Case report

Nasal spindle cell tumor with rhabdomyoblastic features: A rare and diagnostically difficult case

Kenichi Mizutani[1*], Motona Kumagai[2], Akane Aikawa[3], Shintaro Terahata[4], Shin Ishizawa[3], Hiroshi Minato[5], Takayuki Nojima[6], Sohsuke Yamada[1]

[1]Department of Pathology and Laboratory Medicine, Kanazawa Medical University, 1-1 Daigaku, Uchinada, Kahoku, Ishikawa, 920-0293, Japan; [2]Department of Pathophysiological and Experimental Pathology, Kanazawa Medical University, 1-1 Daigaku, Uchinada, Kahoku, Ishikawa, 920-0293, Japan; [3]Department of Pathology, Toyama Prefectural Central Hospital, 2-2-78 Nishinagae, Toyama, Toyama, 930-8550, Japan; [4]Department of Pathology, Tonami General Hospital, 1-61 Shintomi-cho, Tonami, Toyama, 939-1395, Japan; [5]Department of Diagnostic Pathology, Ishikawa Prefectural Central Hospital, 2-1 Kuratsukihigashi, Kanazawa, Ishikawa, 920-8530, Japan; and [6]Department of Diagnostic Pathology, Kanazawa University Hospital, 13-1 Takara-machi, Kanazawa, Ishikawa, 920-8641, Japan.

Short running title: Nasal spindle cell tumor with rhabdomyoblastic features

Word count: 1194 words (Abstract 154 words); References: 15; and 2 Figures.

*Corresponding author: Kenichi Mizutani, Department of Pathology and Laboratory Medicine, Kanazawa Medical University, 1-1 Daigaku, Uchinada, Kahoku, Ishikawa, 920-0293, Japan. Tel: 81-76-286-2211; and E-mail: kmupalm@gmail.com

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Consent was obtained for the publication of this case report.

Availability of data and material

The dataset supporting the findings and conclusions of this case report is included within this article.

Funding

The authors declare that there is no funding.

Conflicts of interests

The authors declare that they have no conflicts of interests.

Authors' contributions

Manuscript concepts and design: KM, MK, and SY. Manuscript preparation: KM. Manuscript review: MK and SY. Corresponding author: KM. KM, MK, AA, ST, SI, HM, TN, and SY were associated with the interpretation of this case.

Acknowledgements

We would like to thank all members who were associated with this case for their expert technical assistance, helpful comments and general support.

Abstract

Nasal spindle cell rhabdomyosarcoma is very rare. The tumor is sometimes confused with other spindle cell tumors. We herein report a case of nasal spindle cell tumor in a 62-year-old woman. The patient first presented herself to a medical doctor's office after an episode of left epistaxis. An intranasal tumor was found and resected. The tumor was composed of spindle cells, and she was diagnosed with desmoid-type fibromatosis. Five years after the initial episode, an intranasal tumor was found again. The tumor showed a fascicular growth pattern with high cellularity and was predominantly composed of spindle cells. Scattered eosinophilic rhabdomyoblasts were also observed. She was diagnosed with spindle cell rhabdomyosarcoma. This is a unique case report not only because nasal spindle cell rhabdomyosarcoma is very rare but also because the tumor was initially diagnosed as desmoid-type fibromatosis. It is important to consider spindle cell rhabdomyosarcoma as a differential diagnosis of nasal spindle cell tumors.

Keywords: spindle cell rhabdomyosarcoma, rhabdomyosarcoma, spindle cell tumor, desmoid-type fibromatosis, nasal

Background

Rhabdomyosarcoma is a common soft tissue sarcoma in adolescents and young adults but rarer in patients over 40 years old [1]. Spindle cell rhabdomyosarcoma is a minor subtype of rhabdomyosarcoma, accounting for approximately 5% to 10% of all rhabdomyosarcoma [1]. It affects both children and adults and occurs more frequently in males than in females [2]. The tumor commonly arises in the paratesticular region in pediatric patients or in head and neck deep soft tissue in adults; however, nasal spindle cell rhabdomyosarcoma is very rare [2-4]. The tumor predominantly consists of spindle cells. Scattered rhabdomyoblasts may be observed; however, when rhabdomyoblastic features are not clear, the tumor can be mistaken for other benign or malignant tumors, such as fibromatosis, leiomyosarcoma, and fibrosarcoma [1,5-7]. Although the spindle cell variant generally has a better prognosis than other subtypes of rhabdomyosarcoma [1], the outcome in adults is worse than in pediatric patients, with a recurrence and metastasis rate of 40% to 50% [2], and MYOD1-mutant spindle cell and sclerosing rhabdomyosarcoma show a poor prognosis, irrespective of age [8].

We herein report a case of recurrent nasal spindle cell rhabdomyosarcoma that was initially diagnosed with desmoid-type fibromatosis.

Case presentation

A 62-year-old female first presented herself to a medical doctor's office five years previously after an

episode of left epistaxis. An intranasal tumor was found and resected. A microscopic study of the tumor revealed a poorly circumscribed lesion (Figure 1A). The tumor showed a fascicular fashion with moderate cellularity (Figure 1B). The tumor was composed of spindle cells with mild to moderate nuclear atypia (Figure 1C). Immunohistochemically, the tumor cells were positive for vimentin, focally positive for S-100 protein, and negative for cytokeratin AE1/AE3, α-smooth muscle actin (α-SMA), and CD34. They were considered to be reactive for nuclear β-catenin (Figure 1D) and negative for desmin. The Ki-67 labeling index was less than 5%. Based on these findings, she was diagnosed with desmoid-type fibromatosis.

There were subsequently no symptoms for five years after the initial episode; however, she noted nasal hemorrhage again four months ago and was admitted to a hospital. Magnetic resonance imaging (MRI) revealed a 43-mm tumor in the left nasal cavity with suggestion of orbit involvement (Figure 1E). Positron emission tomography-computed tomography (PET-CT) showed no metastasis. Recurrence of the desmoid-type fibromatosis was clinically considered, and the tumor was surgically removed, weighing 16 g in total and showing a tan colored cut surface (Figure 1F). Microscopically, the lesion was poorly circumscribed and intermingled with hemorrhage (Figure 2A). The tumor displayed a fascicular growth pattern with high cellularity and was predominantly composed of atypical spindle cells with elongated nuclei and scant cytoplasm (Figure 2B, C). In addition, scattered eosinophilic rhabdomyoblasts and cross-striations in the tumor cells were present (Figure 2D, E).

Immunohistochemistry revealed that the tumor cells were not reactive for nuclear β-catenin (Figure 2F) but were positive for myogenin (Figure 2G), myoglobin, desmin, MyoD1 (Figure 2H), α-SMA, HHF 35, cytokeratin CAM5.2, and EMA. They were negative for cytokeratin AE1/AE3, S-100 protein, HMB 45, and melan A. The Ki-67 labeling index was 9%, especially in hot spots. As these findings suggested spindle cell rhabdomyosarcoma as a diagnosis, the re-evaluation of the initial tumor was performed, revealing that the initial tumor had not been reactive for nuclear β-catenin but was positive for myogenin, myoglobin and desmin.

She was finally diagnosed with recurrent spindle cell rhabdomyosarcoma. There was no metastasis, and relapse was not reported for four years after the second resection.

Discussion

This is a unique case report not only because nasal spindle cell rhabdomyosarcoma is very rare [3, 4] but also because the tumor was initially diagnosed as desmoid-type fibromatosis.

In the initial tumor, compared with the recurrent one, rhabdomyoblastic features were not clear. In addition, cytoplasmic strong reactivity for β-catenin of the tumor cells was retrospectively considered to have been confused with nuclear reactivity. In that sense, multiple samplings of tumor tissue may lead to its correct diagnosis. Moreover, nuclear reactivity for β-catenin were also reported in other spindle cell tumors in the sinonasal or oral region, such as sinonasal glomangiopericytoma,

solitary fibrous tumor and synovial sarcoma [9-11]. Our case indicates that nuclear positivity for β-catenin alone is not useful in the investigation of nasal spindle cell tumors and that a broader immunohistochemical evaluation is necessary, including myogenin and MyoD1.

Our second tumor morphologically showed rhabdomyoblastic features and was immunohistochemically positive for myogenin, MyoD1 and desmin, which are sensitive markers for rhabdomyosarcoma, suggesting rhabdomyoblastic differentiation; however, rhabdomyoblastic differentiation is also seen in other spindle cell tumors [12]. Malignant peripheral nerve sheaths tumor may show rhabdomyoblastic features (malignant triton tumor), and on immunohistochemistry, the tumor is focally positive for S-100 protein; however, our second tumor was negative for S-100 protein. In addition, our re-evaluation of initial and second tumors showed that they were positive for H3K27me3 (Figure 2I), the complete loss of which can be seen in malignant peripheral nerve sheaths tumor. Biphenotypic sinonasal sarcoma is a rare low-grade sarcoma that was first described in 2012 as low-grade sinonasal sarcoma with neural and myogenic features, including rhabdomyoblastic differentiation [13,14]. It characteristically demonstrates rearrangement of PAX3 [13,14] and shows the immunohistochemical expression of PAX3 and S-100 protein [13,14]. A study revealed that PAX8 is also positive for biphenotypic sinonasal sarcoma, possibly due to cross-reactivity with PAX3 [15]. As this might be a relatively new entity, it was not considered as a differential diagnosis of our tumors when they were diagnosed. We therefore re-evaluated our second tumor, revealing positivity for PAX8.

We were not able to investigate the immunohistochemical PAX3 expression or the genetic profile of PAX3 due to the limitation of our study. The expression of PAX3 and PAX8 has also been reported in spindle cell rhabdomyosarcoma [15]; however, we cannot exclude the possibility that our tumor was biphenotypic sinonasal sarcoma.

Conclusion

We reported a case of nasal spindle cell tumor that was initially considered as desmoid-type fibromatosis and finally diagnosed with spindle cell rhabdomyosarcoma. Although further investigation may be required, this notable and diagnostically difficult case is worth reporting. It is important to keep in mind that spindle cell rhabdomyosarcoma is a rare but possible differential diagnoses of nasal spindle cell tumors.

List of abbreviations

α-SMA, α-smooth muscle actin; MRI, magnetic resonance imaging; and PET-CT, positron emission tomography-computed tomography.

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Consent was obtained for the publication of this case report.

Availability of data and material

The dataset supporting the findings and conclusions of this case report is included within this article.

Funding

The authors declare that there is no funding.

Conflicts of interests

The authors declare that they have no conflicts of interests.

References

1. Goldblum JR, Folpe AL, Weiss SW. Rhabdomyosarcoma. *Enzinger and Weiss's Soft Tissue Tumors*. 7th ed. Philadelphia: Elsevier, 2019, pp. 652-696.
2. Nascimento AF, Barr FG. Spindle cell/sclerosing rhabdomyosarcoma. In: Fletcher CDM, Bridge JA, Hogendoorn PCW, et al (eds). *WHO classification of tumours of soft tissue and bone*. 4th ed. Lyon: International agency for research on cancer, 2013, pp. 134-135.
3. Franchi A, Flucke U, Thompson LDR. Rhabdomyosarcoma. In: El-Naggar AK, Chan JKC, Grandis JR, et al (eds). *WHO classification of head and neck tumours*. 4th ed. Lyon: International agency for research on cancer, 2017, pp. 36-38.
4. Hartmann S, Lessner G, Mentzel T, et al. An adult spindle cell rhabdomyosarcoma in the head and neck region with long-term survival: a case report. *J Med Case Rep*. 2014; 8: 208.
5. Kraft SM, Singh V, Sykes KJ, et al. Differentiating between congenital rhabdomyosarcoma versus fibromatosis of the pediatric tongue. *Int J Pediatr Otorhinolaryngol*. 2010; 74: 781-785.
6. Carrol SJ, Nodit L. Spindle cell rhabdomyosarcoma: a brief diagnostic review and differential diagnosis. *Arch Pathol Lab Med*. 2013; 137: 1155-1158.
7. Gupta A, Maddalozzo J, Win Htin T, et al. Spindle cell rhabdomyosarcoma of the tongue in an infant: a case report with emphasis on differential diagnosis of childhood spindle cell lesions.

Pathol Res Pract. 2004; 200: 537-543.

8. Agaram NP, LaQuaglia MP, Alaggio R, et al. MYOD1-mutant spindle cell and sclerosing rhabdomyosarcoma: an aggressive subtype irrespective of age. A reappraisal for molecular classification and risk stratification. *Mod Pathol*.2019; 32: 27-36.

9. Jo VY, Fletcher CDM. Nuclear β-catenin expression is frequent in sinonasal hemangiopericytoma and its mimics. *Head Neck Pathol*. 2017; 11: 119–123.

10. Thompson LDR, Flucke U, Weing BM. Sinonasal glomangiopericytoma. In: El-Naggar AK, Chan JKC, Grandis JR, et al (eds). *WHO classification of head and neck tumours*, 4th ed. Lyon: International agency for research on cancer, 2017, pp. 44-45.

11. Goldblum JR, Folpe AL, Weiss SW. Perivascular tumors. *Enzinger and Weiss's Soft Tissue Tumors*. 7th ed. Philadelphia: Elsevier, 2019, pp. 837-862.

12. Leiner J, Le Loarer F. The current landscape of rhabdomyosarcomas: an update. *Virchows Arch*. 2020; 476: 97–108.

13. Lewis JE, Oliveria AM. Biphenotypic sinonasal sarcoma. In: El-Naggar AK, Chan JKC, Grandis JR, et al, (eds). *WHO classification of head and neck tumours*. 4th ed. Lyon: International agency for research on cancer, 2017, pp. 40-42.

14. Goldblum JR, Folpe AL, Weiss SW. Soft tissue tumors of intermediate malignancy of uncertain type. *Enzinger and Weiss's Soft Tissue Tumors*. 7th ed. Philadelphia: Elsevier, 2019, pp. 1107-

1174.

15. Jo VY, Mariño-Enríquez A, Fletcher CDM, et al. Expression of PAX3 distinguishes biphenotypic sinonasal sarcoma from histologic mimics. *Am J Surg Pathol*. 2018; 42: 1275-1285.

Figure legends

Figure 1. Microscopic findings of the tumor resected five years previously, and an MRI scan and macroscopic findings of the recurrent tumor. (A) A low-power view of the tumor revealed a poorly circumscribed lesion. Bar = 1.0 mm (H&E staining; original magnification: × 12.5). (B) The tumor showed a fascicular pattern with moderate cellularity. Bar = 200 μm (H&E staining; original magnification: × 100). (C) The tumor was composed of spindle cells with mild to moderate nuclear atypia. Bar = 50.0 μm (H&E staining; original magnification: × 400). (D) The tumor cells were considered to be reactive for nuclear β-catenin. Bar = 50.0 μm (original magnification: × 400). (E) Enhanced T1-weighted MRI showed a 43-mm tumor in the left nasal cavity. The orbit adjacent to the tumor was slightly unclear. (F) The tumor tissue resected from the nasal cavity, weighed 16 g (in total) and had a tan color.

Figure 2. Microscopic and immunohistochemical findings of the recurrent tumor. (A) A low-power view showed a poorly circumscribed lesion intermingled with hemorrhage. Bar = 1.0 mm (H&E staining; original magnification: × 12.5). (B) The tumor showed a fascicular growth pattern with high cellularity. Bar = 200 μm (H&E staining; original magnification: × 100). (C) The tumor was predominantly composed of atypical spindle cells with elongated nuclei and scant cytoplasm. Bar =

50.0 μm (H&E staining; original magnification: × 400). (D) Scattered eosinophilic rhabdomyoblasts were present. Bar = 50.0 μm (H&E staining; original magnification: × 400). (E) A high-power view of tumor cells with cross-striations. Bar = 20.0 μm (H&E staining; original magnification: × 1000). (F-H) The tumor cells were not reactive for nuclear β-catenin (F) but were positive for myogenin (G) and MyoD1 (H). Bar = 50.0 μm (original magnification: × 400). (I) The tumor was positive for H3K27me3. Bar = 50.0 μm (original magnification: × 400).

Figure 1

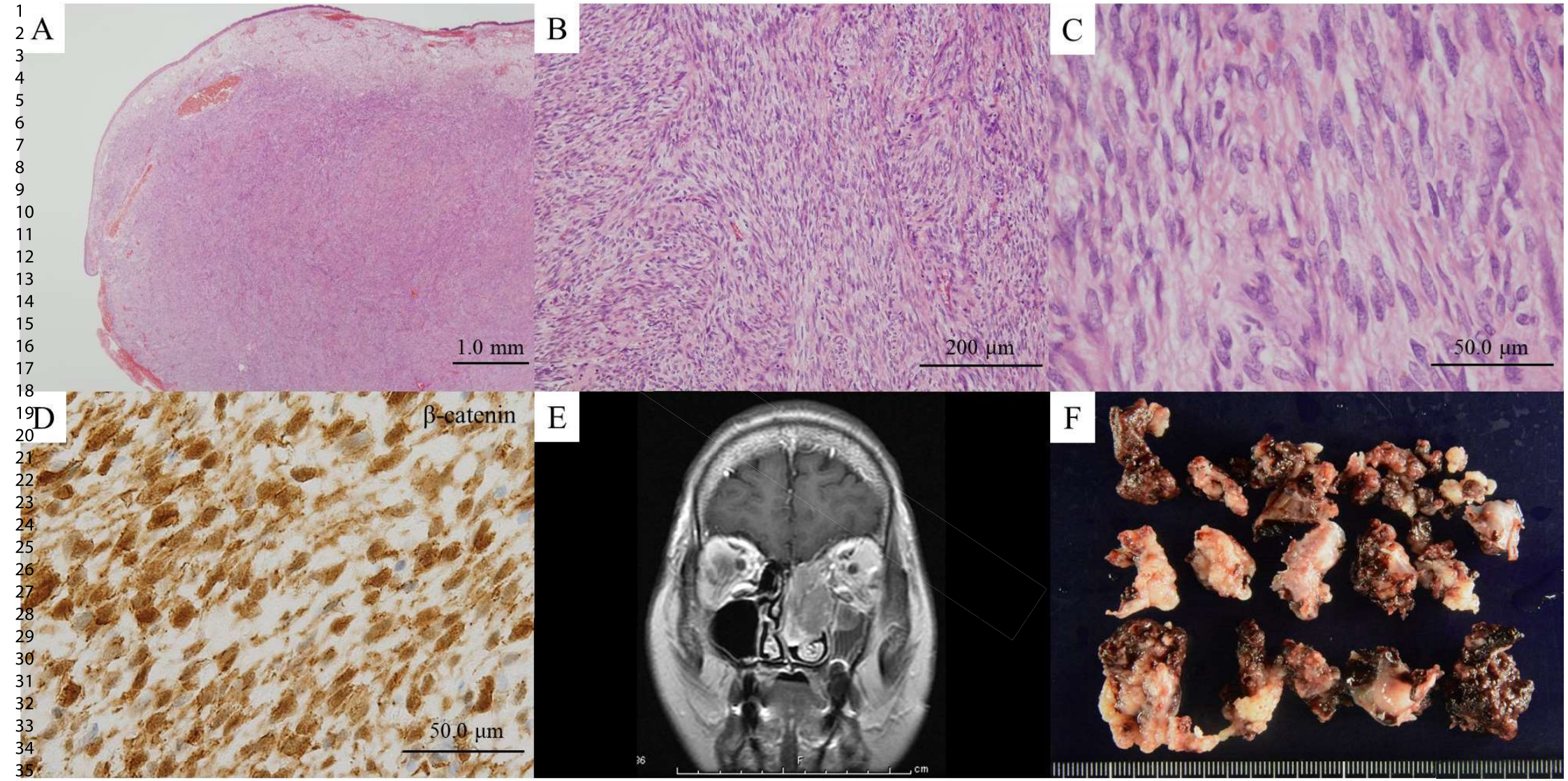
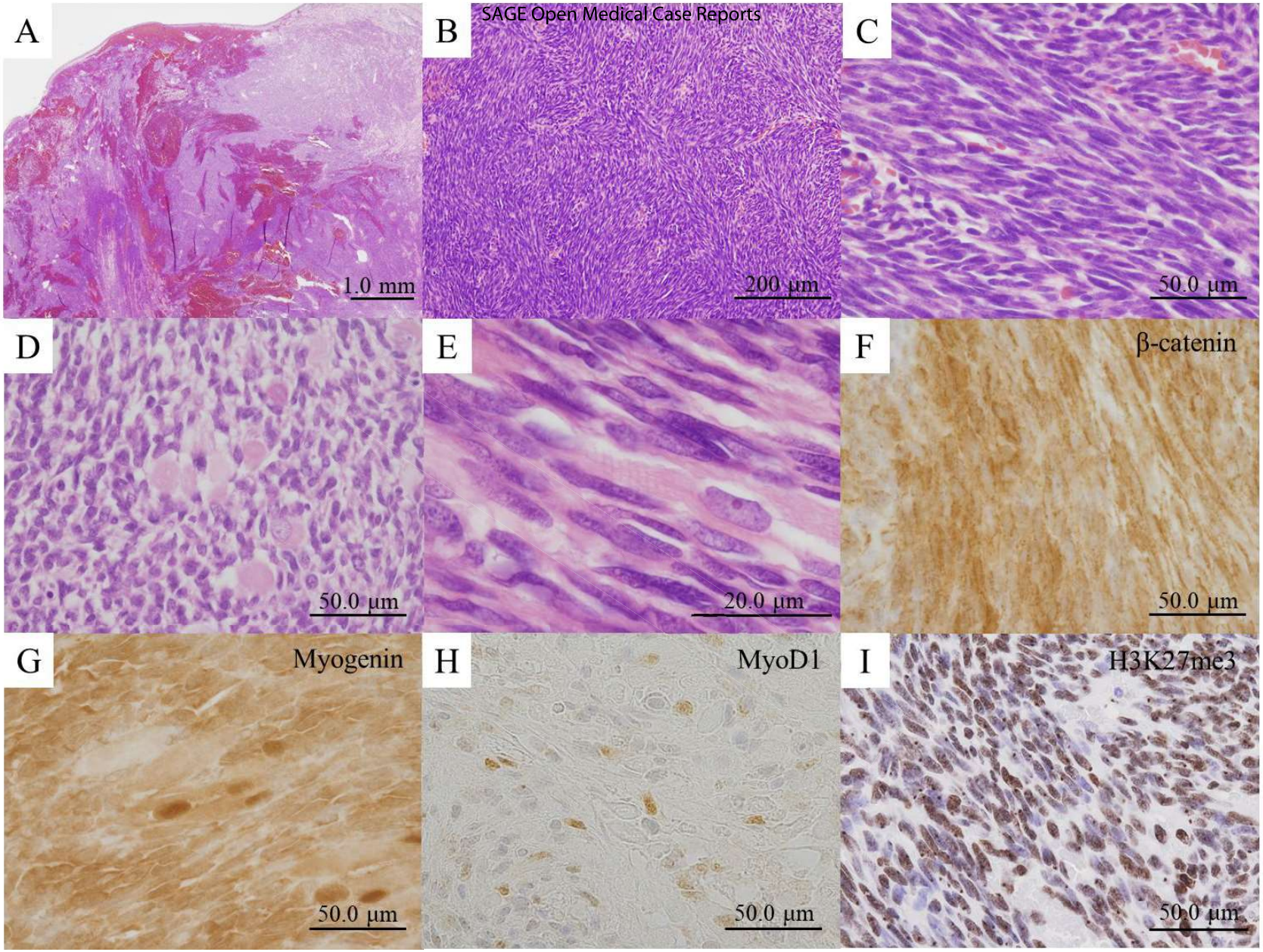


Figure 2


A
1.0 mm
B
200 μm
C
50.0 μm
D
50.0 μm
E
20.0 μm
F
β-catenin
50.0 μm
G
Myogenin
50.0 μm
H
MyoD1
50.0 μm
I
H3K27me3
50.0 μm