

Sentinel Lymph Node Biopsy Reveals a Positive Popliteal Node in Clear Cell Sarcoma

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Abstract. Clear cell sarcoma of the tendons and aponeuroses is an aggressive, rare soft tissue tumor with frequent metastases to regional lymph nodes. Sentinel lymph node biopsy, which has dramatically changed the management of melanoma, was used for clear cell sarcoma for an evaluation of popliteal and groin lymph node status. Although all isosulfan blue-stained groin lymph nodes were negative for malignancy, a popliteal lymph node was positive. Adjuvant 50 Gy of radiotherapy to the popliteal node might have been effective for local control for one year.

Clear cell sarcoma of tendons and aponeuroses (CCSTA) is a rare malignant tumor that occurs predominantly in the extremities, constituting 1% of all soft tissue sarcomas (1). CCSTA was first described as a distinct clinicopathological entity by Enzinger in 1965 (2). CCSTA was originally considered to be malignant melanoma, due to the histological features similar to malignant melanoma, such as the presence of melanin and positive melanoma-associated immunostaining with HMB-45 (2). The presence of a reciprocal translocation, t(12;22)(q13;q12), has been detected in the majority of CCSTA cases, resulting in fusion of the *EWS* and *ATF1* genes (3). The absence of this translocation in malignant melanoma led to the distinction between CCSTA and malignant melanoma.

As for all groups of soft tissue sarcomas, complete surgical resection is the mainstay of the treatment for CCSTA, with or without radiotherapy (1, 4, 5). Though the overall incidence of regional lymph node metastases in sarcoma is low (6), approximately one-third of the CCSTA patients develop regional lymph node metastases during the follow-up (1, 4, 5), and many patients with lymph node metastasis will develop distant metastasis (2, 5, 7, 8).

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Intra-operative lymphatic mapping and sentinel lymph node (SLN) biopsy are the techniques to assess the presence of metastatic disease in the regional lymphatic basin, and have recently been introduced for patients with melanoma and patients with breast cancer (9-11). The core concept of SLN biopsy is that the SLN is the first lymph node in the lymphatic basin to receive lymphatic flow from the tumor. Therefore, the histopathological analysis of SLN reflects the disease status of the entire lymphatic field (11). In utilizing SLN biopsy to evaluate the regional lymphatic basin, surgeons could avoid massive lymphadenectomy in the case of SLN-negative patients. On the other hand, in SLN-positive cases, additional complete lymph node dissection or adjuvant therapy should be considered.

We present the case of a patient with a clear cell sarcoma on the lateral aspect of her right ankle, on whom we performed SLN biopsy on both the popliteal and groin lymph nodes using isosulfan blue dye. Histological examination of SLN revealed one positive popliteal node and no positive inguinal nodes.

Case Report

A 13-year-old female presented to her general practitioner with a 1-year history of a slowly enlarging painless palpable mass in the lateral aspect of her right ankle, and was referred to our institution. She had no family history of malignancy. On clinical examination, there was a 3 x 3 cm mass above the lateral malleolus of her right ankle (Figure 1), but no tenderness and no skin pigmentation. There were several small palpable lymph nodes in the groin, but not at the poplitea. The patient underwent biopsy with local anesthesia. Histology confirmed the presence of a clear cell sarcoma. After obtaining informed consent from the patient and family, and approval from the Institutional Review Board of our hospital, 1 ml of isosulfan blue dye (Patent Blue V, Guerbet, France) was intraoperatively injected intra- and

sub-dermally around the primary site, and 5-10 min were allowed to pass. Six inguinal and 1 popliteal stained lymph nodes were identified (Figure 2). All the identified nodes were resected and subjected to histological examination of the frozen section. None of the 6 inguinal lymph nodes were positive for malignancy, while 1 popliteal node was positive. To examine whether the SLN biopsy was truly negative, unstained lymph nodes in the groin were all dissected and subjected to histological examination. All of the nodes were confirmed as negative. Subsequently, the primary tumor was excised with a 3-cm skin margin, and lateral malleolus, parts of the talus, calcaneus, tibia, navicular and cuboid bones were resected with the tumor. The peroneus longus and brevis and the extensor digitorum longus were also sacrificed. Arthrodesis was performed for all the resected joints with a free bone graft obtained from the ilium. Tendons of the extensor digitorum longus were fixed to the residual tarsal bones. The defect in the soft tissue was reconstructed with a free vascularized latissimus dorsi flap. The final histological diagnosis revealed that the margins were all clear. Postoperatively, the patient underwent 50 Gy of radiotherapy at the poplitea, and there was no remarkable complication. One year later, the patient remained free of disease in the follow-up and can walk without any assistance.

Discussion

CCSTA is an extremely rare, slow-growing malignant tumor, affecting mainly adults in their thirties and forties (1). The tumor usually arises in the lower extremities, particularly in the foot and ankle, in association with tendons and aponeuroses. At presentation, most of the tumors are smaller than 5 cm in greater diameter, however, they behave as very aggressive tumors because of the high incidence of local recurrence, regional lymph node and distant metastasis (12). Several prognostic factors have been suggested, including regional lymph node metastasis and local recurrence as adverse prognostic features (5). To clarify the stage of lymph node, SLN biopsy is widely utilized to avoid radical lymphadenectomies for node-negative patients, reducing the number of complications, such as lymphedema (13). In CCSTA patients, the incidence of lymph node metastases is almost as common as lung metastases, indicating prophylactic selective regional lymph node dissection as part of the therapy (14). To our knowledge, there are only 2 reports concerning SLN biopsy for patients of clear cell sarcoma (15, 16). Al-Refaie *et al.* (15) described three cases of CCSTA in whom simultaneous SLN biopsy was performed. In two of the cases identified lymph nodes were negative for malignancy, and one of the cases revealed positive

inguinal lymph nodes, whereas popliteal lymph nodes were negative. In our case, all confirmed inguinal lymph nodes were negative, whereas one blue-stained popliteal lymph node was positive for malignancy, differing from the typical cases in malignant melanoma. Given that the pathway of lymphatic drainage between the malignant melanoma and CCSTA seemed to be similar because of the location of these tumors, the percentage of lymphatic drainage to the popliteal basin in patients with CCSTA will not be far from the percentage of malignant melanoma. In malignant melanoma, lymphatic drainage to the popliteal basin occurred in 6%-9% of patients at or distal to the knee (17, 18). 6%-9% patients have popliteal drainage, however, less than 0.4% of all patients with malignant melanoma develop metastatic disease in popliteal lesion (17), suggesting a low metastatic rate to the popliteal basin. The current case showed a deep, subfascial node that was blue-stained and diagnosed as positive for malignancy, thus suggesting that popliteal lymph nodes are first-order sentinel nodes in this case.

There have been difficulties in developing the optimal management of CCSTA due to the rarity of this disease and the poor response to chemotherapy. Adjuvant radiotherapy seems to be beneficial for improving local control in CCSTA, both in cases of inadequate surgical margins (5) and wide excision (19), leading to the idea that it might exert effects on local control of regional lymph nodes. There are 2-6 popliteal lymph nodes in general, lying within the fat surrounding the major vessels and nerves. In this case, radical lymphadenectomy for popliteal lymph nodes was not performed considering the high complications, but the patient received adjuvant 50 Gy of radiation post-operatively.

To our knowledge, this is the first case that a positive popliteal lymph node and negative inguinal lymph nodes for malignancy were confirmed by SLN biopsy in CCSTA. Long-term follow-up of this case, the pathway of lymphatic drainage to the popliteal and groin basin in CCSTA, the significance of SLN biopsy and the effectiveness of adjuvant therapy for this disease should be further studied.

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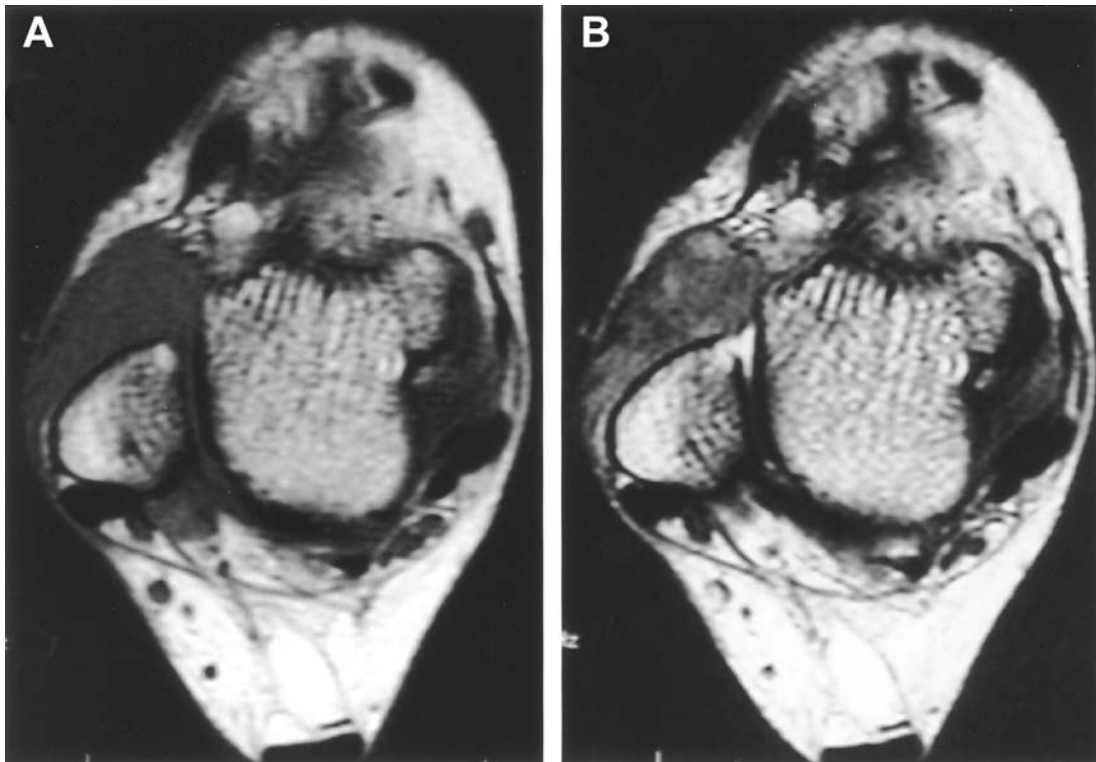


Figure 1. Magnetic resonance image (MRI) axial section. T1-weighted image shows low signal intensity lesion adjacent to lateral malleolus (A). T2-weighted image shows low and high intensity lesion. The low intensity area may represent the lesion of melanin pigmentation.

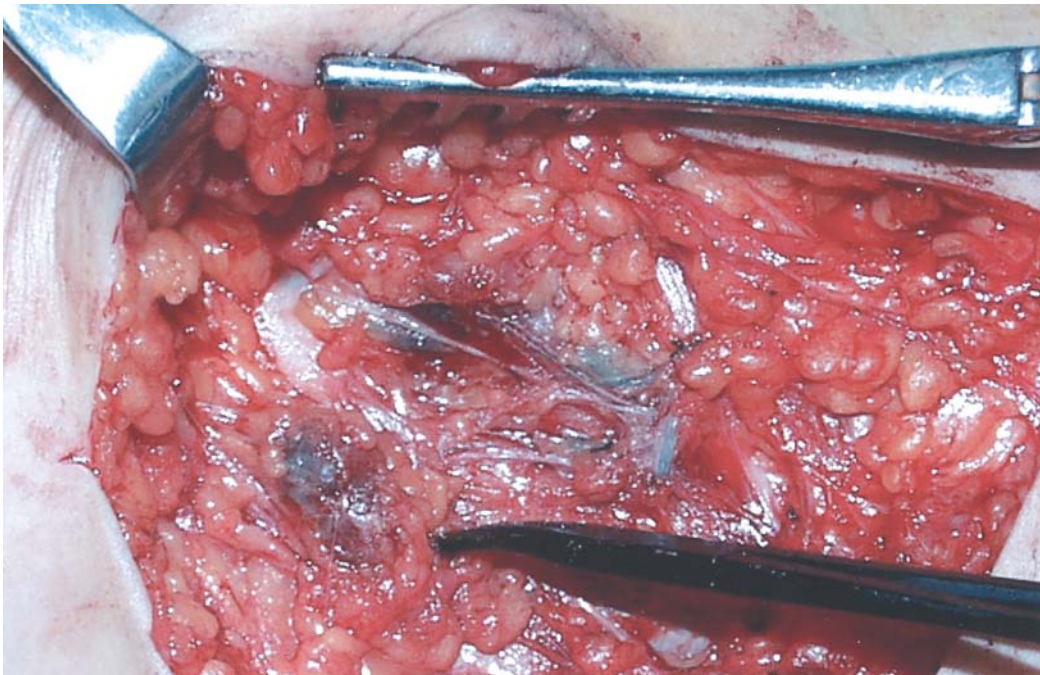


Figure 2. Dark blue-stained lymph nodes. One ml of Patent Blue was injected, followed by exposure of the right superficial inguinal lymph nodes.

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