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Characterization of cartilaginous tumors with ^{201}Tl scintigraphy

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Histological diagnosis and grading of cartilaginous tumors are closely correlated with patient prognosis; consequently, they are essential elements. We attempted to clarify the characteristics of ^{201}Tl uptake in various histological types of cartilaginous tumors and to assess its clinical value. ***Methods:*** Twenty-two cases with histologically proven cartilaginous tumors (3 enchondromas, 15 conventional chondrosarcomas (grade I = 9, II = 5, III = 1), 3 mesenchymal chondrosarcomas, and 1 de-differentiated chondrosarcoma) were examined retrospectively. Planar ^{201}Tl images were recorded 15 min following intravenous injection of ^{201}Tl (111 MBq). ^{201}Tl uptake in the tumor was evaluated visually employing a five-grade scoring system: 0 = no appreciable uptake, 1 = faint uptake above the background level, 2 = moderate uptake, 3 = intense uptake but lower than heart uptake and 4 = uptake higher than heart uptake. ***Results:*** ^{201}Tl uptake scores were 0 in 3 of 3 enchondromas, 9 of 9 grade I, and 4 of 5 grade II conventional chondrosarcomas. ^{201}Tl uptake scores were 1 among 1 of 5 grades II and a grade III conventional chondrosarcoma. Mesenchymal chondrosarcoma and de-differentiated chondrosarcoma displayed ^{201}Tl uptake scores of 2 or 3. ***Conclusions:*** Absence of elevated ^{201}Tl uptake in cartilaginous tumors was indicative of enchondroma or low-grade conventional chondrosarcoma. However, in instances in which ^{201}Tl uptake is obvious, high-grade chondrosarcoma or variant types should be considered.

Key words: ^{201}Tl, bone and soft tissue sarcoma, chondrosarcoma

INTRODUCTION

CARTILAGINOUS TUMORS, which include both benign and malignant lesions, are one of the most common neoplasms of bone and soft tissues. They are characterized by the presence of chondrocytes within and surrounded by cartilaginous matrix. Chondrosarcoma comprises approximately 10% of malignant primary bone tumors.[1,2] Conventional chondrosarcomas are generally classified by a three-grade system based on their histological features including cellularity and nuclear atypia. Variants including dedifferentiated chondrosarcoma, mesenchymal chondrosarcoma and clear cell chondrosarcoma are rare but do occur. The risk of metastasis is highly dependent on tumor histology and grade.[3–5] Therefore, radiological methods could play an important role in terms of evaluation of the grade of malignancy. However, CT, MRI and angiography do not possess sufficient ability in this regard.[6–9]

^{201}Tl scintigraphy is a tumor imaging technique employed for visualization of the nature of lesions.[10] Numerous reports in the literature have demonstrated the benefit of ^{201}Tl scintigraphy with respect to differentiation of malignant and benign tumors on the basis of the degree of tracer uptake in various organs.[11–18] Currently, however, no detailed documentation exists which describes ^{201}Tl uptake in cartilaginous tumors.[19]

Consequently, the objective of this study was to elucidate the features of ^{201}Tl uptake in various cartilaginous tumors from a perspective of histological diagnosis and grading. The clinical importance of ^{201}Tl scintigraphy for the evaluation of cartilaginous tumors is also discussed on the basis of our scintigraphic findings.

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MATERIALS AND METHODS

Patients

Twenty-two patients presenting with bone and soft tissue tumors, who underwent ^{201}Tl scintigraphy and whose lesions were subsequently shown to be cartilaginous tumors by histological examination with the surgically removed specimen, were enrolled in this retrospective study. There were 3 enchondromas, 15 conventional chondrosarcomas (grade I = 9, II = 5, III = 1), 3 mesenchymal chondrosarcomas, and one de-differentiated chondrosarcoma.

Thallium-201 Scintigraphy

A dose of 111 MBq of ^{201}Tl chloride was injected intravenously followed by planar imaging at 15 minutes follow-

Table 1 Tl-201 uptake score and uptake ratio in various kinds of cartilaginous tumor

Patient number	Sex	Age	Pathological diagnosis	Location	Size (cm)	Uptake score*	Uptake ratio**
1	M	59	enchondroma	femur	7	0	—
2	F	25	enchondroma	femur	8	0	—
3	F	34	enchondroma	humerus	6	0	—
4	M	37	chondrosarcoma grade I	sacral	7	0	—
5	F	32	chondrosarcoma grade I	femur	8	0	—
6	M	28	chondrosarcoma grade I	acetabulum-pubes	15	0	—
7	F	61	chondrosarcoma grade I	ilium	10	0	—
8	M	40	chondrosarcoma grade I	vertebra	15	0	—
9	F	53	chondrosarcoma grade I	pelvis	10.5	0	—
10	M	35	chondrosarcoma grade I	femur	12	0	—
11	M	54	chondrosarcoma grade I	scapula	13	0	—
12	F	63	chondrosarcoma grade I	ilium	3.8	0	—
13	F	55	chondrosarcoma grade II	pelvis	7	0	—
14	F	49	chondrosarcoma grade II	pelvis	15	0	—
15	M	67	chondrosarcoma grade II	acetabulum	5	0	—
16	F	42	chondrosarcoma grade II	scapula	12	0	—
17	F	73	chondrosarcoma grade II	femur	16	1	1.17
18	M	57	chondrosarcoma grade III	femur	12	1	2.10
19	F	80	dedifferentiated chondrosarcoma	tibia	12	3	3.70
20	F	66	mesenchymal chondrosarcoma	buttock	9	2	1.45
21	M	32	mesenchymal chondrosarcoma	thigh	13	2	1.43
22	M	36	mesenchymal chondrosarcoma	calf	4	2	3.06

* Visually evaluated score the Tl-201 uptake employing a five-grade scoring system

** Ratios calculated by dividing the count density of the ROI of the lesion by that of the background ROI

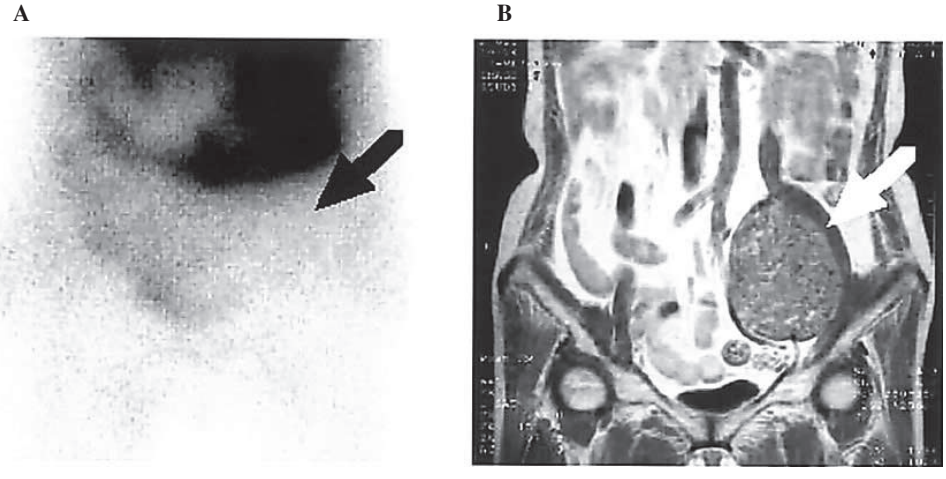

Fig. 1 Planar ^{201}Tl (A) and coronal T1-weighted magnetic resonance (B) images of a patient presenting with conventional grade I chondrosarcoma of the pelvis (patient number 9). Increased ^{201}Tl uptake was not observed in the lesion corresponding to the tumor location disclosed by intermediate signal intensity on the magnetic resonance images (*arrows*).

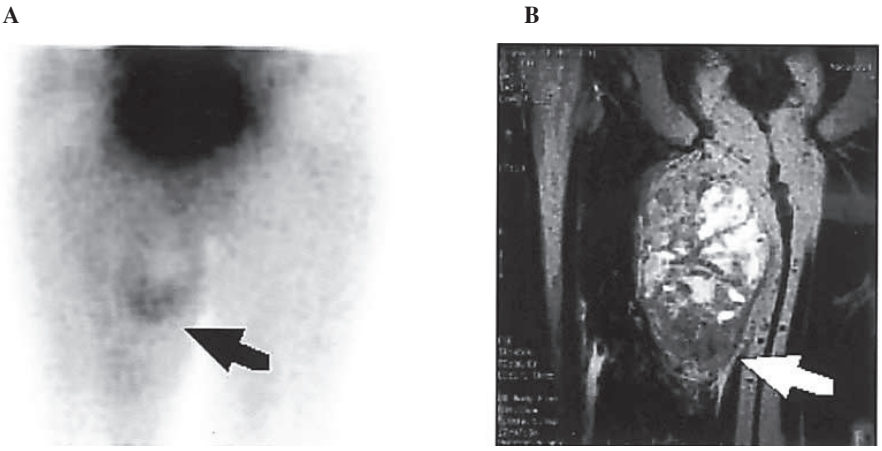

Fig. 2 Planar ^{201}Tl (A) and coronal T2-weighted magnetic resonance (B) images of a patient presenting with mesenchymal chondrosarcoma of the thigh (patient number 21). A distal portion of the tumor displayed increased ^{201}Tl uptake (*black arrow*), which corresponded to an area of decreased signal intensity on the T2-weighted magnetic resonance image (*white arrow*) also indicating the increased cellularity in the portion.

ing tracer injection with a two-headed gamma camera equipped with low-energy, high-resolution parallel-hole collimators. ^{201}Tl uptake in the tumor was evaluated visually employing a five-grade scoring system: 0 = no appreciable uptake, 1 = faint uptake above the background, 2 = moderate uptake, 3 = intense uptake but lower than heart uptake, and 4 = uptake equal to or greater than heart uptake. When the uptake was observed only in a limited portion in the tumor lesion, the visual scoring was perfomed based on the strongest uptake in the tumor lesion. Semi-quantitative analyses were also performed for those lesions demonstrating ^{201}Tl uptake in the visual evaluation. A region of interest (ROI) was set manually on the entire lesion and a symmetrical ROI was set on the contralateral normal area or the adjacent area as a background. When necessary, CT or MRI was referenced for the tumor location. The uptake ratio was then calculated by dividing the count density of the ROI of the lesion by that of the background ROI.

RESULTS

All patient data are summarized in Table 1. Enchondroma displayed no increase in ^{201}Tl uptake. None of the grade I and 4 of 5 grade II conventional chondrosarcomas exhibited any increase in ^{201}Tl uptake either, which precluded differentiation from enchondroma. However, grade III chondrosarcoma and all variant types of chondrosarcoma (mesenchymal (n = 3) and de-differentiated (n = 1)) demonstrated increased ^{201}Tl uptake. Representative images of conventional (grade I) and mesenchymal chondrosarcomas are presented in Figure 1 and Figure 2.

DISCUSSION

Histological diagnosis and grading of cartilaginous tumors are strongly correlated with patient prognosis; as a result, these factors are extremely important in terms of patient management[4]; conventional high grade, de-differentiated and mesenchymal chondrosarcomas exhibit aggressive clinical features and a poor prognosis. Enchondromas and most cases with conventional grades I and II chondrosarcoma displayed no increased ^{201}Tl uptake in the lesion. Therefore, differentiation of enchondroma from conventional low grade chondrosarcoma by ^{201}Tl imaging is not feasible. However, all lesions commonly characterized by aggressive clinical features including grade III, mesenchymal and de-differentiated chondrosarcoma demonstrated a significant increase in tracer uptake. Consequently, ^{201}Tl scintigraphy should be of limited yet significant value for grading of cartilaginous tumors as a non-invasive method.

Several radiopharmaceuticals, which are governed by distinct mechanisms of localization in tumors, are currently available for tumor imaging, including ^{201}Tl, ^{99m}Tc-MIBI, ^{99m}Tc-tetrofosmin and ^{18}F-FDG. Among these radioisotopes, ^{201}Tl behaves in a manner similar to potassium chloride in biologic systems; moreover, tumor uptake is believed to reflect various factors including the malignant nature of the lesion, blood flow and vascular permeability, cell viability and number of cells in the tumors, activities of Na^+-K^+ ATPase system and co-transport system.[10,20] Several reports have documented the clinical diagnostic value of ^{201}Tl scintigraphy in cases with malignancies such as lung,[17,18,21] thyroid[22] and brain[12,23] tumors. In general, malignant tumors exhibit higher ^{201}Tl uptake relative to benign neoplasms.

However, oftentimes, exceptional findings exist with respect to tumors in the bone and soft tissue due to histological variability of tissue components, cell number and vascularity. Intense ^{201}Tl uptake in benign giant cell tumor of bone is a noteworthy example.[16,19] Therefore, characteristics of ^{201}Tl uptake in each histological grade of bone and soft tissue tumor should be analyzed.

Low grade chondrosarcomas demonstrated no increased ^{201}Tl uptake, despite their classification as malignant tumors. Cell number and vascularity are relatively low in low grade conventional chondrosarcoma in comparison with other types of malignant neoplasms,[24–26] which may be one of the reasons for negative ^{201}Tl uptake. In contrast, high grade conventional and variant chondrosarcomas (mesenchymal and de-differentiated) commonly exhibit increased cell proliferative activities, dense cell component and hypervascularity.[24–26] These histological characteristics may contribute to increased ^{201}Tl uptake in the lesion.

In addition, ^{201}Tl scintigraphy may be valuable for the determination of biopsy site. In the event that ^{201}Tl localization occurs in specific areas of the tumor, the particular uptake site may be a high grade region, which can serve as a representative site reflecting patient prognosis (Fig. 2). Another possible benefit of ^{201}Tl scintigraphy is the early assessment of therapeutic effects.

We assessed the ^{201}Tl uptake in both visual scoring (uptake score) and semi-quantitative analyses (uptake ratio). The visual score was graded based on the strongest uptake part in the lesion, and the semi-quantitative analysis was perfomed based on the ROI on the entire lesion. These differences resulted in some discrepancies between the two methods; uptake scores in patient number 20 and 21 were higher than that in patient number 18, whereas uptake ratios in number 20 and 21 were lower than number 18. When uptake is observed in a limited part of the tumor lesions, the uptake ratio tended to be lower. The semi-quantitative analysis is an objective method compared to visual analysis. However, the most malignant portions of the tumor influence patient outcome, and therefore the visual analysis has some advantages in this point.

In our patient group, all four highly malignant lesions (grade III, mesenchymal and de-differentiated chondrosarcoma) demonstrated significantly increased tracer uptake. However, additional data in large patient groups are required to verify if there are no exceptions in the increased uptake in such histological types. Besides, comparison between other imaging modalities such as plain X-ray, X-ray CT or MRI should be performed to confirm the clinical usefulness of ^{201}Tl scintigraphy for the assessment chondrosarcoma.

CONCLUSION

No appreciable ^{201}Tl uptake was observed in enchondroma or low grade conventional chondrosarcoma. However, high grade and variant types of chondrosarcoma were characterized by increased ^{201}Tl uptake. As a result, ^{201}Tl scintigraphy facilitates evaluation of the grade of malignancy of cartilaginous tumors; consequently, scintigraphic findings might reflect prognosis in patients presenting with cartilaginous tumors.

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