

# Spindle Cell Lipoma: A Case Report and Literature Review on Japanese Patients

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## Spindle Cell Lipoma: A Case Report and Literature Review on Japanese Patients

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### Key Clinical Message

Spindle cell lipoma is a subtype of lipoma consisting of spindle-shaped cells, collagen fibers, and proliferated mature adipocytes. The review of 85 cases showed its continuous growth and its imaging findings indistinguishable from malignant tumors.

### Introduction

Spindle cell lipoma (SCL), proposed by Enzinger and Harvey [1] in 1975, is a benign soft tissue tumor. It is regarded as a subtype of lipoma composed of spindle-shaped cells and collagen fibers in various percentages among enlarged mature adipocytes. Tumor cells are positive for CD34 and negative for S-100 protein and murine double minute 2 (MDM2). Since SCL is rare, accounting for only 1.5% of lipomas [2], its characteristics remain unclear. Furthermore, SCL is often difficult to distinguish from atypical lipomatous tumors and liposarcoma in imaging examinations. Therefore, the clinical characteristics of SCL warrant further study.

Racial differences have been reported in some mesenchymal tumors, such as Kaposi's sarcoma, dermatofibrosarcoma protuberance, angiosarcoma, and leiomyosarcoma [3], and, thus, need to be examined in each racial population. The characteristics of SCL have not yet been investigated in a single racial population. Therefore, we herein report the findings of a Japanese case of SCL and review a Japanese case series of SCL.

### Materials and Methods

## Patient and Data

The Ethics Committee of the Jikei University School of Medicine approved the case report with written informed consent from our patient. In the review of the case series, we searched for case reports of SCL between 1979 and 2022 in the Japan Medical Abstracts Society, a database of Japanese medical literature. We collected data including age, sex, the period from perception of the tumor to the first hospital visit, the site of occurrence, size, heterogeneity in imaging examinations, enhancement on enhanced imaging, the presence or absence of a capsule in macroscopic findings, the presence or absence of recurrence, and a follow-up period.

A statistical analysis was performed using the commercial software, SPSS (IBM, Armonk, NY). A linear regression analysis was conducted to investigate the relationships between two types of quantitative parameters. The Mann-Whitney U test was used to examine differences in quantitative parameters between two groups. Pearson's chi-square test was employed to analyze differences among qualitative parameters.  $P < 0.05$  was considered to be significant.

## Results

### Case report

A 45-year-old Japanese man was referred to us with a few day-history of a subcutaneous mass in the left shoulder area. The patient had arrhythmogenic right ventricular cardiomyopathy associated with arrhythmia after cardioverter-defibrillator implantation and dyslipidemia. There was no family history of mesenchymal tumors or a previous history of trauma to the left shoulder area.

A physical examination revealed a 7-cm dome-shaped subcutaneous mass on the left shoulder with poor mobility to the lower floor (**Figure 1a**). Magnetic resonance imaging (MRI) showed a subcutaneous mass measuring approximately  $6.0 \times 5.0 \times 2.5$  cm without findings of invasion into the deep muscle layer (**Figure 1b**). The tumor had a well-demarcated margin from the surrounding tissue and a heterogeneous structure with a septum. Fat-suppressed T1-weighted images revealed fat-suppressed areas, suggesting the presence of a fatty component (**Figure 1c**). Based on these findings, we initially considered the tumor to be an atypical lipomatous tumor or liposarcoma. Therefore, we dissected the tumor with a narrow margin for a histopathological examination. Dissection from the surrounding tissues was relatively easy. The excised mass was covered with an elastic, soft, and thin capsule that was yellowish in color and contained hard, whitish nodules.

The histopathological examination showed the lobular proliferation of mature adipocytes, bundles of collagen fibers, and spindle-shaped cells (**Figure 1d and 1e**). Adipocytes and spindle-shaped cells had neither atypical nuclei nor mitosis. Immunohistochemical staining revealed that spindle-shaped cells were positive for CD34 and negative for S100 protein, MDM2,  $\alpha$ -smooth muscle actin ( $\alpha$ SMA), cyclin-dependent kinase 4 (CDK4), signal transducer and activator of transcription 6 (STAT6), and desmin. Less than 5% of tumor cells were positive for mindbomb E3 ubiquitin protein ligase 1 (MIB1) (**Figure 2**). Based on these results, the patient was diagnosed with SCL. Twelve months after surgery, neither recurrence nor postoperative complications have been observed.

### Review

A total of 128 Japanese cases, including the case described above, were reported during the period examined. Eighty-five cases were positive for CD34 and negative for S-100 protein and MDM2 and, thus, were regarded as definitive SCL [4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62] (**Supplementary Table 1**).

The average age of patients at the first hospital visit was  $59.2 \pm 12.2$  years (**Table 1**). The male-to-female ratio was approximately 4:1 (69 males and 16 females). The tumor appeared in the neck in 26 cases (30.6%), the oral cavity in 13 (15.3%), the lower extremities in 12 (14.1%), the shoulder in 9 (10.6%), the back in 7

(8.2%), the head in 7 (8.2%), the chest in 3 (3.5%), the groin and genital area in 3 (3.5%), the abdomen in 2 (2.4%), and the upper extremities in 2 (2.4%), except for 1 case had multiple occurrences across many regions. Among 71 cases with relevant data, the tumor occurred in subcutaneous tissue in 64 cases (90.1%), muscle tissue in 6 (7.1%), and submuscular tissue in 1 (1.2%). Among 66 cases with relevant data, the imaging examination showed a well-demarcated margin in 63 cases (95.5%) and an irregular margin in 3 (4.5%). Among 65 cases with relevant data, the imaging examination showed heterogeneity in 50 cases (76.9%) and homogeneity in 15 (23.1%). Among 33 cases with relevant data, the imaging examination also showed the presence of enhancement in 30 cases (90.9%) and its absence in 3 (9.1%). Among 41 cases with relevant data, the capsule of dissected tumors was present in 38 (92.7%) and absent in 3 (7.3%). Among 80 cases with relevant data, tumors were dissected with a narrow margin in 69 cases (86.3%) and a wide margin in 11 (13.8%). The average follow-up period was  $1.3 \pm 1.4$  years in 65 cases with relevant data on the follow-up period. Recurrence was detected in one (1.5%) of the 65 cases followed up.

We performed statistical analyses of the data described above. Age at the first hospital visit was significantly older in male patients than in female patients;  $60.7 \pm 11.8$  years in male patients vs.  $52.6 \pm 12.8$  years in female patients ( $p = 0.029$ , the Mann-Whitney U test, **Table 2**). A significant difference was observed in tumor occurrence sites between male and female patients; the tumor occurred in the lower extremities in 7 female patients (43.8%) and the neck in 25 male patients (36.8%) ( $p = 0.014$ , Pearson's chi-square test; **Table 2**). A positive correlation was noted between the maximum gross tumor diameter and the period from perception of the tumor to the first hospital visit ( $p = 0.004$ , a linear regression analysis) (**Figure 3**). Furthermore, a correlation was observed between the maximum gross tumor diameter and contrast enhancement in imaging studies ( $p = 0.05$ , the Mann-Whitney U test). However, the period from perception of the tumor to the first hospital visit did not correlate with tumor heterogeneity on imaging.

## Discussion

The present study described the findings of a Japanese case of SCL and reviewed a Japanese case series of SCL, which were described by researchers in various medical departments in a cross-sectional manner, including orthopedics, plastic surgery, dentistry, otorhinolaryngology, radiology, respiratory medicine, pathology, urology, surgery, and dermatology. The results obtained suggest that SCL continuously grows, and its imaging findings may become indistinguishable from those of malignant soft tissue tumors over the long period from its onset.

Previous studies reported that the peak age of onset of SCL was between 45 and 65 years [1, 2]. These findings are consistent with the present results, showing an average age of 59.2 years. SCL commonly occurs in subcutaneous tissue in the nuchal region, shoulder, and back [1]. In addition to these findings, the present study indicated the oral cavity and lower extremities as sites predisposed to developing SCL, at least in Japanese patients.

According to the classification in the World Health Organization, lipomatous tumors are classified based on the prognosis of patients. SCL, an atypical lipomatous tumor, and liposarcoma are regarded as benign, intermediate malignant, and malignant lipomatous tumors, respectively [63]. Previous findings and the present results indicate that SCL often shows heterogeneity and enhancement in imaging examinations, suggesting malignancy in contrast to banal lipoma. An imaging examination was not useful for reaching a diagnosis in the present case, which was indistinguishable from malignant lipomatous tumors because of its heterogeneity. Therefore, the definite diagnosis of SCL required a histopathological examination.

Banal lipoma does not show a significant sex difference [64]. In contrast, previous findings and the present results indicated significant sex differences in SCL. Furthermore, the present study demonstrated that SCL was approximately 4-fold more common in males than in females, which was consistent with previous findings, showing the male predominance of SCL [65]. The present study also showed that tumors were more likely to develop at a significantly older age in Japanese males than in Japanese females. Furthermore, the site of occurrence of SCL significantly differed between the sexes. The most common site of occurrence was the lower extremities in women (7/16 cases), and the neck in men (25/68 cases), which may be attributed to sex

hormones; however, the underlying mechanisms remain unknown.

The present study revealed the clinical importance of the period from perception of the tumor to the first hospital visit. The results obtained showed that i) the period from perception to the first hospital visit positively correlated with the maximum gross tumor diameter, and ii) the period from perception to the first hospital visit was significantly longer in patients with enhancement than in those without. On the other hand, statistical analyses failed to show that the period from perception to the first hospital visit was significantly longer in patients with tumor heterogeneity on images than in those without. This may be due to a delay in perception of the tumor in many patients, which also led to an underestimation of the period from the onset of the tumor to the first hospital visit. In the present case, the 7-cm tumor was only perceived a few days before the first hospital visit.

In the present study, a correlation was observed between enhancement and the period from perception to the first hospital visit, but not between the period and heterogeneity referring to structures with different densities/signal intensities regardless of the administration of a contrast agent. Thus, studies reporting heterogeneity may have been performed without a contrast agent, which may explain the higher sensitivity in the detection of enhancement than heterogeneity among the reported cases.

There are a number of limitations that need to be addressed. The present study was conducted to review various case reports from multiple institutes. Therefore, the quality of imaging examinations was not standardized. Furthermore, there was a lack of relevant clinical data in some case reports, which may have affected the reliability of the statistical analysis.

## Conclusion

The present study described the characteristics of SCL in Japanese patients. Physicians need to be aware that SCL may continuously grow, and its imaging findings may become indistinguishable from those of malignant soft tissue tumors over the long period from its onset.

**Acknowledgments:** Not applicable.

**Statement of Ethics:** The study protocol was approved by The Ethics Committee of The Jikei University School of Medicine and the patient provided written informed consent.

**Consent statement:** Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

**Availability of data and material:** Data that support the results of the present study are available from the corresponding author, Y.N., upon reasonable request.

**Competing interests:** The authors declare that they have no competing interests.

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**Authors' contributions:** K.H. contributed to data collection, data analysis, results interpretation, a literature review, and writing the draft manuscript. M.O. contributed to data collection. Y.N. contributed to the study conception, study design, and writing the final manuscript draft. A.A. contributed to supervision. All authors read and approved the final manuscript.

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## Figure legends

### Figure 1. Macroscopic, imaging, and microscopic findings of the present case

**a)** Macroscopic findings. A 7-cm dome-shaped subcutaneous mass is observed on the left shoulder. **b)** T1-weighted magnetic resonance image. A subcutaneous mass measuring approximately  $6.0 \times 5.0 \times 2.5$  cm is present in the left shoulder region. The mass is well-demarcated from the surrounding area without invasion into the deep muscular layer. The signal is heterogeneous, ranging from low to high, with a septal-like structure. **c)** Fat-suppressed T1-weighted magnetic resonance imaging. The overall signal is decreased. **d)** Microscopic findings (hematoxylin and eosin staining,  $\times 40$ ). The lobular proliferation of mature adipocytes, bundles of collagen fibers, and spindle-shaped cells are evident. **e)** Microscopic findings (hematoxylin and eosin staining,  $\times 400$ ). Adipocytes and spindle-shaped cells have neither atypical nuclei nor mitosis.

## Figure 2. Immunohistochemistry

The immunohistochemical findings of a typical region in the tumor in the present case are represented ( $\times 40$ ). An image of hematoxylin and eosin staining is presented as a control in the same section. **a)** Hematoxylin and eosin, **b)** CD34, **c)** MIB1, **d)** CDK4, **e)** MDM2, **f)** STAT6, **g)** S-100 protein, **h)**  $\alpha$ SMA, and **i)** desmin.

## Figure 3. Relationship between the tumor diameter and period from its perception

The relationship between the maximum gross tumor diameter and the period from its perception to the first hospital visit is represented as a scatter plot graph. The horizontal axis indicates the period from perception of the tumor to the first hospital visit (years). The vertical axis indicates the maximum gross tumor diameter (cm).

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