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Sentinel node biopsy in synovial sarcoma

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Abstract

Aims: To examine the relevance of sentinel node biopsy in patients with synovial sarcoma.
Methods: Between July 2004 and February 2007 11 consecutive patients with synovial sarcoma treated in our clinic underwent sentinel node biopsy after a preoperative lymphoscintigraphy. A handheld γ-probe was used during the procedure to identify the sentinel nodes, which were then resected and submitted for histopathologic evaluation.
Results: At least one sentinel node was identified in every patient. Of a total of 15 sentinels, one was positive and 14 negative. The patient with the positive sentinel underwent a regional lymph node dissection and remains disease-free 17 months later. One patient developed regional nodal metastases despite negative sentinel node biopsy and died 12 months after the procedure. No biopsy-associated complications were observed.
Conclusions: Sentinel node biopsy can be successfully and safely applied to patients with synovial sarcoma. Further prospective studies are required to determine the optimal treatment approach, the false negative rate and the prognostic significance of a positive sentinel node biopsy.

Keywords: Synovial sarcoma; Lymphatic mapping; Sentinel node biopsy; Multimodal treatment

Introduction

Synovial sarcoma is a rare, highly aggressive tumor, representing 5–10% of all soft tissue sarcomas.[1–4] The median age of patients at the time of diagnosis lies in the third decade of life, with approximately 30% of the cases being children and adolescents younger than 20 years of age.[3,5] A slight male predominance has been reported.[6]

The most common location of synovial sarcoma is the lower extremity, followed by the upper extremity.[3,4] An extracompartmental growth is frequently exhibited.[2] Despite its name, synovial sarcoma is not thought to derive from synovial tissue, usually arising near rather than within a joint.[5–7] The tissue of origin remains unknown.[6,7] Due to the presence of two morphologically distinct cell types in varying proportions, epithelial and spindle cells, synovial sarcomas are divided into four histological subtypes: biphasic, monophasic fibrous, monophasic epithelial and poorly differentiated, the first two being those most commonly encountered.[7,8] On the molecular level, more than 90% of synovial sarcomas demonstrate a specific translocation *t*(X;18)(p11.2;q11.2), producing the distinct chimeric gene SYT-SSX, which appears in both cell types of the tumors.[7,8]

As in other sarcomas, the most frequent site of metastasis is the lung.[1,9,10] However, unlike most soft tissue sarcomas, regional lymph node metastases are described in 6–14% of patients with synovial sarcoma.[1,2,11] Data regarding the prognosis vary significantly, with pediatric trials reporting 5-year survival rates of up to 80%,[5] compared to 57–75% in adult series.[4,10] Several studies suggest that this could be attributed to the different therapy strategies applied in children and adults.[1,5,9] Whereas approximately 80% of pediatric patients additionally receive a systemic chemotherapy, usually within clinical or

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cooperative group trials,[5] the respective ratio for adults lies at 40–50%,[4,10] with the exact role of adjuvant chemotherapy in both children and adults with grossly resected synovial sarcoma remaining controversial due to the lack of prospective randomized trials.[1,5,12,13] However, complete surgical removal of the primary tumor and of all metastases remains, with or without radiotherapy, the cornerstone of curative treatment modalities in both groups.[1,3,7,14]

A potentially useful diagnostic tool for detecting lymph node metastases is the sentinel lymph node biopsy. The concept of this technique is that the sentinel represents the first node to receive lymphatic drainage from a tumor; an involvement of this lymph node could therefore indicate a potential tumor spread in the entire regional basin, whereas a tumor-free sentinel would render nodal involvement unlikely.[15,16] Sentinel node biopsy has been established over the years in the treatment of malignant melanoma[17] and breast cancer,[18] while its role is being currently explored in cancers of the gastrointestinal tract[19] and numerous other carcinomas.[16] However the possible advantages of implementing sentinel node biopsy in patients with synovial sarcoma have yet to be investigated.

The aim of this preliminary prospective study was to examine the relevance of sentinel node biopsy in patients with synovial sarcoma and report our experience with this technique.

Patients and methods

Patients

Eleven consecutive patients with synovial sarcoma, 7 women and 4 men, treated in our clinic between July 2004 and February 2007, underwent lymphatic mapping with sentinel node biopsy. Their age ranged from 17 to 72 years (median, 41 years). The tumor was located in the lower extremity in nine patients and in the upper extremity in two patients. Four patients presented with a primary tumor, one with a local recurrence, one with a subcutaneous metastasis in the lower limb, while five patients were referred to us from other centers after marginal resection of a synovial sarcoma. The patient presenting with the subcutaneous metastasis had received adjuvant radiochemotherapy during the treatment of the primary tumor, while a further patient presenting with a primary tumor received neoadjuvant chemotherapy prior to wide resection and sentinel node biopsy; the remaining patients had not received radiation or chemotherapy at the time of the sentinel node biopsy. All patients were subjected to a complete staging, including a clinical and sonographic evaluation of the regional lymph nodes. Follow-up data was either acquired at the surgical policlinic in the routine aftercare or provided by the referral physician.

Lymphatic mapping

The sentinel node biopsy was performed in the same session as another operating procedure in all but one patient. Our protocol involved a preoperative lymphoscintigraphy after four injections of ^{99} ^{m}Tc-labelled colloidal albumin (Nanocoll®, GE Healthcare Buchler GmbH & Co. KG, Germany) around the primary tumor or its resection site. The distribution of the nanocolloid was detected using a γ-camera (DigiCam® MB9100, Gamma-Budapest, Hungary) in defined intervals up to 19 h post injection; the lymph node closest to the tumor identified was marked on the skin surface using waterproof ink.

During the operation a small incision was made through the marked area, in a way that a future, potentially necessary lymph node dissection would incorporate the incision tract. The operation site was explored using a handheld, sterile covered γ-probe (G100 Gamma Finder®, World of Medicine AG, Germany), sentinel nodes being defined as those considerably radioactive above background. A specific sentinel-to-background ratio was not determined in the protocol, as the background count has been reported to be quite variable depending on the location of the primary tumor and the placement of the probe.[20] The site was re-examined with the γ-probe until no further substantially radioactive nodes could be identified.

Histopathologic analysis

All lymph nodes resected were fixed in formalin and submitted for serial, 500 μm step sections of the entire nodes. Analysis was performed with hematoxylin-eosin stains, as well as with various immunostains (usually Cytokeratin and EMA, depending on the immunohistochemistry of the primary tumor).[7] Given the lack of data regarding sentinel biopsy in synovial sarcoma, intraoperative frozen sections were not performed.

Results

At least one sentinel node was identified in each patient (mean, 1.36; range, 1–2 nodes). Of a total of 15 sentinels, one was positive and 14 negative. No patient developed complications associated with the biopsy. One patient underwent isolated limb perfusion (ILP) and is currently awaiting surgical removal of the tumor; the mean follow-up of the remaining patients was 17.6 months (range, 7–34 months). ILP was performed in a total of four patients, always subsequent to the sentinel node biopsy. In all patients the regional lymph nodes were neither dissected nor perfused during the ILP.

The positive sentinel node was identified microscopically on hematoxylin and eosin staining in a patient referred to us after marginal resection of a synovial sarcoma of the upper extremity. He subsequently underwent axillary lymph node dissection; no further evidence of nodal disease was detected and staging had been negative for systemic metastases, so that no additional treatment was recommended. 17 months after surgery the patient remains disease free.