International Orthopaedics (SICOT) (2005) 29: 403–405
DOI 10.1007/s00264-005-0004-8

ORIGINAL PAPER

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Diffuse pigmented villonodular synovitis of the foot and ankle treated with surgery and radiotherapy

Received: 1 May 2005 / Accepted: 1 June 2005 / Published online: 30 August 2005

Abstract We followed up seven patients with histologically confirmed diffuse pigmented villonodular synovitis in a prospective study between 1992 and 2001. The mean age at diagnosis was 30.7 years. The patients underwent synovectomy, followed by radiotherapy with a total dose of 35 Gy in 20 fractions. In all cases, the excision was considered incomplete when examined histologically. At an average follow up of 24 (18–36) months, six patients reported better function and reduced levels of pain. One patient remained symptomatic but did not have a recurrence. We conclude that a combined approach to a primary pigmented villonodular synovitis of the foot and ankle may reduce the risk of recurrence without functional impairment.

Résumé Nous avons suivi sept malades avec une synovite villonodulaire pigmentée diffuse confirmé histologiquement dans une étude prospective entre 1992 et 2001. L'âge moyen au diagnostic était de 30,7 ans. Les malades ont subi une synovectomie suivie d'une radiothérapie avec une dose totale de 35 Gy en 20 fractions. Dans tous les cas, la résection a été considérée incomplète à l'examen histologique. À une moyenne de suivi de 24 (18–36) mois, six malades ont une meilleure fonction et un niveau réduit de douleur. Un malade est resté symptomatique, mais sans récidive. Nous concluons qu'un traitement combiné d'une synovite villonodulaire pigmenté du pied et de la cheville peut réduire le risque de récidive sans dégradation fonctionnelle.

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Introduction

Pigmented villonodular synovitis (PVNS) is a rare but potentially aggressive lesion that attacks the synovium of joints, tendon sheaths or bursae; 2.5% of cases occur in the foot and ankle. Granowitz and Mankin [4] divided PVNS into two forms: localised (nodular) and diffuse. Both forms can occur in the foot and ankle. A nodular variant, the giant cell tumour of tendon sheath (GCT), occurs in the flexor or extensor tendon sheaths of digits. Although now considered a benign tumour, PVNS was considered to be a low-grade synovial malignancy. The spectrum of clinical presentations ranges from a painless nodule or swelling to a diffusely painful, stiff joint. Most cases are monarticular and do not metastasise although they may be locally destructive.

Diagnosis is made on clinical features, aspiration of the joint, radiographic features and magnetic resonance imaging (MRI), which is the most useful. The lesion has a pathognomonic appearance first described by Kottal et al. [6]. The T1-weighted images with a short TR/TE show the lesion to have density similar to muscle while the T2-weighted images with a long TR/TE show the lesion as dark due to a signal void created by the ferromagnetic haemosiderin in the lesion (Figs. 1 and 2).

As the natural history of PVNS is one of potential aggression, it is accepted that surgical excision is the only curative treatment, and total synovectomy is required for the diffuse form where recurrence is common. Marginal or intra-lesional excision by curettage may not eliminate the disorder. The nature of the anatomy in the foot and ankle makes complete excision difficult to achieve.

Radiotherapy (RT) has been used in the management of recurrent disease with moderate radiation doses. Where complete synovectomy cannot be achieved, local recur-

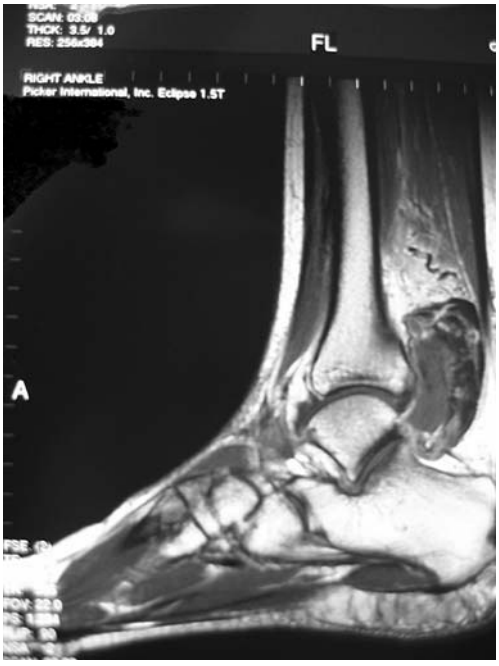

Fig. 1 T1-weighted magnetic resonance imaging (MRI) demonstrating a heterogeneous lesion with surrounding low signal intensity characteristic of haemosiderin deposition

rences have been treated with RT. Blanco et al. [1] combined partial arthroscopic synovectomy with external-beam RT at a dose of 26 Gy for cases of PVNS in the knee where posterior joint access was difficult and only partial excision could be achieved. A recurrence rate of 14% within 1 year of surgery was reported. We present the results of a similar combined approach to PVNS of the foot and ankle.

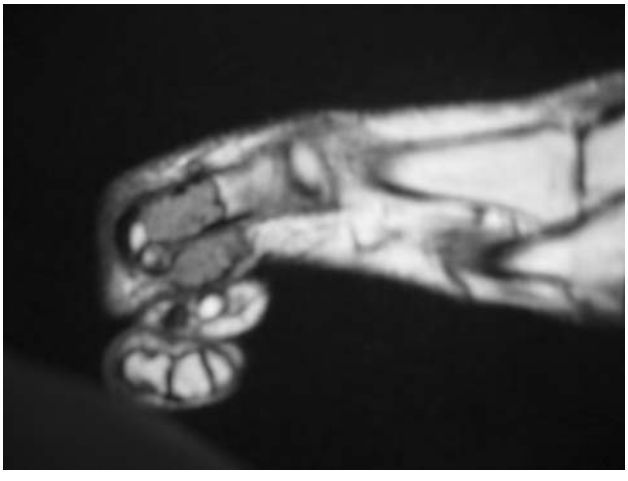

Fig. 2 T1-weighted magnetic resonance imaging (MRI) demonstrating pigmented villonodular synovitis (PVNS) lesion of the great toe with invasion of the proximal phalanx

Table 1 Patient characteristics, location of lesions and combined management

Patient	Age/ Gender	Location of lesion	Follow-up (months)
1	25/M	2nd toe MTP joint	22
2	22/M	Calcaneum, navicular, cuboid, sinus tarsi	19
3	42/M	Proximal phalanx great toe	20
4	14/F	Posterior aspect ankle	18
5	25/F	Navicular, cuneiform 2nd and 3rd intermetatarsal spaces	27
6	56/M	Anterior ankle	26
7	31/F	Anterolateral ankle	36

Patients and methods

Seven patients with clinical, MRI and histologically confirmed PVNS of the foot and ankle were followed up in a prospective study between 1992 and 2001 at the Royal National Orthopaedic Hospital, Stanmore (Table 1). There were four males and three females, with a mean age of 30.7 (14–56) years at diagnosis. In four cases, the disease was located in the foot; in two cases it was found in the ankle. One patient had disease in both sites. The average time from diagnosis to operation was 75 days.

The patients underwent open synovectomy. Two surgeons performed the operations. In all cases, the disease was classified as diffuse in appearance, and all specimens had incomplete resection margins. Post-operatively, upon receipt of formal histology, the patients were treated with RT with a total dose of 35 Gy in 20 fractions over 4 weeks. In all cases, parallel opposed fields were used to encompass the whole joint and all affected extra-articular tissue as defined clinically and on CT or MRI of the joint. Patients were reviewed at regular multi-disciplinary clinics with orthopaedic and RT team members.

Results

Criteria for determining outcomes at follow-up were patient-reported symptoms and MRI. Pre- and post-treatment symptoms were compared at each outpatient visit (Table 2). At an average follow-up of 24 (18–36) months, six patients reported reduced levels of pain and improved function

Table 2 Comparison of pre- and post-treatment symptoms at an average of 24 months

	Patients with pre-treatment symptoms	Patients with post-treatment symptoms
Pain	7	1
Swelling	5	2
Erythema	5	0
Stiffness	7	1

compared with pre-treatment symptoms. One patient reported persistent swelling and pain although a recurrence of the lesion was not found. In all cases, no recurrence was identified on MRI.

Discussion

PVNS is an aggressive disease, and there is a substantial incidence of re-growth. When found in the foot and ankle, the large number of joints in this region and the lack of integrity of the superficial muscle layers assist in allowing spread to adjacent articular spaces. Complete excision is therefore difficult to achieve. Radiation oncologists have been reluctant to employ radiation in the treatment of benign disease for several reasons: (1) the small but not negligible risk of late appearance of radiation-induced malignant tumours; (2) the need to reduce the radiation dose if an independent neoplasm was to arise in the same region of the body; and (3) non-malignant tissue changes that might appear subsequently and complicate healing of surgical wounds.

However, the clinical seriousness of many benign processes has liberalised the use of radiation, and clinical data indicate that moderate radiation doses can be effective. The Princess Margaret Hospital reported on their experience with 14 patients with advanced recurrent disease [9]. The dose was 30–50 Gy. There was a complete response in 13 of the 14 patients. These data suggest that a moderate radiation dose is an attractive option in recurrent disease. An alternative has been the injection of radioactive yttrium 90 locally. Blanco et al. [1] combined anterior arthroscopic synovectomy and post-operative RT with a total dose of 2,600 cGy for primary diffuse PVNS of the knee. At an average follow-up of 33 months, 86% of cases did not show signs of recurrence, and there were no apparent harmful effects from RT.

Research is continuing into the anti-inflammatory properties of radiation and the optimal treatment regimes [12], and some of the mechanisms are becoming clear. For example, low radiation doses may have an anti-inflammatory effect through modulation of the NO pathway in macrophages [5]. Since the pathogenesis of PVNS is unclear, it is not possible to infer that radiation affects the disease through the same pathways, but it seems likely that chronic inflammation has some role, and this may be why RT can improve symptoms and prevent recurrence.

Estimates of risk after low radiation doses to joints are also difficult to define. Many studies have addressed the incidence of second malignancy after treatment for childhood cancers and common adult tumours [2, 5, 7, 8]. These studies, whilst instructive for specific populations, should not necessarily be used to estimate risk for patients without malignant disease. This is highlighted by the fact that some of these tumours occur with increasing frequency at non-irradiated sites and are therefore due to factors unrelated to treatment—possibly genetic pre-disposition [10]. After treatment for benign disease such as Grave's ophthalmopathy in young patients, an absolute lifetime risk of radiation-induced cancer has been estimated at 0.3% [3]. After treatment for joint disease at the knee or ankle in an adult, the only organ for which there is a quantifiable risk of second malignancy is skin, and the estimated absolute lifetime risk is 22×10^{-8} per Gy [11]. For the typical field size used in this study, this gives a risk estimate of three per 100,000. This small risk may be justified in patients with significant disability who may otherwise require radical surgery in order to achieve complete excision.

Although this study is too small to fully evaluate the benefit of radiation in these patients, we have demonstrated that low-dose RT can be an effective adjuvant to surgery.

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