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| メールアドレス: | |
| 所属: | |
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Dedifferentiated liposarcoma of the oral floor: A case study and literature review of 50 cases of head and neck neoplasm

FUMIKAZU NIMURA1, TOSHIYUKI NAKASONE2, HIROFUMI MATSUMOTO3, TESSHO MARUYAMA1,2, AKIRA MATAYOSHI2, NOBUYUKI MARUYAMA1,2, NAOKI YOSHIMI3,4, AKIRA ARASAKI1,2 and KAZUHIDE NISHIHARA1,2

1Department of Oral and Maxillofacial Functional Rehabilitation, Graduate School of Medicine, University of the Ryukyus; Departments of 2Oral and Maxillofacial Surgery and 3Pathology, University Hospital of the Ryukyus; 4Department of Pathology and Oncology, Graduate School of Medicine, University of the Ryukyus, Nishihara, Okinawa 903-0215, Japan

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Correspondence to: Dr Tessho Maruyama, Department of Oral and Maxillofacial Functional Rehabilitation, Graduate School of Medicine, University of the Ryukyus, 207 Uehara, Nishihara, Okinawa 903-0215, Japan
E-mail: h075324@eve.u-ryukyu.ac.jp

Abstract. Dedifferentiated liposarcoma (DDLs) has a relatively poor prognosis, however this neoplasm rarely occurs in the head and neck. To date, no definite protocol has been established for the diagnosis and treatment of head and neck DDLs. The present study reports the case of a 69-year-old male patient with DDLs of the oral floor. To the best of our knowledge, this is the first documented case of oral floor DDLs. In addition, this is the first reported case with the development of a second primary malignancy following the treatment of head and neck DDLs. A literature review of 50 cases of head and neck DDLs revealed that preoperative biopsy is not reliable for the diagnosis of these tumors and an accurate pathological diagnosis with total resection is preferred.

Introduction

Liposarcoma (LS) is the most common tumor among sarcomas of the soft tissue (~20% of the tumors in adults) (1). This neoplasm was first described by Virchow (2) in 1857 and has been well documented thereafter (3,4). LS is categorized into four subgroups: atypical lipomatous tumor (ALT)/well-differentiated liposarcoma (WDLS), myxoid liposarcoma, pleomorphic liposarcoma, and dedifferentiated liposarcoma (DDLs) (5). Among these, DDLs is defined as a subtype of ALT/WDLS with non-lipogenic lesions (heterogenous lesions in one tumor) (5). DDLs has a high degree of malignancy; hence, its recurrence and metastasis rates are higher than those of other types of LS (6,7). DDLs can develop anywhere in the body; however, the head and neck (H&N) is a relatively rare site of occurrence of this lesion (7,8). The pathological features of DDLs are well defined (5,9). Here we report the case of a 69-year-old male patient with DDLs of the oral floor. It was difficult to determine the diagnosis clinically. Furthermore, to date, no definite protocol has been established for the diagnosis and treatment of H&N DDLs.

Case study

Written informed consent was obtained from the patient for the publication of this case report and accompanying images. The report was submitted for ethical review to the Ethics Committee of the University of the Ryukyus (Okinawa, Japan), which waived the requirement for review per institutional protocol because the study does not contain content that requires ethical approval. The Ethics Committee approved the submission and publication of the manuscript.

A 69-year-old man presented to the Department of Oral and Maxillofacial Surgery at Ryukyu University Hospital. He had noticed a slow-growing mass in his mouth and experienced difficulty in talking for approximately 1 year. Physical examination revealed a painless, smooth, and non-tender (firm) mass at the floor of the mouth (Fig. 1). The mass was covered by an intact mucosa. The Wharton duct was not involved by the mass, and clear saliva could be expressed from the sublingual gland duct. The patient's facial appearance was symmetrical, and there was no cervical lymphadenopathy. He had a history of alcohol consumption and was a current smoker, with no history of malignancy. The patient was being treated for diabetes mellitus. His brother had a history of colorectal cancer. Contrast-enhanced computed tomography (CT) demonstrated a large heterogenous mass under the tongue that seemed to push the hyoglossus muscles,
but no invasive lesion was present. The margins of the lesion were well defined. The adipose-like section of the mass was partially suspected. No other lesions were detected in the H&N, bones, and lungs. Contrast-enhanced magnetic resonance imaging (MRI) demonstrated a 50x39x43 mm lesion that pushed the hyoglossus muscle into the sublingual space and seemed to contain heterogeneous components (Fig. 2).

Most of the mass revealed low-signal in T1-weighted image and high-signal in T2-image. On the other hand, at the bottom of the mass, fat signals were partially detected. No other lesion was present. Based on the findings, the oral floor lesion was considered a tumor or cyst; however, an apparent clinical diagnosis could not be made. Moreover, performing biopsy for an oral floor is difficult (10). Therefore, we planned for surgical resection and accurate pathological examination.

The patient underwent surgical resection of the mass under general anesthesia. The mass had no adhesions to the surrounding tissue. The excised specimen was a 60x45x45 mm capsulated mass. The resected mass showed two areas: A pale yellow (fatty) area and milky-white (non-fatty) area; however, no cystic lesion was found (Fig. 3). Histopathological examination also revealed two distinct areas, but the findings were contrasting (Fig. 4A): i) The milky-white area contained a dedifferentiated area which was composed of spindle cell and pleomorphic cell with patchy necrosis. Spindle cell showed a fascicular architecture with hyperchromatic nuclei and eosinophilic cytoplasm. Bizarre multinucleate giant cells were occasionally seen (Fig. 4B); ii) the yellow area was a well-differentiated area, which demonstrated adipocytic proliferation with hyperchromatic stromal cells (Fig. 4C). The two areas mostly transitioned abruptly, and partly transitioned gradually. Immunohistochemical examination revealed positive results for S-100 in the adipocytic cells, whereas it revealed partial positive results for SMA, desmin and CDK4, but negative for caldesmon or MDM2 in the dedifferentiated component. Based on the findings, DDLS (FNCLCC system grade 2) was diagnosed. The tumor was clinically resected; however, histological surgical margin was positive. Therefore, postoperative radiotherapy (RT) (total 60 Gy) was performed to treat the residual tumor and to prevent the recurrence or metastasis of the disease (3,11). At 5 years 8 months postoperatively, no sign of local recurrence or distant metastasis of DDLS had been found, until the time of writing this report. However, pleomorphic LS of the chest wall was detected after 5 years 2 months postoperatively. The patient was treated and followed up at another hospital (Fukuoka University Hospital, Fukuoka, Japan) to this writing. Histologically, atypical spindle-shaped cells, bizarre giant cells, and lipoblast-like cells were revealed in the chest wall tumor. These cells were negative for MDM2 or CDK4. Further, no DDLS component was observed. Therefore, the chest wall tumor was considered a second primary tumor rather than a metastasis of DDLS.

Discussion

To the best of our knowledge, this is the first documented case of oral floor DDLS. Furthermore, our case is the first to exhibit the development of a second primary malignancy (SPM) after the treatment of H&N DDLS. We searched the English literature for H&N DDLS cases that occurred between 1979 and 2017, using PubMed and Google Scholar. The exclusion criteria were i) cases from non-English literature, ii) cases in which DDLS metastasis from non-H&N regions was apparent (12,13) and iii) a case in which it could not be determined whether the lesion was a DDLS or WDLS (14). We identified 50 cases (excluding the cases in Tirumani et al (12) study, where the number of cases was stated as ‘not applicable’ (NA), which are listed in Table I (7,11,12,15–42). However, no patient had oral floor DDLS. This list includes 2 cases of tongue DDLS (19,22), but clinical information regarding these cases was sparse. Therefore, we could not confirm whether the DDLSs involved the oral floor in these cases. As described in Table I, DDLS has been reported to develop at various sites in the H&N region (7,11,12,15–42). Among these, the most common site was the larynx (6 patients), followed by the cheek (5 patients), neck (3 patients), orbit (3 patients), pyriform sinuses (3 patients), buccal area (2 patients), tongue (2 patients), parotid gland, pharyngeal space, posterior neck, paralaryngeal area, nose, maxillary gingiva, and oral floor (current case), i.e., anywhere in the H&N region (Table I). The mean age was 58.7±17.27 years (range, 20-86 years), with a male/female ratio of 1.8:1. Most of the patients (except for the NA case) underwent contrast-enhanced CT or MRI for initial staging; however, no patient underwent positron emission tomography (PET) for initial staging (date not shown in Table I). Some patients underwent PET as an additional detection test after the first surgery (31) or as follow-up of radical surgery (37,42). For H&N DDLS, the outcomes are reportedly good with wide surgical excision (11). No patients underwent preoperative therapy, but 12 patients (including our case) underwent postoperative RT. No patient underwent postoperative chemotherapy, but one patient underwent therapy for the recurrence of the tumor (15). Given the sparse clinical details, the present literature review was unable to report any conclusions regarding treatment suggestions. Of 24 patients (except for the NA case), 3 (12.5%) reported recurrence and 1 (our case) developed SPM (4.2%); no patient with regional recurrence or distant metastasis was identified. However, case reports with long-term follow-up are limited. Of the 20 patients whose follow-up duration was reported, only 6 (30%) and 8 (40%) patients were followed up for >5 and 2 years, respectively. Meanwhile, cases of recurrence after 23 years of follow-up (16) and six recurrences over 26 years of follow-up (22) have been reported. Our case exhibited no recurrence or metastasis during 5 years of follow-up; however, SPM (pleomorphic LS of the chest wall) developed at 5 years after the H&N DDLS resection. We could not determine why the current patient developed SPM because there have been no reports of SPM in H&N DDLS cases to date. Lupo et al (43), reported on the statistical analysis of 8,785 sarcoma (at all regions of the body, including H&N) survivors diagnosed between 1992 and 2012 from the Surveillance, Epidemiology, and End Results database, using standardized incidence ratios. Among these, LS survivors (257 patients) had a relatively high SPM risk; however, there were no details regarding the DDLS survivors (30 patients) (43). To date, reports of SPMs in DDLS (at all regions of the body) cases are sparse (44). Therefore, our case indicates the possibility of SPM developing not only in the H&N region but also at all DDLS sites. According to the size of oral region LSs, lesions of >5.0 or >3.6 cm were reported as prognostic factors for recurrence, metastasis, or death (22,45). We researched the relationship between the size of H&N DDLS...
lesions and recurrence; however, no definitive data were found because of the sparsity of clinical information.

So far, no accurate protocol for DDLS (in all regions of the body, including H&N) management has been established (5,9). For both LS of the whole body and H&N, surgical resection is the standard treatment (7). However, the effects of pre- and postoperative therapy have been inaccurately reported so far (38). DDLS is a rare condition, and experimental DDLS models are lacking, leading to a delay in the development of suitable therapeutic strategies (46). Furthermore, DDLS may have site-specific characteristics. Henricks et al (17), studied 155 DDLS cases and concluded that retroperitoneal DDLS has a significantly worse prognosis than does DDLS at other sites. However, reports of H&N DDLS cases remain sparse because this is a relatively rare site for this tumor (7,37). Therefore, the accumulation of H&N DDLS cases with detailed clinical information and long-term follow-up is needed to establish a novel therapeutic protocol. We speculate that hidden H&N DDLS cases of recurrence, metastasis, or SPM exist.

Another important issue highlighted in this study is that biopsy (either incisional biopsy or fine needle aspiration) is not reliable for the diagnosis of DDLS. Table 1 shows that biopsy results have reported in 13 cases; however, DDLS was diagnosed in only 3 cases (23.1%). Even worse, 6 cases (46.2%) were misdiagnosed as benign lesions (5 cases) or ‘failures’ (1 case). DDLS generally involves heterogeneous lesions and occasionally presents as kinds of lesions (11,34,35,37). Petersson and Murugasu (37), reported a case of a unique DDLS lesion.
| First author | Year | Age | Gender | Site             | Size (cm) | Type of diagnosis based on biopsy findings | Histological type of DDLS | Grade and histological findings | Postoperative RT | Follow-up data                | (Refs.) |
|--------------|------|-----|--------|-----------------|-----------|-------------------------------------------|---------------------------|---------------------------------|-----------------|------------------------------|---------|
| Tobey        | 1979 | 61  | M      | Larynx          | NA        | (+)                                       | LS                         | (-)                             | (-)             | Approximately 6 months; recurrence and mortality | (15)    |
| McCormick    | 1994 | 62  | M      | Larynx          | NA        | NA                                        | NA                        | NA                              | NA              | 23 years; recurrence | (16)    |
| Henricks     | 1997 | NA  | NA     | H&N             | NA        | NA                                        | NA                        | NA                              | NA              | NA                           | (17)    |
| Henricks     | 1997 | NA  | NA     | Larynx          | NA        | NA                                        | NA                        | NA                              | NA              | NA                           | (17)    |
| Cai          | 2001 | 54  | F      | Orbit           | >2        | NA                                        | (-)                       | NA                              | NA              | 6 months; NED | (19)    |
| Nascimento   | 2002 | 83  | F      | Tongue          | 2.5       | NA                                        | NA                        | NA                              | NA              | 23 years; NED | (19)    |
| Diamond      | 2002 | 57  | M      | Cheek           | NA        | (+)                                       | Suggestive of neurofibroma| (-)                            | (+): 66 Gy | 12 months; NED | (20)    |
| Gonzalez-Lois| 2002 | 69  | M      | Pyriform sinus  | >3        | (+)                                       | Lipoma                    | (-)                             | (-)             | 6 months; NED | (21)    |
| Fanburg-Smith| 2002 | 39  | M      | Tongue          | 6         | NA                                        | Low-grade                 | NA                              | 6 years; NED | (22)            |
| Fanburg-Smith| 2002 | 56  | M      | Buccal (mucosa) | 5         | NA                                        | High-grade, focal myxoid features | NA                          | 26 years; 6 recurrences, but alive | (22)    |
| Fanburg-Smith| 2002 | 57  | F      | Parotid grand   | 5.5       | NA                                        | High-grade                | NA                              | 17 years; NED | (22)            |
| Roza         | 2004 | 61  | M      | Cheek           | 7         | (-)                                       | (-)                       | (-)                             | (+)             | Lost to follow-up | (23)    |
| Cunha        | 2005 | 42  | F      | Cheek           | 6         | (-)                                       | (-)                       | (-)                             | (+)             | 1 year; NED | (24)    |
| Angiero      | 2006 | 62  | M      | Cheek           | 3         | Incisional                                | LS                        | NA                              | (-)             | 7 years; NED | (25)    |
| Giordano     | 2006 | 50  | M      | Pyriform sinus  | 5         | (-)                                       | Low-grade                 | (-)                             | 6 months; NED | (26)            |
| Powitzky     | 2007 | 63  | M      | Larynx          | 4.5       | (+)                                       | Myxoid LS                 | High-grade, with myxomatous degeneration and element rhabdomyosarcoma | (+): 70.2 Gy | 16 months; NED | (11)    |
| Saeed        | 2007 | 56  | F      | Orbit           | NA        | (+)                                       | DDLS grade 2              | Grade 2                        | (+): 60 Gy | NED             | (27)    |
| Rogers       | 2010 | 83  | M      | Pharyngeal space| 8.6       | FNA                                       | No evidence of malignancy | NA                              | (+): 64 Gy | 19 months; NED | (28)    |
| Gritli       | 2010 | NA  | NA     | Neck            | NA        | NA                                        | NA                        | NA                              | (+)             | NED             | (29)    |
| First Author   | Year | Age | Gender | Site              | Size (cm) | Type of on biopsy | Histological diagnosis based on biopsy findings | Grade and histological type of DDLS | Postoperative RT | Follow-up data | (Refs.) |
|----------------|------|-----|--------|-------------------|-----------|-------------------|-----------------------------------------------|------------------------------------|-----------------|---------------|---------|
| Endo           | 2010 | 48  | M      | Neck              | 5         | (-)               | Low-grade                                     | (-)                               | 1 year; NED     | (30)          |
| Makeieff       | 2010 | 62  | F      | Larynx           | 8         | (+)               | NA                                            | (+)                               | NED             | (31)          |
| Stomeo         | 2012 | 76  | M      | Cheek             | 12+10     | Incisional        | Lipomatous lesion                              | NA                                | (Refused by the patient) | 2 years; death with NED | (32)          |
| Zhang          | 2011 | 23  | F      | Orbit            | NA        | (-)               | NA                                            | (-)                               | (+)             | 16 months; NED | (33)          |
| Blumberg       | 2012 | 65  | M      | Paratracheal     | 4.7       | FNA               | Failure                                       | NA                                | (-)             | NED           | (34)          |
| Wang           | 2012 | 20  | F      | Neck             | 5         | (-)               | With an osteosarcomatous component            | (-)                               | 5 months; NED   | (35)          |
| Zreik          | 2015 | 86  | M      | Posterior neck   | 9.3       | US guided FNA     | Suggestive of DDLS                            | NA                                | (+)             | 4 months; NED | (36)          |
| Gerry          | 2014 | NA  | NA     | H&N (number of cases, 16) | NA        | NA    | NA                                            | NA                                | NA              | NA            | (7)           |
| Petersson      | 2014 | 61  | F      | Paralaryngeal    | 6         | CT guided         | Deceptively mild histopathological features (benign) | Suggestive of a partially benign dedifferentiated component | (+)             | The case was reported during postoperative RT | (37)          |
| Jour           | 2015 | NA  | NA     | Larynx           | NA        | NA    | NA                                            | NA                                | NA              | NA            | (38)          |
| Tirumani       | 2015 | NA  | NA     | H&N (number of cases, NA) | NA        | NA    | NA                                            | NA                                | NA              | NA            | (12)          |
| Saâda-Bouzid   | 2015 | 63  | M      | Nose             | NA        | NA    | NA                                            | NA                                | NA              | NA            | (39)          |
| Ishii          | 2016 | NA  | NA     | H&N (number of cases, 2) | NA        | NA    | NA                                            | NA                                | NA              | NA            | (40)          |
| Riva           | 2016 | 81  | M      | Pyriform sinus   | 21        | (-)               | Grade 2 according to FNCLCC                    | (-)                               | 1 year; NED     | (41)          |
| Enomoto        | 2017 | 28  | F      | Maxillary gingiva | NA        | (+)               | DDLS                                         | Grade 3 according to FNCLCC        | (-)             | 30 months; NED | (42)          |
with a partly deceptively benign-appearing dedifferentiated component, leading to the misdiagnosis of DDLS on biopsy. Some studies have confirmed that WDLS and DDLS belong to the same group (14,47,48) because DDLS is well defined as a disease caused by progression from WDLS to a high- or low-grade lesion (34,38). Importantly, DDLS has a poorer 5-year disease-specific and overall survival rates compared with WDLS (7). Therefore, accurate pathological diagnosis with total resection is preferred to clearly distinguish DDLS from other LSs.

In conclusion, the current patient was the first documented case of oral floor DDLS. Furthermore, our case was the first reported case of SPM development after the treatment of H&N DDLS. After the first DDLS description in 1979 (49), the present study detected 50 cases of H&N DDLS. Our literature review indicated that preoperative biopsy is not reliable for the diagnosis of H&N DDLS, and accurate pathological diagnosis with total resection is preferred. Statistical analyses could not be performed, due to the small number of patients and sparse clinical information. Therefore, additional cases with long-term follow-up and well-described clinical information are needed to develop new protocols for H&N DDLS patients.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors’ contributions

FN and TM acquired the data, performed the literature review and edited the manuscript. AA made substantial contributions to the concept and design of the study. TN, AM, NM and KN acquired the data and gave clinical advice. HM, NM and AA revised the manuscript. HM and NY evaluated the specimens and gave histopathological advice. TM was a major contributor in writing the manuscript.

Ethics approval and consent to participate

The report was submitted for ethical review to the Ethics Committee of the University of the Ryukyus (Okinawa, Japan), which waived the requirement for a review, since the study does not contain any protocols requiring ethical approval. The Ethics Committee approved the submission and publication of the manuscript.
Consent for publication
Written informed consent was obtained from the patient for the publication of this case report, including their clinical data and accompanying images.

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

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