of late asymptomatic recurrence (9 years), diagnosed radiologically on the follow-up MRI. The functional results remained good at follow-up (MMTS 77%, AOFAS 71, OMAS 71). Five of the six patients returned to their daily activities. At revision, no sign of osteoarthritis was observed. No risk factor for recurrence was demonstrated.

Discussion/conclusion: The hypothesis was confirmed with the existence of asymptomatic recurrence at revision, underscoring the value of systematic MRI at follow-up. Other than major joint destruction, the prognosis remains good even in case of recurrence. The literature emphasizes the existence of an initial diffuse form and partial surgical resection as risk factors of recurrence. None of the reports in the literature has proven that adjuvant treatment, whose modalities do not meet with consensus, reduces this risk.

Level of evidence: Retrospective series, level IV.

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1. Introduction

Villonodular synovitis (VNS) is a rare disease [1,2] with an incidence of 1.8 new cases per 1,000,000 inhabitants [3]. This synovial proliferation is marked by villous or nodular hyperplasia [4] causing alteration of the joints, bursae, synovial membranes, and tendons [1] that can progress to joint destruction. It can be localized or diffuse [4] and all joints can be involved with a strong predominance for the knee. It exceptionally affects the ankle. Seventy-four cases (with the majority corresponding to the diffuse form [51/74, 69%]) have been reported in the literature with follow-up from 1 to 5 years [5–14]. The radiological and clinical results have been deemed satisfactory. The mean recurrence rate is approximately 11% (8/74), ranging from 0% to 50% depending on the series (Table 1). Most authors recommend synovectomy, as wide as possible, with complete resection via the conventional approach. Only Rochwerger et al. [14] proposed arthroscopic resection with satisfactory results and no recurrence. No consensus exists on the value of adjuvant treatment or on the modalities to adopt vis-à-vis the risk of recurrence. Four series used adjuvant treatment (radiotherapy or isotopic synoviorthesis) with two cases of recurrence in 25 patients (8%) at follow-up [5,9,11,12].
### Table 1
Series reported in the literature (ankle VNS).

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of patients</th>
<th>Sex ratio (males/females)</th>
<th>Form (diffuse/localized)</th>
<th>Mean age (years)</th>
<th>Study period</th>
<th>Main treatment</th>
<th>Adjuvant treatment</th>
<th>Follow-up (years)</th>
<th>Clinical score</th>
<th>MRI</th>
<th>Recurrence at revision</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shabat et al. [12] 2002</td>
<td>3</td>
<td>2/1</td>
<td>3/0</td>
<td>31.6</td>
<td>1989–1998</td>
<td>CS</td>
<td>Isotopic synoviorthesis</td>
<td>5</td>
<td>–</td>
<td>Annual MRI</td>
<td>0</td>
</tr>
<tr>
<td>Bisbinas et al. [9] 2004</td>
<td>9</td>
<td>0/9</td>
<td>2/7</td>
<td>27</td>
<td>1990–2002</td>
<td>CS</td>
<td>Radiotherapy for 2 diffuse forms</td>
<td>3.4</td>
<td>–</td>
<td>–</td>
<td>2</td>
</tr>
<tr>
<td>Saxena and Perez [10] 2004</td>
<td>10</td>
<td>NC</td>
<td>5/5</td>
<td>40</td>
<td>NC</td>
<td>CS</td>
<td>–</td>
<td>4.5</td>
<td>–</td>
<td>–</td>
<td>2</td>
</tr>
<tr>
<td>Brien et al. [11] 2004</td>
<td>10</td>
<td>NC</td>
<td>10/0</td>
<td>35</td>
<td>NC</td>
<td>CS</td>
<td>Radiotherapy in 4 cases Radiotherapy</td>
<td>3.5</td>
<td>–</td>
<td>–</td>
<td>0</td>
</tr>
<tr>
<td>Sharma et al. [8] 2006</td>
<td>8</td>
<td>5/3</td>
<td>26</td>
<td>NC</td>
<td>CS</td>
<td>–</td>
<td>4.6</td>
<td>–</td>
<td>–</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Stevenson et al. [7] 2013</td>
<td>18</td>
<td>7/11</td>
<td>11/7</td>
<td>42</td>
<td>2000–2012</td>
<td>CS (no treatment for 4 patients)</td>
<td>–</td>
<td>5</td>
<td>MMTS 93.8 AOFAS 89</td>
<td>–</td>
<td>0</td>
</tr>
<tr>
<td>Korim et al. [6] 2014</td>
<td>7</td>
<td>2/5</td>
<td>6/1</td>
<td>37</td>
<td>2000–2010</td>
<td>CS</td>
<td>Isotopic synoviorthesis in 4 cases</td>
<td>6.5</td>
<td>MMTS 77 AOFAS 71 OMAS 71</td>
<td>MRI</td>
<td>2</td>
</tr>
<tr>
<td>Our series</td>
<td>7</td>
<td>6/1</td>
<td>2/5</td>
<td>42</td>
<td>2002–2011</td>
<td>CS</td>
<td>–</td>
<td>4</td>
<td>–</td>
<td>–</td>
<td>1</td>
</tr>
</tbody>
</table>

NC: not communicated; CS: conventional synovectomy.
We report a continuous retrospective series of operated ankle VNS. The main objective of the study was to analyze the radiological and clinical results while searching for possible recurrence at the medium term and risk factors for recurrence. At revision, the main endpoint of the study was the existence of local recurrence (radiological and clinical) and the secondary endpoint was the existence of osteoarthritis. The working hypothesis was that recurrence could be subclinical, therefore warranting systematic imaging in the follow-up.

2. Material and methods

2.1. The series

Patients with VNS were identified in the database of the Strasbourg University Hospital's anatomopathology department. Between 1995 and 2014, 88 patients were found, seven of whom had ankle locations treated between 2002 and 2011. The initial diagnosis of these ankle locations was made based on an anatomopathological examination of the surgically excised specimens, suspected on preoperative MRI. In one case, a primary biopsy was performed. The patient files and the surgical report were examined to collect the type of VNS (localized or diffuse), the surgical procedures (conventional or arthroscopic synovectomy, total or partial resection judged by the operator), any adjuvant treatment, and the onset of any complications. The majority were males (n = 6). The mean age was 42 years (range, 26–66 years). The initial symptoms described by the patients were for the most part edema, swelling, mixed pain (at rest and with exercise), and general discomfort when walking (Table 2).

2.2. Treatment

Treatment consisted in tumor resection as wide as possible via the conventional approach using arthroscopy with resection in the healthy macroscopic area (according to the analysis of the surgical report) for all patients. Surgery was performed by surgeons experienced in tumor surgery. The approaches were determined by the tumor location (Table 2). After analysis of the surgical report, the resection was judged “total and complete” by the operator in five cases (four localized forms and one diffuse form). Four patients received adjuvant isotopic synoviotherapy treatment (two localized and two diffuse forms; Table 2).

2.3. Evaluation

Assessment occurred after the patient had been informed and informed consent was obtained by an independent examiner (MC). The study’s main endpoint was the appearance of recurrence (radiological and clinical) and the secondary endpoint was the existence of osteoarthritis, based on radiological and clinical examination. Three clinical scores were used, specific of ankle and tumor pathologies: The Musculoskeletal Tumor Society Rating Scale (MSTS) [15], The American Orthopaedic Foot and Ankle Society score (AOFAS): the Ankle Hindfoot Scale [16,17], and the Olerud-Molander Ankle Score (OMAS) [18]. The radiological workup included an x-ray of the ankle (AP and lateral) searching for degenerative involvement. An MRI of the ankle searching for recurrence was proposed to each patient. The MRI was analyzed independently by a radiologist specialized in osteoarticulare diseases (GB).

3. Results

Six of the seven patients (one was lost to follow-up) were seen at a mean follow-up of 77 months (range, 35–114 months).

3.1. Clinical results

Five patients returned to daily activities with no restrictions. The mean results of the clinical scores were good, with 77% (range, 50–97%) for the MMTS, 71 points (range, 39–100 points) for the AOFAS score, and 71 points (range, 20–100 points) for the OMAS score, confirming good functional recovery and satisfactory range of motion (Table 3).

Concerning the localized forms, three of the four patients (cases 1, 4, 6) were able to return to professional and sports activities with no restrictions and good functional results. One patient (case 5) complained of discomfort preventing her from totally returning to activities despite relatively modest objective functional repercussions.

Concerning the diffuse forms, patient 2 was able to return to work and personal activities with no modification. The second patient (case 3), whose initial progression was marked by major radiological and clinical recurrence with joint destruction requiring arthrodesis, was required to change occupations and discontinue sports.

3.2. Radiological results

One case of early recurrence (at 4 years) (case 3) was observed, with local progression marked by the appearance of major tibial osteoarthrosis and subtalar pain requiring arthrodesis using retrograde nailing. Radiological reassessment at the follow-up visit 4 years after surgery showed no recurrence (Fig. 1).

The MRI performed at revision demonstrated one case (case 1) of late recurrence at 9 years of follow-up, which was completely asymptomatic (Fig. 2). This was located at the plantar arch of the foot, outside the initial approach, which was anteromedial. It should be noted that one patient (case 2) refused this reassessment MRI. No progression to osteoarthrosis was observed at revision for the six cases reassessed with standard x-rays (Table 3).

4. Discussion

4.1. The working hypothesis

The working hypothesis was confirmed with one late asymptomatic recurrence (9 years) diagnosed on the reassessment MRI. At revision, no progression to osteoarthrosis was demonstrated. However, one case of multiple recurrence at 4 years after the first surgery evolved catastrophically with joint destruction requiring secondary arthrodesis, which remained stable and with no recurrence at 4 years. The clinical results were satisfactory at the mean follow-up of 6.5 years for the entire series.

4.2. Study’s limitations

This study presents a number of limitations. Its design was retrospective and the series was small, inherent to the rarity of the disease and the location. The complete removal of the tumor, evaluated based on only the analysis of the surgical report, remained a subjective assessment by the operator. However, this study presented several strengths: the follow-up was one of the longest found in the literature (6.5 years) and the evaluation at revision included an MRI, which has rarely been noted in the literature [5,12].

4.3. Major risk of VNS

The major risk of VNS is recurrence, with an 11% rate (8/74) (range, 0–50%) found in the literature for the ankle. This is lower than the rate found in the present study (28%) considering all the
Fig. 1. Joint destruction secondary to multiple recurrence. Arthrodesis at 4 years. a, b: preoperative MRI with erosive hypointense mass in the ankle (a: T2-weighted sagittal Fat-Sat) (b: coronal T1); c: scan (AP and lateral) 4 years after the first synovectomy; d: arthrodesis fused at the last follow-up at 4 years (AP and lateral); e: MRI at revision (T2-weighted sagittal Fat-Sat). No sign of recurrence.

Fig. 2. Recurrence at 9 years at the medial part of the plantar arch (initially ankle villonodular synovitis [VNS]). Round mass with an intermediary signal and low-signal areas indicating VNS. T1-weighted coronal MRI image (a) and T2-weighted axial Fat-Sat (b).
recurrences (two out of seven: one clinical and one radiological), but comparable if only clinical recurrence is retained (14%, one case at 4 years). The recurrence rate in the literature is probably underestimated because it is based exclusively on clinical manifestation. Only two teams [5,12], with only six patients, undertook systematic MRI verification, with no recurrences demonstrated. In our opinion, case 1 in the present series underscores the need for systematic MRI assessment. The result of this workup will not necessarily result immediately in surgery if the ankle is perfectly asymptomatic; however, the follow-up will be more rigorous and more frequent and the patient will be informed. Comparison of clinical results remains delicate because only two series [6,7], collecting 25 patients, reported clinical scores (Table 1).

The secondary assessment criterion was the existence of osteoarthritis at revision. None was demonstrated by the imaging studies. The major risk factor of secondary osteoarthritis onset seems to be the existence of aggressive recurrence, as in case 3. Secondary osteoarthritis was not precisely analyzed in the different series reported in the literature and no risk factors were emphasized.

4.4. Most important predictive factor in terms of the risk of recurrence

The most important predictive factor in terms of the risk of recurrence seems to be the existence of a diffuse form of the

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Details of the series.</th>
</tr>
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<tbody>
<tr>
<td>Age (years)</td>
<td>Gender</td>
</tr>
<tr>
<td>1</td>
<td>66</td>
</tr>
<tr>
<td>2</td>
<td>59</td>
</tr>
<tr>
<td>3</td>
<td>56</td>
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<td>4</td>
<td>29</td>
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<td>5</td>
<td>26</td>
</tr>
<tr>
<td>6</td>
<td>27</td>
</tr>
<tr>
<td>7</td>
<td>31</td>
</tr>
</tbody>
</table>

R: right; L: left; VNS: villonodular synovitis; M: male; F: female; TT: tibiotalar.

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Radiological and clinical results at last follow-up.</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Diffuse</td>
</tr>
<tr>
<td>3</td>
<td>Diffuse</td>
</tr>
<tr>
<td>1</td>
<td>Localized</td>
</tr>
<tr>
<td>4</td>
<td>Localized</td>
</tr>
<tr>
<td>5</td>
<td>Localized</td>
</tr>
<tr>
<td>6</td>
<td>Localized</td>
</tr>
</tbody>
</table>

VNS: villonodular synovitis; functional score: MMTS [15], AOFAS [16,17], OMAS [18].
disease. Korim et al. [6] reported one case for a diffuse form, Sharma et al. [8] two cases, Saxena and Perez [10] two cases, and Ghert et al. [13] one case. The predominance of the localized form in our series (five out of seven) should result in a lower recurrence rate, which unfortunately was not the case.

Complete surgical resection is recommended, implying conventional surgery, which is defended by the literature [4,9,19,20]. The resection was deemed partial by the operator for two of our cases of recurrence, a second fundamental risk factor for recurrence.

With the objective of reducing this risk of recurrence, some authors have proposed adjuvant treatment. The knowledge of the use of these adjuvant therapies is greater in hemophilic arthropathies. No specific recommendations or consensus exist for VNS, and even less so for the ankle. The only protocol proposed was described by Ottaviani et al. [21] with an injection of rhenium 2 mCi. The literature reports the most frequently used adjuvant treatment was radiotherapy, but this does not seem to guarantee the desired result, since Bissibas et al. [9] reported two cases of recurrence. We have no experience in this treatment. Four adjuvant treatments were prescribed to our patients: hexatrione alone in one case, isotopic synoviothertesis with rhenium in three cases: two diffuse forms and two localized forms. No particular explanation for the adjuvant treatment indication for the two localized forms was found in the surgical report. Unfortunately, this did not suffice to prevent recurrence for case 3.

5. Conclusion

Our hypothesis was confirmed. Given the possibility of recurrence with little or no clinical manifestation, we recommend regular MRI follow-up. The risk factors for recurrence identified in the literature are a diffuse form and incomplete tumor resection. Adjuvant treatment does not seem to have proven its efficacy in terms of this risk. Finally, the risk of secondary osteoarthritis onset does not seem to be increased, subject to the absence of aggressive recurrence.

Disclosure of interest

The authors declare that they have no competing interest.

Outside of this work: FB is an educational consultant for Serr® and Amplitude®. ME is an educational consultant for Depuy-Synthes® and Groupe Lépine®. PA is an educational consultant for Depuy-Synthes®.

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