



Title	A case of cerebral astroblastoma with rhabdoid features : a cytological, histological, and immunohistochemical study
Author(s)	Yuzawa, Sayaka; Nishihara, Hiroshi; Tanino, Mishie; Kimura, Taichi; Moriya, Jun; Kamoshima, Yuuta; Nagashima, Kazuo; Tanaka, Shinya
Citation	Brain tumor pathology, 33(1), 63-70 <a href="https://doi.org/10.1007/s10014-015-0241-5">https://doi.org/10.1007/s10014-015-0241-5</a>
Issue Date	2016-01
Doc URL	<a href="http://hdl.handle.net/2115/63975">http://hdl.handle.net/2115/63975</a>
Rights	The final publication is available at <a href="http://link.springer.com">link.springer.com</a>
Type	article (author version)
File Information	Astroblastoma_yuzawa_HUSCAP.pdf



[Instructions for use](#)

## Case report

### **A case of cerebral astroblastoma with rhabdoid features: a cytological, histological, and immunohistochemical study**

Sayaka Yuzawa<sup>1</sup>, Hiroshi Nishihara<sup>2,3</sup>, Mishie Tanino<sup>1</sup>, Taichi Kimura<sup>2,3</sup>, Jun Moriya<sup>1</sup>, Yuuta Kamoshima<sup>4,5</sup>, Kazuo Nagashima<sup>6</sup>, and Shinya Tanaka<sup>1,2</sup>.

<sup>1</sup>Department of Cancer Pathology, Hokkaido University Graduate School of Medicine, North 15, West 7, Kita-ku, Sapporo, 060-8638, Japan.

<sup>2</sup>Department of Translational Pathology, Hokkaido University Graduate School of Medicine, Sapporo, Japan.

<sup>3</sup>Translational Research Laboratory, Hokkaido University Hospital, Clinical Research and Medical Innovation Center, Sapporo, Japan.

<sup>4</sup>Sapporo Azabu Neurosurgical Hospital, Sapporo, Japan.

<sup>5</sup>Department of Neurosurgery, Hokkaido University Graduate School of Medicine, Sapporo, Japan.

<sup>6</sup>Higashi Tokushukai Hospital, Sapporo, Japan.

Correspondence: Shinya Tanaka

Department of Cancer Pathology, Hokkaido University Graduate School of Medicine, North 15, West 7, Kita-ku, Sapporo, 060-8638, Japan.

Tel: +81-11-706-5053

Fax: +81-11-706-5902

E-mail: tanaka@med.hokudai.ac.jp

## Abstract

Astroblastoma is a rare neuroepithelial neoplasm of unknown origin, usually occurring in children and young adults. Here we report a case of astroblastoma with uncommon features in an 18-year-old female. The tumor was a well-circumscribed cystic and solid mass with marked gadolinium enhancement in the right frontal lobe. Cytological examination showed polarized monopolar cells with diminished cohesiveness. Tumor cells possessed eccentric round to oval nuclei with abundant eosinophilic cytoplasm, sometimes having cytoplasmic processes. Histopathologically, the tumor showed perivascular pseudorosettes with prominent vascular sclerosis. Foam cells were frequently infiltrated around blood vessels and among tumor cells. In some areas, a solid growth pattern of plump tumor cells with abundant inclusion-like eosinophilic cytoplasm showing rhabdoid appearance was observed. The immunohistochemical study revealed strong and diffuse positivity for vimentin and epithelial membrane antigen (EMA). Tumor cells were focally positive for glial fibrillary acidic protein (GFAP) and cytokeratin AE1/AE3. Nuclear immunoreactivity for INI1 protein was evident. The Ki-67 labeling index was 10.8%. This tumor was finally diagnosed as low-grade astroblastoma and the patient had no evidence of recurrence without postoperative radiotherapy or chemotherapy during the last 6 months of follow-up. This report describes novel cytological, histopathological, and immunohistochemical features of the rare tumor.

**Key Words:** astroblastoma, rhabdoid, foam cell, cytology

## **Introduction**

Astroblastoma is a rare neuroepithelial neoplasm of unknown origin, mainly affecting children, adolescents, and young adults with female predominance. On computed tomography (CT) and magnetic resonance imaging (MRI), the tumor is a well-demarcated, nodular or lobulated cystic mass with conspicuous contrast enhancement, usually located in the cerebral hemisphere [1,2].

The typical histopathological features of astroblastoma are the perivascular pseudorosette of GFAP-positive cells with short and stout cytoplasmic processes, radiating towards central blood vessels that often demonstrate sclerosis [3-5]. Other histological characteristics are lack of fibrillary background and compressing rather than infiltrative margin [6,7]. As histological variation, few cases of astroblastoma with rhabdoid features are reported [8,9].

Here we present a case of cerebral astroblastoma with rhabdoid appearance in an 18-year-old female.

## **Clinical summary**

An 18-year-old female complained of headache for 2 months and nausea for a month. With the development of numbness in the left side of her face and upper limb, she visited our hospital. Neurological examination failed to reveal any significant abnormality. Plain computed tomography (CT) demonstrated a heterogeneous low- to isodensity mass with a large cystic lesion of 7.5 cm in diameter in the right frontal lobe extending from the cortex to periventricular region (Fig. 1A). Magnetic resonance imaging (MRI) revealed a large, well-circumscribed, solid and cystic lesion with little perilesional edema (Fig. 1B and 1C). The solid lesion was hypo- to isointense to gray matter on both T1- and T2-weighted sequences with a bubbly appearance. After gadolinium administration, the solid lesion and a part of the cyst wall showed marked enhancement (Fig. 1D). Calcification was not apparent.

Based on these findings, differential diagnoses of pleomorphic xanthoastrocytoma (PXA), primitive neuroectodermal tumor (PNET), and anaplastic ependymoma were raised, and a right frontal craniotomy was performed. The tumor was intraparenchymal and the solid lesion was very hard. The tumor margin was well-demarcated from the surrounding brain tissue and gross total resection was achieved. The cyst wall was also totally resected according to intraoperative rapid diagnosis of the presence of tumor cells in the cyst wall. The patient made an uneventful recovery in the postoperative period and neurological examination did not reveal any additional neurological deficits. The patient had no evidence of recurrence of

tumor without adjuvant radiotherapy or chemotherapy during the last 6 months of follow-up.

## **Pathological findings**

Cytological examination showed polarized monopolar cells with diminished cohesiveness (Fig. 2). Tumor cells possessed eccentric round to oval nuclei with abundant eosinophilic cytoplasm, sometimes exhibiting short cytoplasmic processes. Nuclear atypia was mild and pleomorphism was not observed. Perivascular pseudorosettes, infiltration of foam cells, or hyalinization of blood vessel walls were not apparent.

Histopathological examination of tumor tissue revealed proliferation of polar cells having abundant eosinophilic cytoplasm and eccentrically located nuclei with short stout cytoplasmic processes anchored to blood vessels showing perivascular pseudorosettes, unlike those seen in ependymoma (Fig. 3A). Prominent sclerosis of blood vessels and stroma was observed (Fig. 3B). Degenerative cyst and cholesterol cleft were frequently seen (Fig. 3C). In the intervascular region, tumor cells were poorly cohesive among themselves. Foam cells frequently infiltrated around blood vessels as well as among tumor cells (Fig. 3D and 3E). In some areas, solid growth pattern of plump tumor cells with more abundant inclusion-like eosinophilic cytoplasm showing rhabdoid appearance was observed (Fig. 3F). A few small foci of necrosis without palisading were found (Fig. 3G) but mitosis was infrequent (1–2/10 high power fields (HPFs)) and no microvascular proliferation or palisading necrosis was evident. Fibrillary matrix, true rosettes, or calcification was not observed. Tumor cells were also observed in the cyst wall, but the tumor margin was compressing and well circumscribed

(Fig. 3H).

In the immunohistochemical study, tumor cells were focally positive for glial fibrillary acidic protein (GFAP) (Fig. 4A) and diffusely and strongly positive for vimentin (Fig. 4B).

Inclusion-like cytoplasm was also positive for vimentin. Epithelial membrane antigen (EMA) was strongly and diffusely positive in cytoplasm and cell membrane (Fig. 4C), while in some areas dot-like staining was also observed (Fig. 4D). Ring-like staining of EMA was not evident. S-100 protein (Fig. 4E), cytokeratin AE1/AE3 (Fig. 4F), cytokeratin 34 $\beta$ E12, and cytokeratin 5/6 were focally immunopositive and nuclear immunoreactivity for INI1 protein was evident in most of the tumor cells, including those with rhabdoid appearance (Fig. 4G).

Tumor cells were positive for nestin and negative for Olig2 and cytokeratin CAM5.2.

Immunostaining for IDH1 mutation was negative. The Ki-67 labeling index was 10.8% (Fig. 4H).

Ultrastructurally, tumor cells showed peripherally located nucleus and abundant cytoplasm, which was filled with numerous intermediate filaments and contained few organelles such as Golgi cisternae and mitochondria (Fig. 5). Microvilli, cilia, or junctional complexes were not apparent.

Based on these findings, a histopathological diagnosis of low-grade astroblastoma was established.



## Discussion

Astroblastoma is a very rare neuroepithelial tumor initially described by Bailey and Bucy in 1930 [10]. Astroblastoma accounts for 0.45–2.8% of all neuroglial tumors [11], mainly affecting children, adolescents, and young adults. In the absence of sufficient clinicopathological data, no WHO grade was given to this rare tumor [12].

Distinctive findings on MRI and CT include a well-circumscribed cystic mass with conspicuous enhancement, its being localized usually in the supratentorial region, especially in the frontal, parietal, and temporal lobes [2]. The solid component of the tumor often has a bubbly appearance on MRI, and these lesions have relatively little peritumoral edema for their large size, which may be related to the lack of local tumor infiltration into the surrounding brain tissue [1,7]. The present case showed typical radiological findings with a markedly enhanced solid mass with a large cystic lesion, little peritumoral edema, and a bubbly appearance localized in the frontal lobe.

The histological characteristic of astroblastoma, as described by Bailey and Bucy, is the perivascular arrangement of tumor cells having thick and short cytoplasmic processes with eccentric nuclei, forming perivascular pseudorosettes [10]. The borders of the tumor more often compress, rather than infiltrate, the surrounding tissue. Cytoplasmic immunoreactivity for GFAP, vimentin, and S-100 protein is characteristic for astroblastoma [3,13,14]. EMA expression, especially localized at cytoplasmic margin, is also one of the distinctive features

in astroblastoma [13-15]. Bonnin and Rubinstein divided astroblastoma into two groups from the aspect of malignancy: low-grade (well differentiated) and high-grade (anaplastic). Low-grade astroblastoma was characterized as well-differentiated tumor with a perivascular pattern, little cellular atypia, low to moderate mitotic activity, and prominent sclerosis of the vascular walls. These lesions have an indolent clinical course and patients may have long-term survival after total resection. High-grade astroblastoma had anaplastic features such as high cellularity, cytological atypia, a high mitotic rate, pseudopalisading necrosis, and microvascular hyperplasia without sclerosis of the vessel walls, showing a more aggressive course [3].

In our case, histological features exhibited low-grade astroblastoma: distinct perivascular pseudorosettes of vimentin, GFAP, and S-100 positive tumor cells, prominent sclerosis of vessels, and low mitotic activity (1-2/10 HPFs) without microvascular proliferation. The majority of tumor cells showed cytoplasmic and membranous positivity for EMA and dot-like staining was also observed in some tumor cells. In previous reports, Ki-67 labeling indices varied among cases: 0.5–8% in low-grade astroblastomas and 4–20% in high-grade astroblastomas [13,16-20]. Ki-67 labeling index in the present case was 10.8%, little high as low-grade astroblastoma; however, Ki-67 labeling index alone has not been established as a prognostic marker [12,19]. Non-palisading necrosis like our case also does not indicate malignancy [12]. IDH1 mutation, reported in gliomas, is recently detectable by

immunohistochemistry [21], but IDH1 mutation was absent in this case, which was compatible with previous reports [14,19].

One of the characteristic findings of our case was rhabdoid appearance of tumor cells. Cytoplasmic inclusion composed of numerous intermediate filament with vimentin positivity was observed. There are few case reports of astroblastoma with rhabdoid appearance [8,9,14]. Bannykh et al. reported a case of astroblastoma with rhabdoid features and suggested the malignant potential because of the presence of necrosis, brisk mitotic activity, and elevated Ki-67 index [8]. Fu et al. described a case of astroblastoma with two components, typical astroblastic features and unusual rhabdoid appearance [14]. In their case, GFAP-positive cells around sclerotic blood vessels were observed with low Ki-67 labeling index in the typical astroblastic area, whereas the highly cellular area was composed of many GFAP-negative cells often with a rhabdoid appearance with high mitotic activity and Ki-67 labeling index. Although this case was diagnosed as malignant (anaplastic) astroblastoma, the patient had no evidence of tumor recurrence without postoperative radiotherapy or chemotherapy during the last 2 years of follow-up [14]. Another case of astroblastoma with rhabdoid features and favorable long-term outcome has been reported [9]. These cases indicated that rhabdoid feature by itself does not indicate malignant potency, but other anaplastic features like mitotic activity, microvascular proliferation, or loss of sclerosis of vascular walls should be taken into account when assessing the histological malignancy.

In the present case, differential diagnosis of atypical teratoid/rhabdoid tumor (AT/RT) and rhabdoid or papillary meningioma were made. AT/RT has specific genetic characteristics of loss of nuclear immunoreactivity for INI1 protein [22]. In the present tumor, nuclear expression of INI1 protein was evident in most of the tumor cells, including those with rhabdoid features. Most of rhabdoid meningiomas are mixed with otherwise conventional types of meningioma such as meningothelial meningioma, transitional meningioma, fibrous meningioma, secretory meningioma, and anaplastic meningioma [23-25]. Papillary meningioma is defined by the presence of a perivascular pseudopapillary pattern, which is different from astroblastic pseudorosette showing stout non-tapering cell processes toward vessel walls. Some cases combining papillary architecture with rhabdoid morphology have also been reported [23,26-28]. The diagnosis of rhabdoid or papillary meningioma is secured if typical meningothelial differentiation is identified [27]. Most tumors of rhabdoid or papillary meningioma were immunohistochemically positive for EMA and vimentin, and negative for GFAP, AE1/AE3, and CAM5.2 [27,29-31]. In the present case, other conventional components of meningioma or meningothelial differentiation were not apparent. In addition, tumor cells showed immunopositivity for GFAP and AE1/AE3.

Our case showed prominent foam cell infiltration and this finding is reasonable when considering the nature of this slow-growing tumor. However, infiltration of foam cells in astroblastoma has not been commonly stated. Brat et al. reviewed 17 astroblastomas, and only

18% of the tumors showed infiltration of macrophages [32]. Foam cell infiltration is a consequence of secondary reactions and is also observed in other brain tumors such as schwannoma, ependymoma, meningioma, and PXA. A differential diagnosis of PXA was preoperatively proposed by the clinician; thus, it should be recognized that foam cells sometimes infiltrate in astroblastoma, and the pathological diagnosis of astroblastoma should be made based on other histological features, such as perivascular pseudorosettes and sclerosis of blood vessels.

Cytological findings were not well described compared to histological findings in astroblastoma. Navarro et al. reported the smear findings of astroblastoma as follows: polarized monopolar morphology, rosetting around blood vessels, and lack of cohesiveness [33]. In our case, polarized tumor cells with diminished cohesiveness were observed, although rosette formation was not evident. In addition, some tumor cells were plump with abundant eosinophilic cytoplasm, indicating rhabdoid morphology.

In conclusion, we have described a case of low-grade astroblastoma with rhabdoid appearance in an 18-year-old female. Rhabdoid appearance is sometimes observed in astroblastoma on both cytological and histological examination, but this feature by itself does not indicate malignant potency, so other anaplastic features should be carefully evaluated when assessing histological malignancy. Recognition of foam cell infiltration in astroblastoma is also important for differential diagnoses of other tumors such as PXA or other glial tumors.

### **Acknowledgement**

We appreciate the advice and expertise of Atsushi Sasaki (Saitama Medical University), Takashi Komori (Tokyo Metropolitan Neurological Hospital), Hiroyoshi Suzuki (Sendai Medical Center), Junko Hirato (Gunma University), and Takanori Hirose (Hyogo Cancer Center). We also thank Mami Sato, Tomoko Takenami and Masana Urushido for their technical assistance.

### **Conflict of interest**

The authors have no conflict of interest.

## Reference

1. Port JD, Brat DJ, Burger PC, Pomper MG (2002) Astroblastoma: radiologic-pathologic correlation and distinction from ependymoma. *AJNR Am J Neuroradiol* 23:243-247.
2. Sughrue ME, Choi J, Rutkowski MJ, Aranda D, Kane AJ, Barani IJ, Parsa AT (2011) Clinical features and post-surgical outcome of patients with astroblastoma. *J Clin Neurosci* 18:750-754.
3. Bonnin JM, Rubinstein LJ (1989) Astroblastomas: a pathological study of 23 tumors, with a postoperative follow-up in 13 patients. *Neurosurgery* 25:6-13.
4. Thiessen B, Finlay J, Kulkarni R, Rosenblum MK (1998) Astroblastoma: does histology predict biologic behavior? *Journal of neuro-oncology* 40:59-65.
5. Brat DJ, Hirose Y, Cohen KJ, Feuerstein BG, Burger PC (2000) Astroblastoma: clinicopathologic features and chromosomal abnormalities defined by comparative genomic hybridization. *Brain Pathol* 10:342-352.
6. Agarwal V, Mally R, Palande DA, Velho V (2012) Cerebral astroblastoma: A case report and review of literature. *Asian J Neurosurg* 7:98-100.
7. Singh DK, Singh N, Singh R, Husain N (2014) Cerebral astroblastoma: A radiopathological diagnosis. *J Pediatr Neurosci* 9:45-47.
8. Bannykh SI, Fan X, Black KL (2007) Malignant astroblastoma with rhabdoid morphology. *Journal of neuro-oncology* 83:277-278.
9. Fathi AR, Novoa E, El-Koussy M, Kappeler A, Mariani L, Vajtai I (2008) Astroblastoma with rhabdoid features and favorable long-term outcome: report of a case with a 12-year follow-up. *Pathol Res Pract* 204:345-351.
10. Bailey P, Bucy PC (1930) Astroblastoma of the brain. *Acta Psychiatr Neurol* 5:439-461.
11. Pizer BL, Moss T, Oakhill A, Webb D, Coakham HB (1995) Congenital astroblastoma: an immunohistochemical study. Case report. *Journal of neurosurgery* 83:550-555.
12. Louis. DN, Ohgaki. H, Wiestler. OD, Cavenee. WK (2007) WHO Classification of Tumours of the Central Nervous System. IARC Press, Lyons.
13. Kubota T, Sato K, Arishima H, Takeuchi H, Kitai R, Nakagawa T (2006) Astroblastoma: immunohistochemical and ultrastructural study of distinctive epithelial and probable tanycytic differentiation. *Neuropathology* 26:72-81.
14. Fu YJ, Taniguchi Y, Takeuchi S, Shiga A, Okamoto K, Hirato J, Nobusawa S, Nakazato Y, Kakita A, Takahashi H (2013) Cerebral astroblastoma in an adult: an immunohistochemical, ultrastructural and genetic study. *Neuropathology* 33:312-319.
15. Cabello A, Madero S, Castresana A, Diaz-Lobato R (1991) Astroblastoma: electron microscopy and immunohistochemical findings: case report. *Surgical neurology* 35:116-121.
16. Janz C, Buhl R (2014) Astroblastoma: report of two cases with unexpected clinical

- behavior and review of the literature. *Clin Neurol Neurosurg* 125:114-124.
17. Salvati M, D'Elia A, Brogna C, Frati A, Antonelli M, Giangaspero F, Raco A, Santoro A, Delfini R (2009) Cerebral astroblastoma: analysis of six cases and critical review of treatment options. *Journal of neuro-oncology* 93:369-378.
  18. Hirano H, Yunoue S, Kaji M, Tsuchiya M, Arita K (2008) Consecutive histological changes in an astroblastoma that disseminated to the spinal cord after repeated intracranial recurrences: a case report. *Brain tumor pathology* 25:25-31.
  19. Asha U, Mahadevan A, Sathiyabama D, Ravindra T, Sagar BK, Bhat DI, Aravinda HR, Pandey P, Vilanilam GC (2015) Lack of IDH1 mutation in astroblastomas suggests putative origin from ependymogial cells? *Neuropathology* 35:303-311.
  20. Khosla D, Yadav BS, Kumar R, Agrawal P, Kakkar N, Patel FD, Sharma SC (2012) Pediatric astroblastoma: a rare case with a review of the literature. *Pediatric neurosurgery* 48:122-125.
  21. Kato Y (2015) Specific monoclonal antibodies against IDH1/2 mutations as diagnostic tools for gliomas. *Brain tumor pathology* 32:3-11.
  22. Pfister SM, Korshunov A, Kool M, Hasselblatt M, Eberhart C, Taylor MD (2010) Molecular diagnostics of CNS embryonal tumors. *Acta neuropathologica* 120:553-566.
  23. Karabagli P, Karabagli H, Yavas G (2014) Aggressive rhabdoid meningioma with osseous, papillary and chordoma-like appearance. *Neuropathology* 34:475-483.
  24. Zhou Y, Xie Q, Gong Y, Mao Y, Zhong P, Che X, Jiang C, Huang F, Zheng K, Li S, Gu Y, Bao W, Yang B, Wu J, Wang Y, Chen H, Xie L, Zheng M, Tang H, Wang D, Zhu H, Chen X (2013) Clinicopathological analysis of rhabdoid meningiomas: report of 12 cases and a systematic review of the literature. *World neurosurgery* 79:724-732.
  25. Wu YT, Lin JW, Wang HC, Lee TC, Ho JT, Lin YJ (2010) Clinicopathologic analysis of rhabdoid meningioma. *J Clin Neurosci* 17:1271-1275.
  26. Santhosh K, Kesavadas C, Radhakrishnan VV, Thomas B, Kapilamoorthy TR, Gupta AK (2008) Rhabdoid and papillary meningioma with leptomeningeal dissemination. *Journal of neuroradiology. Journal de neuroradiologie* 35:236-239.
  27. Wu YT, Ho JT, Lin YJ, Lin JW (2011) Rhabdoid papillary meningioma: a clinicopathologic case series study. *Neuropathology* 31:599-605.
  28. Jia W, Sonoda Y, Saito R, Endo T, Watanabe M, Tominaga T (2014) Intracerebral cystic rhabdoid papillary meningioma in an 11-year-old patient. *Childs Nerv Syst* 30:2151-2155.
  29. Martinez-Lage JF, Ferri Niguez B, Sola J, Perez-Espejo MA, Ros de San Pedro J, Fernandez-Cornejo V (2006) Rhabdoid meningioma: a new subtype of malignant meningioma also apt to occur in children. *Childs Nerv Syst* 22:325-329.
  30. Buccoliero AM, Castiglione F, Rossi Degl'Innocenti D, Franchi A, Sanzo M, Cetica V, Giunti L, Sardi I, Mussa F, Giordano F, Genitori L, Taddei GL (2011) Pediatric rhabdoid



meningioma: a morphological, immunohistochemical, ultrastructural and molecular case study. *Neuropathology* 31:59-65.

31. Wang XQ, Chen H, Zhao L, Li ST, Hu J, Mei GH, Jiang CC (2013) Intracranial papillary meningioma: a clinicopathologic study of 30 cases at a single institution. *Neurosurgery* 73:777-790; discussion 789.
32. Brat DJ, Cohen KJ, Sanders JM, Feuerstein BG, Burger PC (1999) Clinicopathologic features of astroblastoma. *Journal of Neuropathology & Experimental Neurology* 58:509.
33. Navarro R, Reitman AJ, de Leon GA, Goldman S, Marymont M, Tomita T (2005) Astroblastoma in childhood: pathological and clinical analysis. *Childs Nerv Syst* 21:211-220.

## Figure legends

**Fig. 1** Radiological findings. (A) Computed tomography image showed heterogeneous low- to isodensity mass with a large cystic lesion in the right frontal lobe extending from the cortex to periventricular region. (B) T1-weighted image and (C) T2-weighted image showed a well-circumscribed solid and cystic lesion with little perilesional edema. The solid lesion was hypo- to isointense to gray matter on both T1- and T2-weighted sequences with a bubbly appearance. (D) After gadolinium administration, the solid lesion and a part of the cystic wall showed marked enhancement.

**Fig. 2** Cytological findings. (A) Hematoxylin and eosin (H&E) staining. (B) Papanicolaou staining. Tumor cells had eccentric round to oval nuclei with abundant eosinophilic cytoplasm with diminished cohesiveness. Some tumor cells had short cytoplasmic processes. Nuclear atypia was mild and pleomorphism was not observed. Scale bars: 50  $\mu\text{m}$ .

**Fig. 3** Histopathological findings. (A) The tumor was composed of polar cells, having eosinophilic cytoplasm and eccentrically placed nuclei with short stout cytoplasmic processes anchored to blood vessels. (B) Prominent sclerosis of stroma and blood vessel walls was observed. (C) Degenerative cyst, cholesterol cleft, and aggregation of foam cells were frequently seen. Many foam cells infiltrated around vessels (D) and among less cohesive

tumor cells (E). (F) In some intervascular regions, tumor cells were plump and had more abundant eosinophilic cytoplasm showing a rhabdoid appearance. (G) A few small foci of necrosis without palisading were found. (H) Tumor cells were seen in the cyst wall, but the tumor margin was compressing and well circumscribed. (A)–(H) H&E staining. Scale bars: 50  $\mu\text{m}$  for (A) and (D)–(G); 100  $\mu\text{m}$  for (B) and (H); 500  $\mu\text{m}$  for (C); 100  $\mu\text{m}$  for (H).

**Fig. 4** Immunohistochemical study. (A) Tumor cells were focally positive for glial fibrillary acidic protein (GFAP). (B) Vimentin was diffusely positive for cytoplasm. Inclusion-like cytoplasm was also positive for vimentin. (C) Epithelial membrane antigen (EMA) was strongly and diffusely positive in cytoplasm and cell membrane. (D) In some areas, tumor cells showed dot-like staining against EMA. (E) S-100 protein was positive for about half of tumor cells. (F) Cytokeratin AE1/AE3 was focally stained in the cytoplasm of tumor cells. (G) Nuclear expression of INI1 was evident. (H) The Ki-67 labeling index of tumor cells was 10.8%. Scale bars: 50  $\mu\text{m}$ .

**Fig. 5** Ultrastructural findings. Intracytoplasmic collection of numerous intermediate filaments was observed. Scale bars: 5  $\mu\text{m}$  for (A); 2  $\mu\text{m}$  for (B).

Figure 1

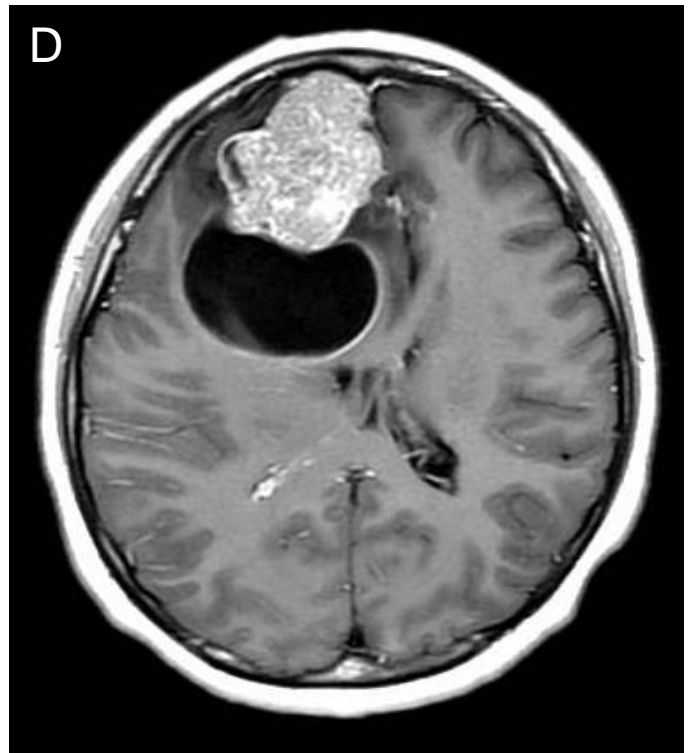
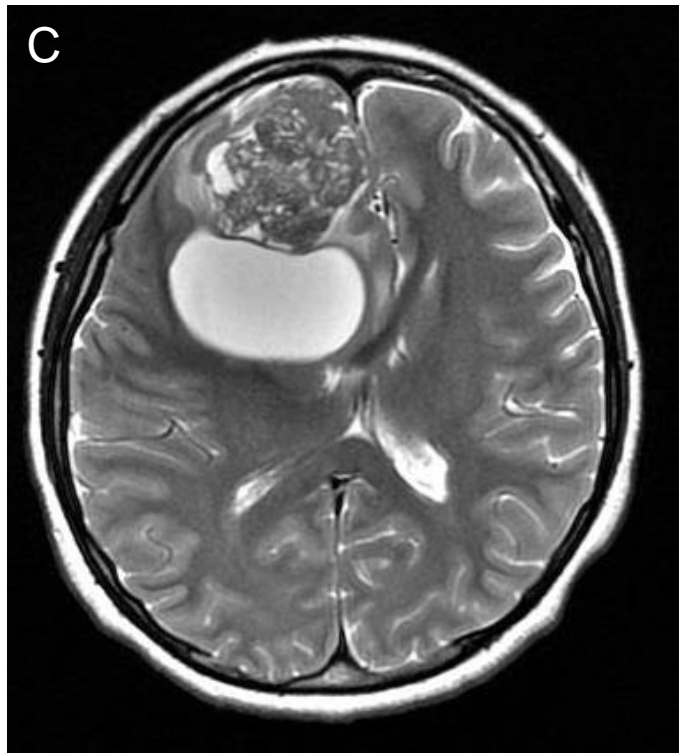
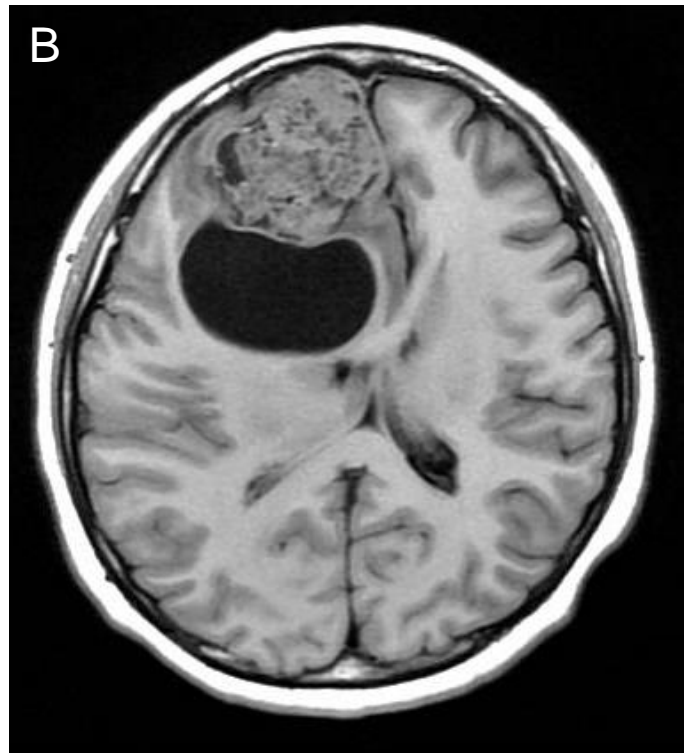
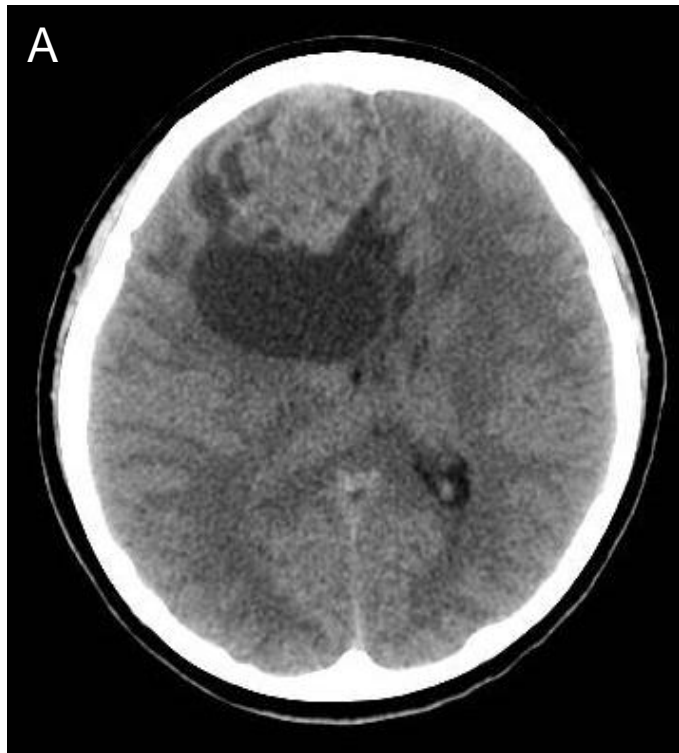


Figure 2

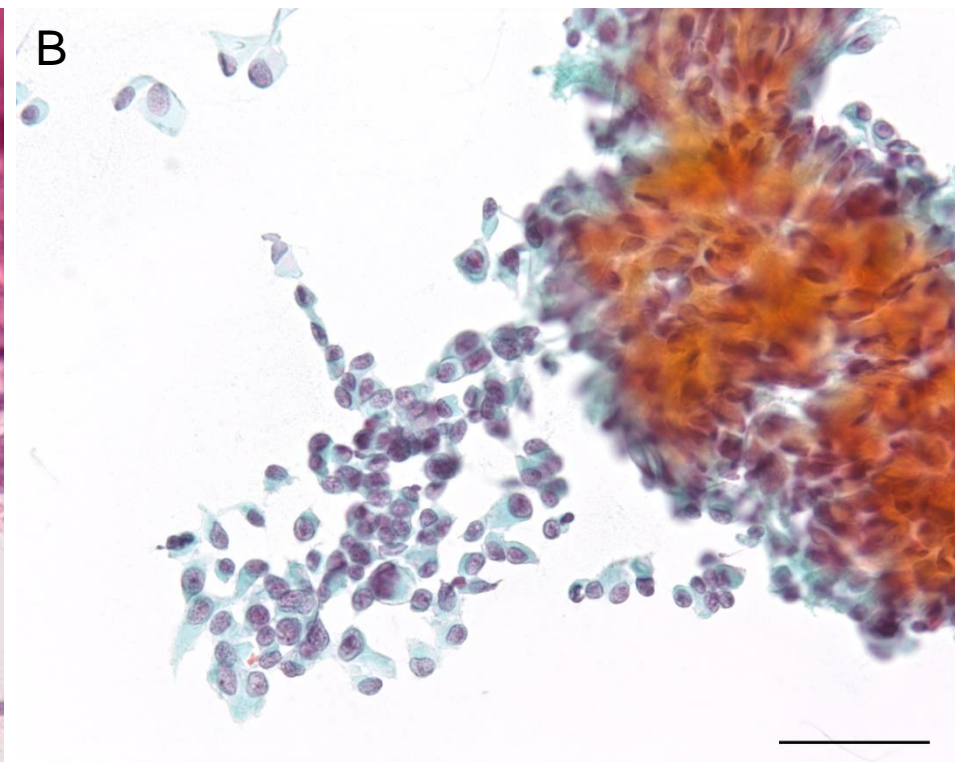
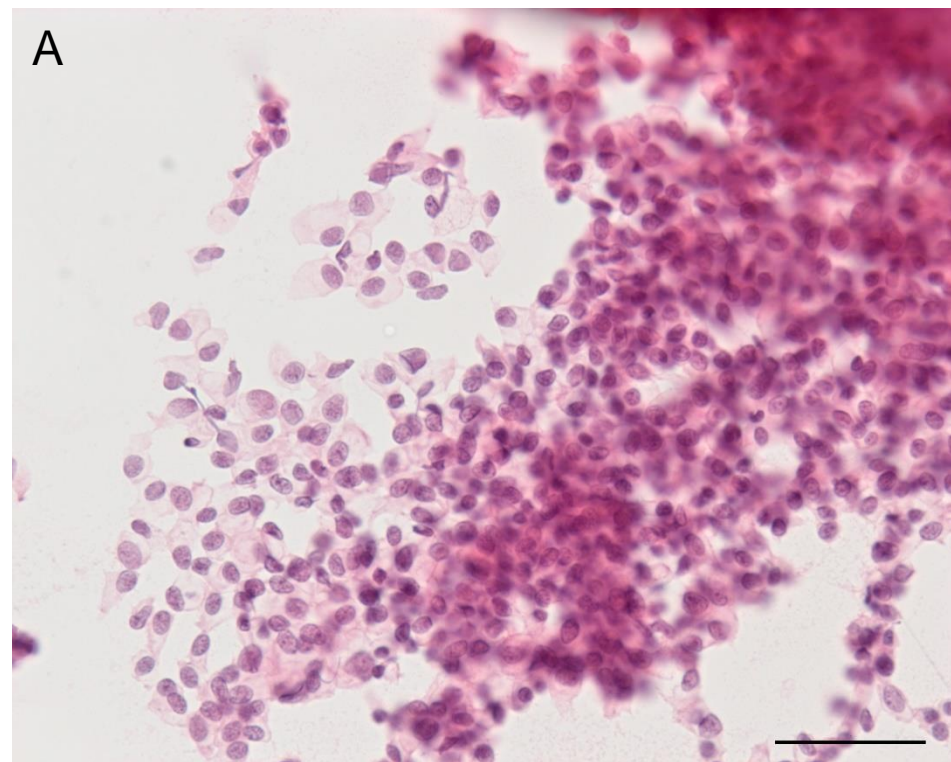


Figure 3

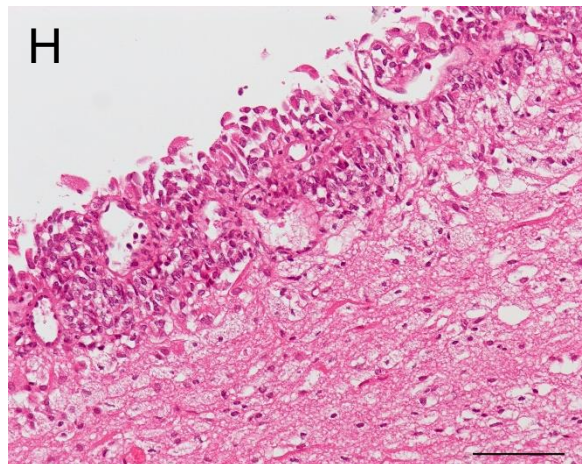
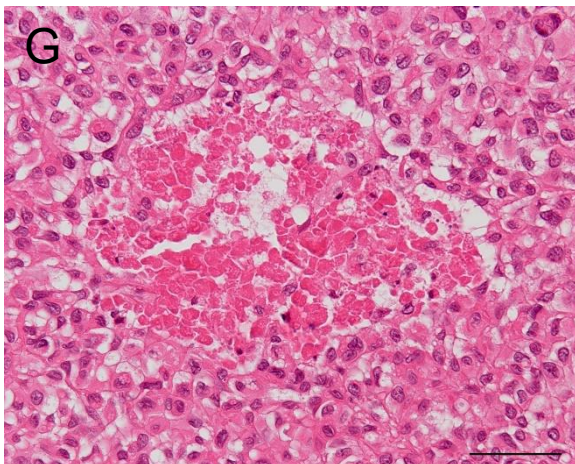
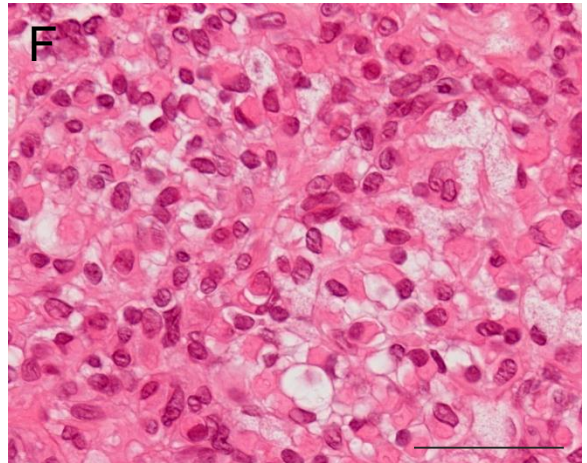
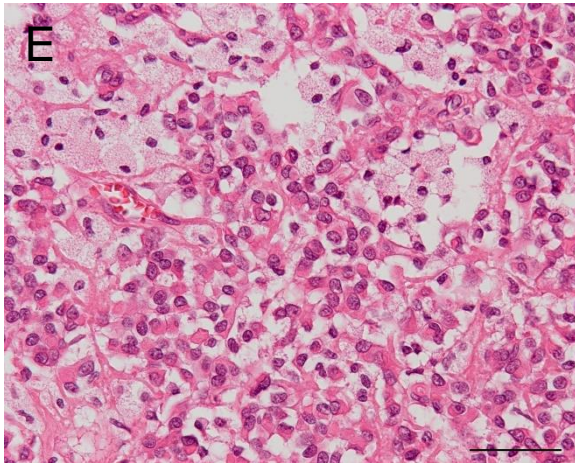
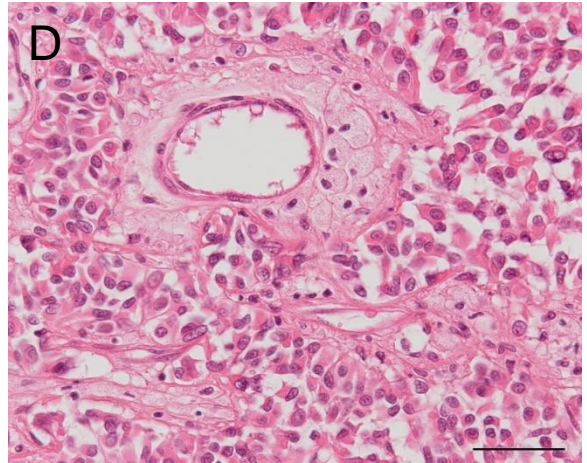
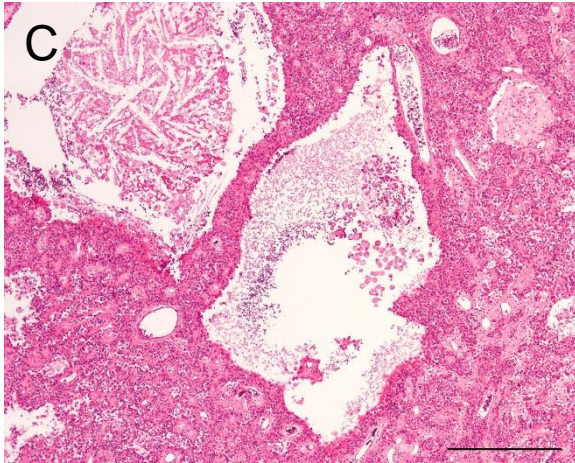
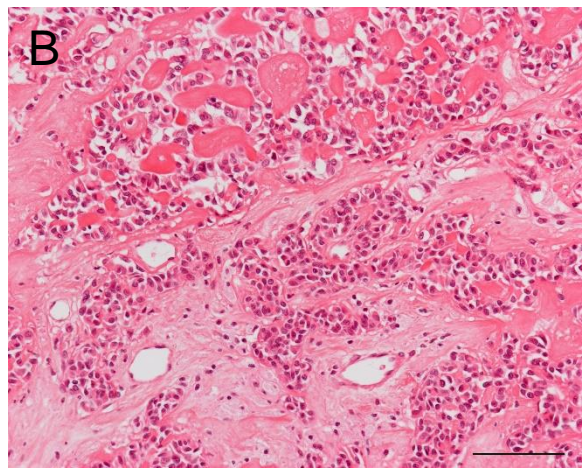
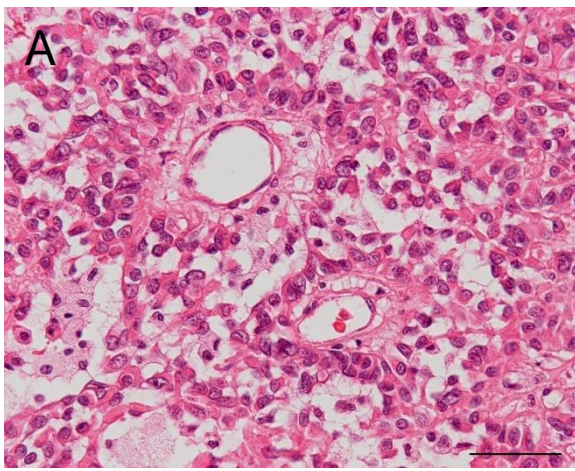


Figure 4

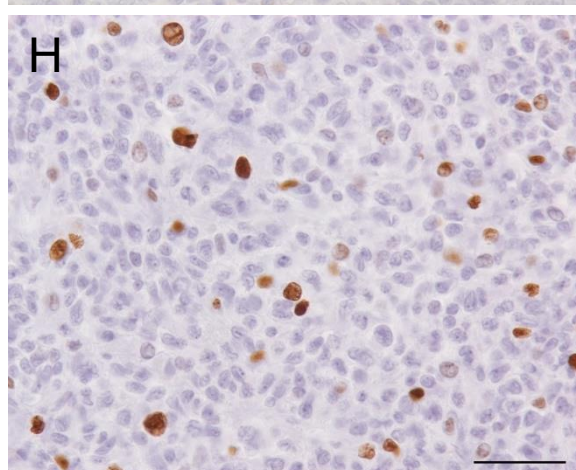
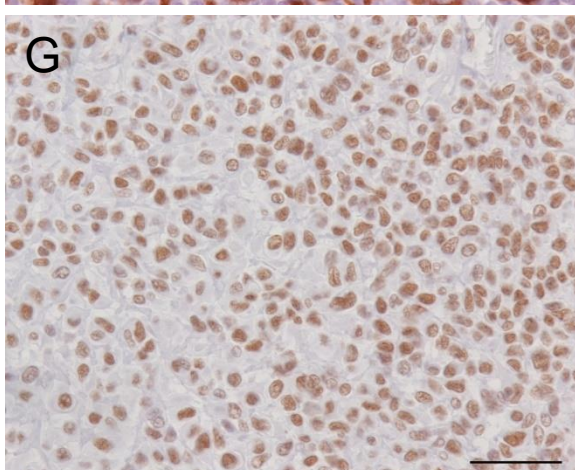
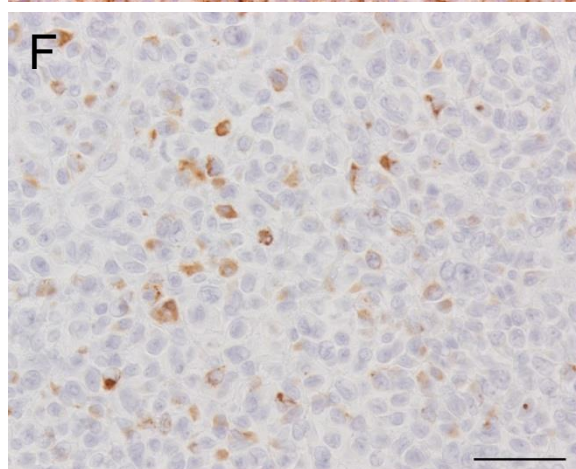
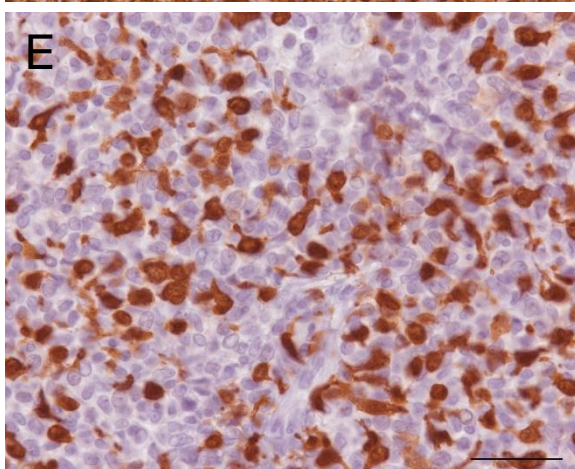
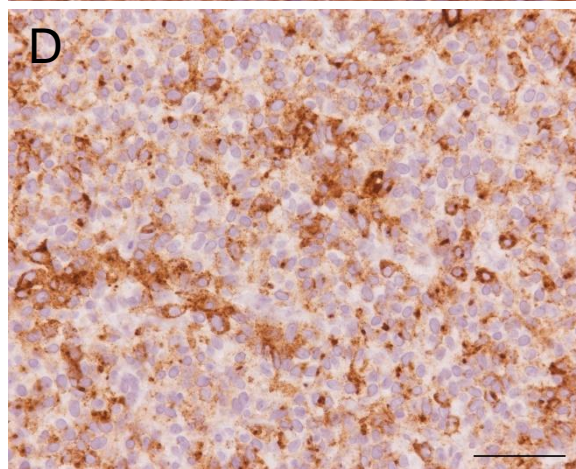
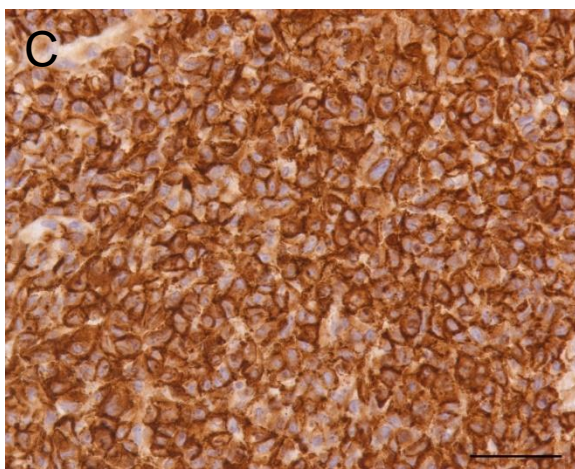
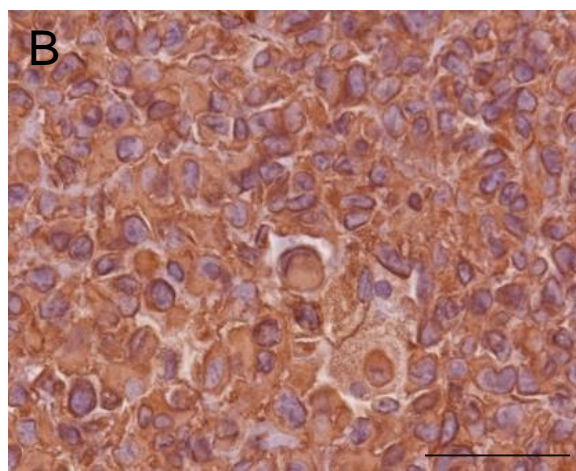
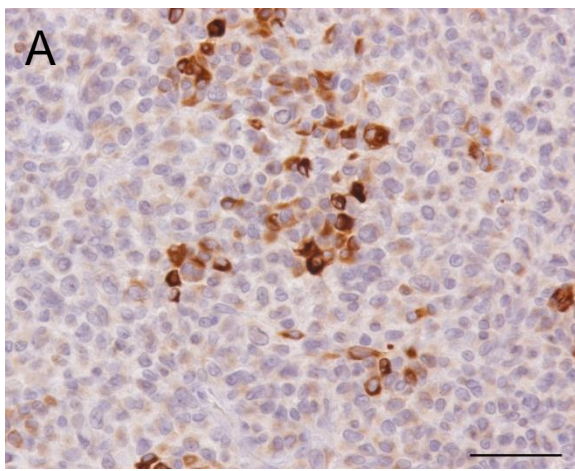


Figure 5

