Original Article

Diagnosis and Differential Diagnosis of Desmoplastic Fibroblastoma by Clinical, Radiological, and Histopathological Analyses

Li-Hua Gong[1], Wei-Feng Liu[2], Yi Ding[1], Yue-Hang Geng[3], Xiao-Qi Sun[1], Xiao-Yuan Huang[1]

[1]Department of Pathology, Beijing Jishuitan Hospital, The Fourth Medical College of Peking University, Beijing 100035, China
[2]Department of Orthopedic Oncology, Beijing Jishuitan Hospital, The Fourth Medical College of Peking University, Beijing 100035, China
[3]Department of Pathology, Peking University Health Science Center, Beijing 100191, China

Abstract

Background: Desmoplastic fibroblastoma (collagenous fibroma) is an uncommon benign soft-tissue tumor, rarely involving bone. It shares some overlapping features with other infiltrate tumors, such as desmoid-type fibromatosis, neurofibroma, and low-grade fibromyxoid sarcoma. The misdiagnosis may cause unnecessary surgical overtreatment, especially for those involving bone. In order to deepen the understanding of the diagnosis and differential diagnosis of desmoplastic fibroblastoma, we planned to analyze the clinical, radiological, and histopathological features and the outcome of desmoplastic fibroblastoma on the basis of case analysis and literature review.

Methods: Sixteen cases were retrieved from the surgical pathology records from May 2011 to April 2016 in the Department of Pathology in Beijing Jishuitan Hospital. Formalin-fixed, paraffin-embedded specimens of 16 cases of desmoplastic fibroblastoma were collected. Hematoxylin and eosin stain and immunohistochemistry were used to observe the histological features of desmoplastic fibroblastoma of soft tissue and bone. The images for diagnosis obtained from the ultrasonic examination, X-ray, magnetic resonance imaging, and computed tomography were used to observe the radiological features. Related literatures were retrieved from the PubMed and CNKI databases.

Results: Sixteen cases of desmoplastic fibroblastoma of soft tissue were located in the hand (n = 7), foot (n = 4), upper arm (n = 1), shoulder (n = 1), forearm (n = 2), and one case occurred in the proximal femur. Age ranged from 32 to 82 years (median age: 58 years). There were six females and ten males. Histologically, the lesions of soft tissue appeared as well-circumscribed masses with abundant collagenous matrix and low vascularity. Tumor cells were stellate- or spindle-shaped and uniformly distributed within the extracellular matrix. In five cases, the desmoplastic fibroblastoma were found to have infiltrated into the skeletal muscle tissue. In one case of desmoplastic fibroblastoma of bone, radiographs revealed osteolytically well-defined lesion. Immunohistochemistry stain showed that vimentin and smooth muscle actin were positive in all cases of desmoplastic fibroblastoma.

Conclusions: Desmoplastic fibroblastoma (collagenous fibroma) has prominent clinical, histopathological, and radiological features. Before the differential diagnosis from other tumors is obtained by thorough analysis and comparison of the similar and different characteristics, the appropriate surgical management and accurate prognosis evaluation could not be delivered to the patient.

Key words: Bone; Collagenous; Desmoplastic; Diagnosis; Differential; Fibroma; Immunohistochemistry; Soft Tissue

Introduction

Desmoplastic fibroblastoma is an uncommon benign soft-tissue tumor, which was first described by Evans in 1995. In 1996, it was renamed as collagenous fibroma, which seemed more appropriate to describe its histological features and reflect its benign prognosis. According to the World Health Organization (WHO) Classification of Tumours of

Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.4103/0366-6999.221274

Address for correspondence: Dr. Li-Hua Gong, Department of Pathology, Beijing Jishuitan Hospital, The Fourth Medical College of Peking University, Beijing 100035, China
E-Mail: lhgong2005@126.com

Received: 13-09-2017 **Edited by:** Ning-Ning Wang
How to cite this article: Gong LH, Liu WF, Ding Y, Geng YH, Sun XQ, Huang XY. Diagnosis and Differential Diagnosis of Desmoplastic Fibroblastoma by Clinical, Radiological, and Histopathological Analyses. Chin Med J 2018;131:32-6.

Soft Tissue and Bone (2013), desmoplastic fibroblastoma was classified as a benign tumor.[1] This tumor occurs predominantly in males, with a male-female ratio of 2.5:1, often between the ages of 16 and 83 years with a median age of 50 years.[2,3] Desmoplastic fibroblastoma is reported to occur mostly in the arm, shoulder, lower limb, back, forearm, hand, and feet,[2,4,5] and rarely in the tongue, palate, and neck.[6-9] It usually manifests as a well-circumscribed, round or oval, painless, and slow-growth mass. The diameter ranged from 1 to 20 cm. Microscopically, the bland spindle- or stellate-shaped fibroblasts are scattered in the abundant and dense collagenous matrix. In order to better understand the characteristics of desmoplastic fibroblastoma, and distinguish it from other soft tissue and bone tumors, we conducted a retrospective study to analyze the clinical pathological features of 16 patients with desmoplastic fibroblastoma (collagenous fibroma).

Methods

Ethical approval

This study was approved by the Ethics Committee of the Beijing Jishuitan Hospital and obtained the waiver of informed consent.

Patients and surgical specimens

Sixteen cases were retrieved from the surgical pathology records between May 2011 and April 2016 in the Department of Pathology in Beijing Jishuitan Hospital. Of the 16 cases of soft-tissue desmoplastic fibroblastoma, 15 were obtained from surgical procedures in the Department of Hand Surgery and one case of bone was derived from a surgical procedure in the Department of Orthopedic Oncology. All tissues were fixed in neutral-buffered formalin and processed routinely with paraffin embedding, while the sections were prepared and stained with hematoxylin and eosin. The histopathological assessment was carried out according to the WHO Classification of Tumors of Soft Tissue and Bone and reviewed by three pathologists, while clinical and radiological information was obtained from online medical records and surgeons.

Tissue samples and immunohistochemistry

Formalin-fixed, paraffin-embedded specimens of 16 cases of desmoplastic fibroblastoma were available for immunohistochemical analysis. Immunohistochemical stain was performed with an automated immunostainer (Autostainer 720, Labvision; BioSurplus, Inc., California, USA) according to standard heat-induced epitope retrieval and the avidin-biotin-peroxidase complex method. The following cytophenotypic markers were detected including: vimentin, cytokeratin pan (CKpan), smooth muscle actin (SMA), S100, CD34, CD68, epithelial membrane antigen (EMA), desmin, and β-catenin. Simultaneously, appropriate positive and negative control sections were used. Tissue of desmoid-type fibromatosis was used as a positive control for vimentin and β-catenin, while tissues of leiomyoma, extrapleural solitary fibrous tumor, and giant cell tumor, respectively, were used as a positive control for SMA, CD34, and CD68. The epithelial tissue, striated muscle, and adipose tissue were used as positive controls for CKpan, EMA desmin, and S-100, respectively. Negative controls were performed by substituting the primary antibody with non-immune mouse serum.

Evaluation of immunohistochemical staining

In order to evaluate S-100 and β-catenin immunoreactivity in this study, tumor cells were considered immunopositive when they displayed a brownish nuclear immunoreactivity. The positive reaction of vimentin, SMA, CD68, and desmin displayed a brownish cytoplasmic immunoreactivity, and the positive reaction of CKpan, CD34, and EMA displayed a brownish membrane and cytoplasmic immunoreactivity. All immunohistochemistry slides were evaluated independently by two pathologists who were not informed of the clinical information. The agreement was reached by careful discussion when the opinions of the two pathologists were different.

Results

Clinical characteristics

The patients included 6 females and 10 males, ranging in age from 32 to 82 years, with a median age of 58 years. Sixteen cases of desmoplastic fibroblastomas were located in the hand ($n = 7$), foot ($n = 4$), upper arm ($n = 1$), forearm ($n = 2$), shoulder ($n = 1$), and femur ($n = 1$; Table 1). None of the patients had reported a history of prior trauma.

Radiological characteristics

In 15 cases of desmoplastic fibroblastomas of soft tissue, ultrasonic examination showed a smooth, heterogeneous hypoechoic mass surrounded by muscular or fat tissue. Magnetic resonance imaging (MRI) revealed an irregularly-shaped, well-circumscribed lesion [Figure 1a], with medium signal intensity on T1-weighted images and low signal intensity on T2-weighted images.

In the one case of desmoplastic fibroblastoma of bone, the X-ray of the right proximal femur showed an osteolytic lesion with a well-defined sclerotic rim, but lack of matrix calcification [Figure 1b]. Furthermore, computed tomography (CT) revealed large erosions in the intertrochanter and femoral neck. Similar to the X-ray report, a thick sclerotic rim was found in the right femur and no calcification was showed. MRI showed that the osteolytic mass filling the proximal femur was hypointense on spin echo T1-weighted images, and slightly hyperintense on spin echo T2-weighted images, which represented a few small bright foci. There were no areas of signal void or hypointense signal to suggest the presence of hemosiderin or calcification. Gadolinium-enhanced spin echo T1-weighted fat suppression images showed almost isointensity signal without contrast enhancement.

Macroscopic features

The desmoplastic fibroblastomas of soft tissue were well circumscribed, round or oval, and covered by a smooth surface [Figure 1c]. The dimension of tumors ranged

Table 1: Clinical summary of desmoplastic fibroblastoma

Case	Sex	Age (years)	Location	Tumor size	Follow-up (months)
1	Female	59	Right upper arm	1.0 cm × 1.0 cm × 0.8 cm	50
2	Male	47	Right forefinger	3.3 cm × 2.5 cm × 0.5 cm	37
3	Male	32	Back of left foot	5.5 cm × 3.5 cm × 3.0 cm	32
4	Male	63	Back of left foot	2.0 cm × 1.5 cm × 1.0 cm	34
5	Male	57	Left forefinger	3.0 cm × 3.0 cm × 1.0 cm	28
6	Male	60	Right forearm	5.5 cm × 4.5 cm × 3.0 cm	29
7	Female	68	Left wrist	3.0 cm × 3.0 cm × 2.0 cm	26
8	Male	82	Palm of right hand	2.0 cm × 2.0 cm × 1.5 cm	27
9	Male	65	Right thumb	3.5 cm × 2.0 cm × 1.5 cm	23
10	Female	56	Right wrist	1.0 cm × 0.8 cm × 0.4 cm	22
11	Male	74	Back of left foot	2.5 cm × 2.0 cm × 1.0 cm	19
12	Female	63	Right forearm	5.5 cm × 4.5 cm × 2.8 cm	18
13	Female	41	Back of left hand	2.2 cm × 1.5 cm × 1.0 cm	18
14	Female	51	Back of left foot	3.0 cm × 1.5 cm × 0.6 cm	12
15	Male	56	Shoulder	2.0 cm × 1.8 cm × 1.5 cm	10
16	Male	46	Proximal femur	1.5 cm × 1.0 cm × 1.0 cm	12

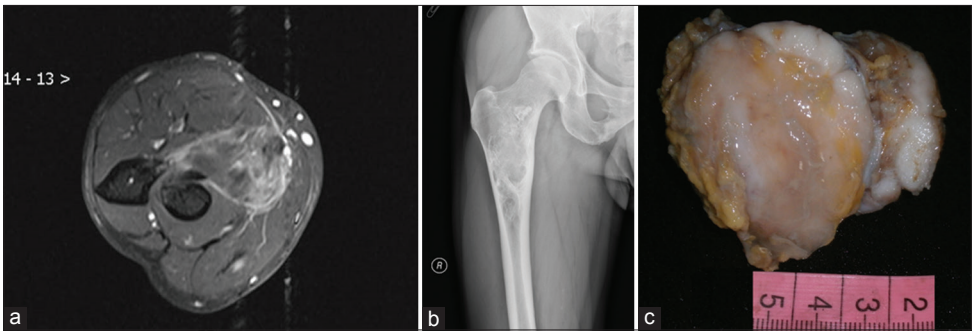

Figure 1: MRI, X-ray, and gross pathological image of desmoplastic fibroblastoma. (a) The MRI reveals an irregularly shaped, well-circumscribed lesion. (b) The X-ray shows an osteolytic lesion in the right proximal femur. (c) Macroscopically, the tumor presented as a well-circumscribed round mass. MRI: Magnetic resonance imaging.

from 1.0 to 5.0 cm, with a median diameter of 2.8 cm, and a cut section appeared to be homogeneously gray-white and firm in nature. The sample of bone desmoplastic fibroblastoma obtained from the curettage surgery showed a gray fragmented tissue, in which some cystic areas existed.

Histological features

The desmoplastic fibroblastomas of soft tissue had a clear border and were surrounded by a thin fibrous capsule [Figure 2a]. Most of them were nodular, but some were lobular. The lesions showed a homogeneous eosinophilic collagenous matrix background, in which some areas displayed hyalinization [Figure 2b]. The cells were scarce and dispersedly distributed in the dense fibrotic tissue, whereas at the periphery area of the tumor, the cells were distributed relatively compactly. The cells were spindle- or stellate-shaped, similar to the activated fibroblasts with eosinophilic cytoplasm. The nuclei were oval without atypia, and the small basophilic nucleoli were prominent [Figure 2c]. Mitotic activity was very low and the mitotic figures were only found in the cells at the periphery of tumors. No necrotic appearance was noted. In the matrix, the blood vessels were rare and small, dilated, and thin walled. Extravasated erythrocytes could be found. In five cases, the tumors were found to have infiltrated the adjacent muscle [Figure 2d]. The histological features of desmoplastic fibroblastoma of bone were similar to those of soft tissue, except cystic degeneration. No invasion into laminar bone was found.

Immunohistochemical results

The immunostaining images showed that the vimentin- and SMA-positive cells existed in all cases [Figure 2e and 2f]. However, the immunostaining signal of other markers was absent in the section of all tissues, which confirmed the diagnosis of desmoplastic fibroblastoma.

Prognosis

All patients have been followed up for 12–50 months (median: 26 months; Table 1). None has shown an evidence of recurrence.

Discussion

In our desmoplastic fibroblastoma cases, except for the one case involving the long bone, others were located in the soft tissue of shoulder, feet, hands, or arms. The low-signal

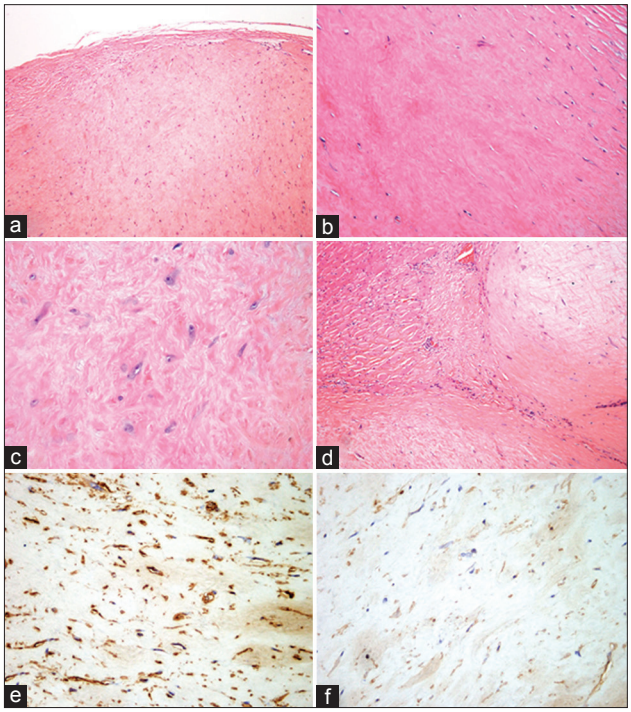

Figure 2: The histopathological and immunohistochemical features of desmoplastic fibroblastoma. (a) The tumor had a clear border and was encapsulated by thin fibrous tissue (H&E staining, ×10); (b) the collagen was homogeneously eosinophilic with hyalinization (H&E staining, ×20); (c) the stellate-shaped tumor cells had eosinophilic cytoplasm and prominent basophilic nucleoli (H&E staining, ×40); (d) the small, thin-walled, and dilated vessels containing erythrocytes (H&E staining, ×20); (e) expression of vimentin in desmoplastic fibroblastoma detected by immunohistochemistry method (×20); (f) expression of SMA in desmoplastic fibroblastoma detected by immunohistochemistry method (×20). SMA: Smooth muscle actin.

intensity lesion on T2-weighted images, an important feature of desmoplastic fibroblastoma, was described in the present study of MRI examination, which was confirmed by the feature of low cellular and abundant collagen fibers in the histopathological examination. The above-mentioned feature might be helpful to make differential diagnosis from other soft-tissue tumors because the majority of soft-tissue tumors were reported to have a high signal intensity on T2-weighted images.[10,11]

Sometimes, the tumors could be found to have invaded adjacent normal tissue. Miettinen *et al*.[1] found that 32 of 63 patients with desmoplastic fibroblastomas emerged conspicuous infiltration into subcutaneous fat, while skeletal muscle infiltration was described in 17 cases, and one-third of the cases were found to have enclosed the nerves. In our present study, the muscle infiltration was found in the 5 of 16 cases, while one enclosed the nerve without symptoms. However, it could not be supposed to be malignant or borderline, although the invasion existed.

Occasionally, invasion of desmoplastic fibroblastoma into the bone tissue was reported;[3,12] but primary tumor that arose in the bone was not found previously. This study reported one case of desmoplastic fibroblastomas primarily located in the femur, while no soft-tissue tumor was found in the adjacent area of bone desmoplastic fibroblastoma. The desmoplastic fibroblastoma of bone might be misdiagnosed as other tumors with abundant collagen, such as desmoid-type fibromatosis of bone. The desmoid-type fibromatosis of bone is a locally aggressive, intermediate tumor, and often recurs after excision. The lesions usually are poorly circumscribed and easily infiltrate into the adjacent soft tissue. The treatment of bone desmoid-type fibromatosis includes marginal or wide resection with or without replacement by allograft, or amputation in certain cases. However, complete surgical excision is a recommended treatment for desmoplastic fibroblastoma due to the benign nature of this neoplasm. Therefore, the distinction between desmoplastic fibroblastoma and desmoid-type fibromatosis of bone is important to avoid unnecessary extensive surgical procedures. The immunohistochemical features might be helpful for the differential diagnosis. Both of the two kinds of tumor cells express vimentin and SMA;[6] but nuclear-positive staining signal of β-catenin was found in approximately 70–75% of desmoid-type fibromatosis,[13] while no positive signal was described in the desmoplastic fibroblastoma. In our present study, only vimentin- and SMA-positive signal was detected in all the cases, which was similar with the previous reports.

Another kind of tumor needs to be distinguished with desmoplastic fibroblastoma is fibroma of the tendon sheath. The two kinds of tumors are reported to show the following overlapping features: first, cytogenetic analysis shows the translocation of t(2;11)(q31;q12) in desmoplastic fibroblastoma, which has also been found in fibromas of the tendon sheath which is usually attached to a tendon.[14,15] Second, ultrastructure shows the features of fibroblast or myofibroblast, while immunohistochemistry shows SMA focally positive in both tumors. Fortunately, the two kinds of tumor have many discrepancies. For example, the fibroma of the tendon sheath usually attaches to a tendon, and the tumor cells are spindle with obvious bundles of collagen formation. There are characteristically elongated thin-walled vessels and formed slit-like clefts, while blood vessels are rare in desmoplastic fibroblastoma just as revealed in the present study.

In addition to the above-mentioned tumors with fibroblast or myofibroblast features, there are still other tumors with different surgical treatment and prognosis needed to be distinguished with desmoplastic fibroblastoma such as nodular fasciitis, sclerotic fibroma, neurofibroma, and low-grade fibromyxoid sarcoma. Nodular fasciitis is a self-limited lesion, which more often occurs in young adults and grows rapidly, but the maximum size is no larger than 5 cm. Histopathologically, it is composed of plump fibroblastic cells and has a loose, tissue culture-like appearance. Small vessels, inflammatory cell infiltration, and extravasated erythrocytes also could be found.[16] Neurofibroma is a benign peripheral nerve sheath tumor with invasive growth. The tumor cells are short, spindle

shaped, loosely dispersed, and surrounded by collagen fiber. This kind of marked collagen formation causes a "shredded carrot's" appearance and S-100 is always positive. Sclerotic fibroma of the skin is a benign fibrous tumor, often situated in the reticular dermis.[17] It is usually solitary and has relative hypocellularity with a prominent feature that thick collagen bundles are arranged in a storiform pattern. The maximum diameter is <1 cm.[18] Low-grade fibromyxoid sarcoma is more cellular, has alternating fibrous and myxoid zones and characteristic whorled growth pattern.[19]

Finally, as a kind of benign tumor, the prognosis of desmoplastic fibroblastoma is good. Up to now, no recurrence has been reported and the longest follow-up period was 12 years. In the present study, we followed up the 16 patients for 12–50 months since the surgery and no recurrence was recorded. The follow-up result is in agreement with the previous studies. Moreover, the good prognosis further supported the benign nature of desmoplastic fibroblastoma although it occasionally exhibits invasive characteristics.

Acknowledgment

We are grateful to Dr. Sajdik C for his assistance in language editing.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Miettinen MM, Bridge JA, Fetsch JF. Desmoplastic fibroblastoma. In: Fletcher CD, Bridge JA, Hogendoom PC, editors. World Health Organization Classification of Tumours of Soft Tissue and Bone. Lyon, France: IARC Press; 2013. p. 60-1.
2. Kim JH, Oh DY, Kim SW, Lee JH, Ahn ST, Rhie JW, *et al.* Desmoplastic fibroblastoma of the finger tip in an adult. Arch Plast Surg 2012;39:84-6. doi: 10.5999/aps.2012.39.1.84.
3. Osipov V, Carrera GF. Collagenous fibroma (desmoplastic fibroblastoma) with vertebral body erosion. Sarcoma 2009;2009:682687. doi: 10.1155/2009/682687.
4. Watanabe H, Ishida Y, Nagashima K, Makino T, Norisugi O, Shimizu T, *et al.* Desmoplastic fibroblastoma (collagenous fibroma). J Dermatol 2008;35:93-7. doi: 10.1111/j.1346-8138.2008.00421.x.
5. Bhagalia S, Jain M, Pardhe N, Sireesha SK. Collagenous fibroma (desmoplastic fibroblastoma) of the oral cavity. J Oral Maxillofac Pathol 2012;16:277-9. doi: 10.4103/0973-029X.99089.
6. Pereira TD, de Lacerda JC, Porto-Matias MD, de Jesus AO, Gomez RS, Mesquita RA, *et al.* Desmoplastic fibroblastoma (collagenous fibroma) of the oral cavity. J Clin Exp Dent 2016;8:e89-92. doi: 10.4317/jced.52605.
7. Nonaka CF, Carvalho Mde V, de Moraes M, de Medeiros AM, Freitas Rde A. Desmoplastic fibroblastoma (collagenous fibroma) of the tongue. J Cutan Pathol 2010;37:911-4. doi: 10.1111/j.1600-0560.2009.01467.
8. Shimoyama T, Horie N, Ide F. Collagenous fibroma (desmoplastic fibroblastoma): A new case originating in the palate. Dentomaxillofac Radiol 2005;34:117-9. doi: 10.1259/dmfr/22428083.
9. Milnes LK, Tennent TD, Pearse EO. An unusual cause of subacromial impingement: A collagenous fibroma in the bursa. J Shoulder Elbow Surg 2010;19:e15-7. doi: 10.1016/j.jse.2010.04.009.
10. Yamamoto A, Abe S, Imamura T, Takada K, Enomoto Y, Harasawa A, *et al.* Three cases of collagenous fibroma with rim enhancement on postcontrast T1-weighted images with fat suppression. Skeletal Radiol 2013;42:141-6. doi: 10.1007/s00256-012-1484-4.
11. Bonardi M, Zaffarana VG, Precerutti M. US and MRI appearance of a collagenous fibroma (desmoplastic fibroblastoma) of the shoulder. J Ultrasound 2014;17:53-6. doi: 10.1007/s40477-013-0051-8.
12. Merriman DJ, Deavers MT, Czerniak BA, Lin PP. Massive desmoplastic fibroblastoma with scapular invasion. Orthopedics 2010;33:601. doi: 10.3928/01477447-20100625-23.
13. Huang PW, Tzen CY. Prognostic factors in desmoid-type fibromatosis: A clinicopathological and immunohistochemical analysis of 46 cases. Pathology 2010;42:147-50. doi: 10.3109/00313020903494078.
14. Kato I, Yoshida A, Ikegami M, Okuma T, Tonooka A, Horiguchi S, *et al.* FOSL1 immunohistochemistry clarifies the distinction between desmoplastic fibroblastoma and fibroma of tendon sheath. Histopathology 2016;69:1012-20. doi: 10.1111/his.13042.
15. Nishio J, Akiho S, Iwasaki H, Naito M. Translocation t(2;11) is characteristic of collagenous fibroma (desmoplastic fibroblastoma). Cancer Genet 2011;204:569-71. doi: 10.1016/j.cancergen.2011.10.003.
16. Lloyd AA, Witheiler D, Menter A. Nodular fasciitis of the lip mucosa: A rare but clinically important entity. Clin Exp Dermatol 2015;40:408-12. doi: 10.1111/ced.12564.
17. Abbas O, Ghosn S, Bahhady R, Salman S. Solitary sclerotic fibroma on the scalp of a young girl: Reactive sclerosis pattern? J Dermatol 2010;37:575-7. doi: 10.1111/j.1346-8138.2010.00843.x.
18. Varghese T, Pillai KS, Sarojini SB, Khosla E. Desmoplastic fibroblastoma (collagenous fibroma) in the oral cavity. J Indian Soc Pedod Prev Dent 2014;32:238-41. doi: 10.4103/0970-4388.135834.
19. Hu SC, Lin CL. Dermal desmoplastic fibroblastoma presenting as a large sacral mass. Australas J Dermatol 2016;57:296-9. doi: 10.1111/ajd.12363.