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Case Report

Cystic Intracranial Recurrence of Olfactory Neuroblastoma without Accumulation on Fluorine-18-fluorodeoxyglucose Positron Emission Tomography

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A 66-year-old man underwent multimodal treatment for olfactory neuroblastoma (ONB). When he was 72 years old, a cystic intracranial lesion without accumulation on fluorine-18-fluorodeoxyglucose positron emission tomography was detected. Surgical resection was performed when the patient was 73 years old. The pathological examination revealed recurrence of ONB, and the patient underwent focal irradiation. At age 81, he presented with a second recurrence in the right occipital lobe with radiological and pathological findings similar to the prior recurrence. This case suggests that pathological confirmation should be considered in cases with atypical radiological findings following the treatment of ONB.

Key words: cystic recurrence, esthesioneuroblastoma, fluorine-18-fluorodeoxyglucose positron emission tomography, intracranial recurrence, olfactory neuroblastoma

Olfactory neuroblastoma (ONB) is a malignant neuroectodermal tumor that originates from the olfactory membrane of the sinonasal tract [1]. Despite the availability of multimodal treatments such as surgery, radiotherapy, and chemotherapy, a subset of patients with ONB experience recurrence over a long-term clinical course [2]. Early detection of recurrence after treatment is important because recurrence is associated with overall survival [2]. In detecting the recurrence of ONB, fluorine-18-fluorodeoxyglucose positron emission tomography (FDG-PET) showed efficacy [3, 4].

Recurrence is common in ONB cases, with the major patterns of recurrence including local recurrence, node metastasis, and distant metastasis [5]. Intracranial recurrence of ONB has been reported [6-10], but radiological findings in such cases have been attributed to recurrent solid tumors. Here, we report a rare case of cystic intracranial repeated recurrences of ONB without accumulation on FDG-PET.

Case Report

A 66-year-old man presenting with rhinorrhea underwent a biopsy of an intranasal lesion at a previous otorhinolaryngological hospital and was pathologically diagnosed with ONB. He was referred to the Department of Otolaryngology at our hospital and underwent neo-

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adjuvant chemotherapy with cisplatin. After 1 month, he underwent surgical resection of the residual tumor (Fig. 1A) with combined surgery using an endoscopic transnasal approach and bifrontal craniotomy. The dura mater of the anterior skull base was incised to examine the olfactory bulb. Gross total resection of the lesion with radical dissection of the olfactory bulb, nasal septum, bilateral middle nasal concha, and frontal sinus mucosa was performed. The dura mater was reconstructed where the filum olfactorium had been penetrated using a pericranial flap. We grossly confirmed that the tumor had not invaded the dura mater of the anterior skull base. Pathological examination revealed densely accumulated tumor cells with round nuclei on hematoxylin and eosin (H&E) staining of specimens from both the nasal cavity and olfactory bulb (Fig. 1B-E), and positive immunohistochemical staining for synaptophysin (Fig. 1F). The pathological diagnosis was ONB of Hyams histological grade 1 [1], and the clinical stage was Kadish stage C [11]. The Ki-67 labeling index was 20%. The resection stump was negative for tumor cells. He underwent focal irradiation (60 gray [Gy]) and was discharged from the hospital without evidence of a tumor.

Although FDG-PET was not performed for the initial tumor, the patient was followed by FDG-PET in addition to magnetic resonance imaging (MRI) in the outpatient clinic. When he was 72 years old, 75 months after the initial treatment, FDG-PET of the head presented a lack of accumulation in the right intracranial space (Fig. 2A). One month before FDG-PET, the patient had a minor head injury. On MRI, a cystic intracranial extra-axial lesion on the right side showed high intensity on T2-weighted imaging (WI) and slightly high intensity on T1WI, and it was hardly enhanced except for the cerebral veins on gadolinium-enhanced T1WI (Fig. 2B-D). Although recurrence of ONB was considered, the patient underwent burr hole drainage surgery with a suspicion of chronic subdural hematoma (CSDH) based on MRI findings and negative accumulation on FDG-PET. Xanthochromic fluid content was confirmed during surgery. He was discharged from the hospital with reduction of the lesion (Fig. 2E) but was readmitted due to regrowth of the lesion after 8 months (Fig. 2F). A second drainage surgery resulted in shrinkage of the lesion (Fig. 2G), but it regrew to its initial size at 2 weeks postoperatively (Fig. 2H). Next, we performed surgical resection with frontotemporal craniotomy when the patient was 73 years of age. During surgery, we confirmed a cystic

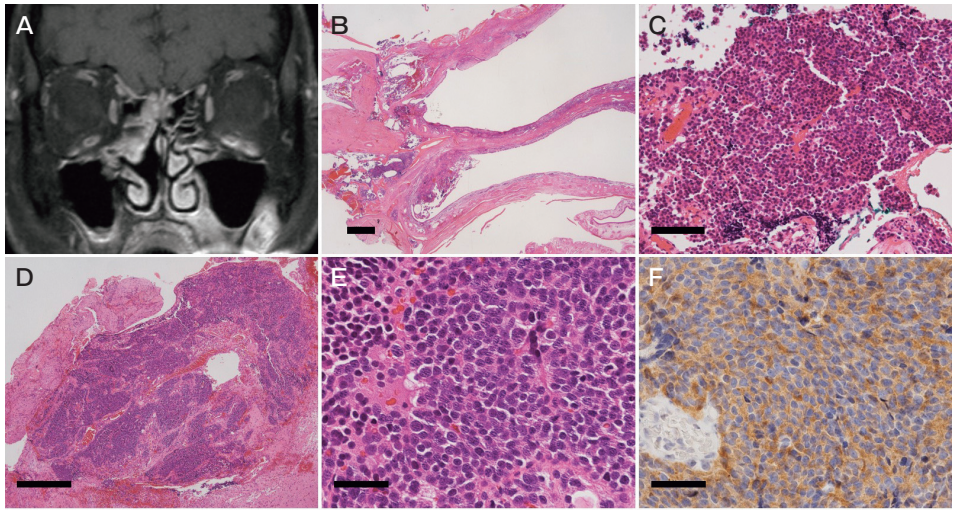

Fig. 1 Radiological and pathological findings at the first surgery. **A**, Preoperative MRI (Gd-T1WI) showing a residual tumor located at the nasal cavity to the anterior skull base; **B**, H&E staining of the specimen at the paranasal cavity (scale bar=1,000 μm) showing tumor cells located in the mucosa and bone; **C**, H&E staining of the specimen at the paranasal cavity (scale bar = 100 μm) showing dense round-shaped tumor cells with large nuclei; **D**, H&E staining of the specimen at the left olfactory bulb (scale bar = 500 μm) showing tumor cells located in the olfactory nerve; **E**, H&E staining of the specimen at the left olfactory bulb (scale bar = 50 μm) showing dense round-shaped tumor cells with large nuclei; **F**, Immunohistochemical staining of the synaptophysin showing positive staining in tumor cells (scale bar = 50 μm).

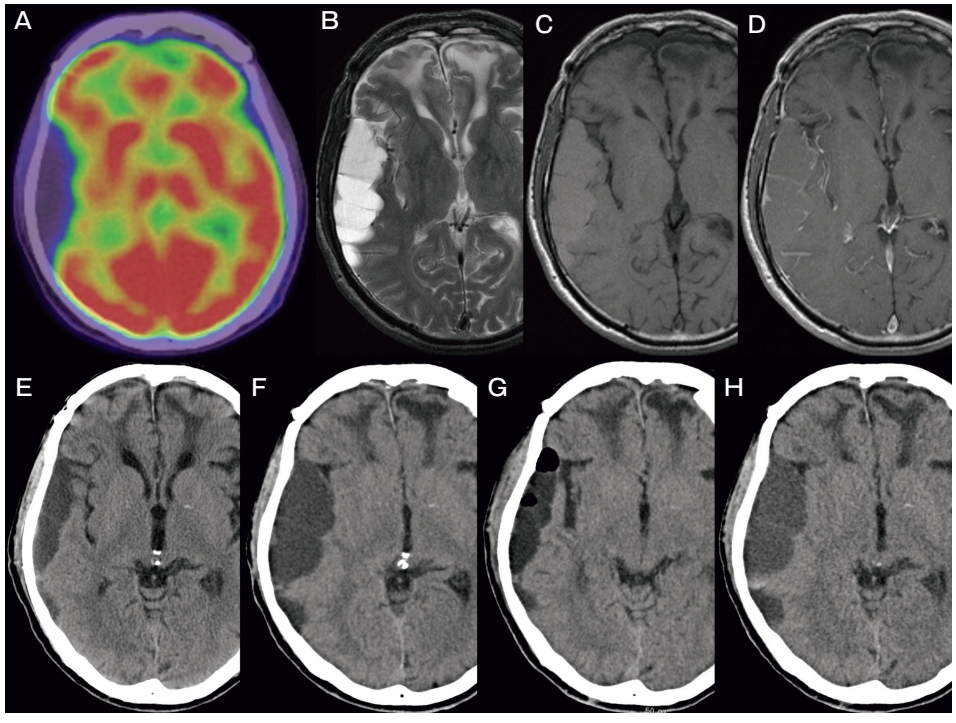

Fig. 2 Radiological findings after the first surgery, chemotherapy, and radiotherapy. **A**, FDG-PET performed 6 years after the first treatment showing an intracranial lesion without FDG accumulation; **B**, T2-weighted MRI showing an intracranial extra-axial lesion with high signal intensity; **C**, T1-weighted MRI showing an intracranial extra-axial lesion with slightly high signal intensity compared with cerebrospinal fluid; **D**, Gadolinium-enhanced T1-weighted MRI showing no apparent enhancement in the lesion except in the cerebral veins; **E**, CT performed 2 weeks after the first drainage surgery showing shrinkage of the lesion; **F**, CT performed 8 months after the first drainage surgery showing regrowth of the lesion; **G**, CT performed 3 days after the second drainage surgery showing shrinkage of the lesion; **H**, CT performed 2 weeks after the second drainage surgery showing regrowth of the lesion.

lesion just under the dura mater (Fig. 3A). The cystic lesion did not firmly adhere to the surrounding tissue, so the cyst wall was easily detached from the dura mater (Fig. 3B) and cerebral cortex (Fig. 3C). Finally, the lesion was resected en bloc (Fig. 3D), and we could not find the apparent origin of the lesion. Pathological examination revealed densely accumulated tumor cells located on the inner side of the cystic lesion on H&E staining (Fig. 4A-C). The morphology and the positive immunohistochemical staining obtained for synaptophysin (Fig. 4D) showed similarity to the specimen observed at the first surgery; therefore, we diagnosed the lesion as a recurrence of ONB. The Ki-67 labeling index was approximately 20%, which was also similar to the first one. The patient underwent additional focal irradiation (50 Gy).

At 96 months after the second irradiation, when the patient was 81 years old, MRI showed a subdural lesion in the right occipital lobe (Fig. 5A-C). FDG-PET showed

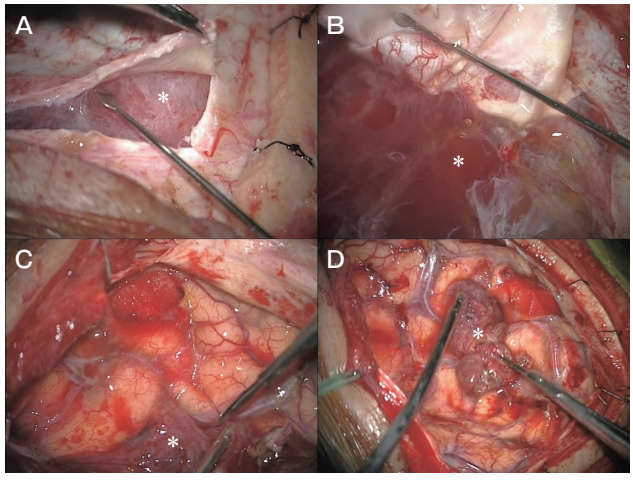

Fig. 3 Intraoperative findings at surgical resection (*indicates the lesion). **A**, The lesion was located at the subdural space; **B**, The lesion was cystic and easily detached from the dura mater; **C**, The lesion was also attached to the cerebral cortex but was easily detached; **D**, The lesion was resected *en bloc*.

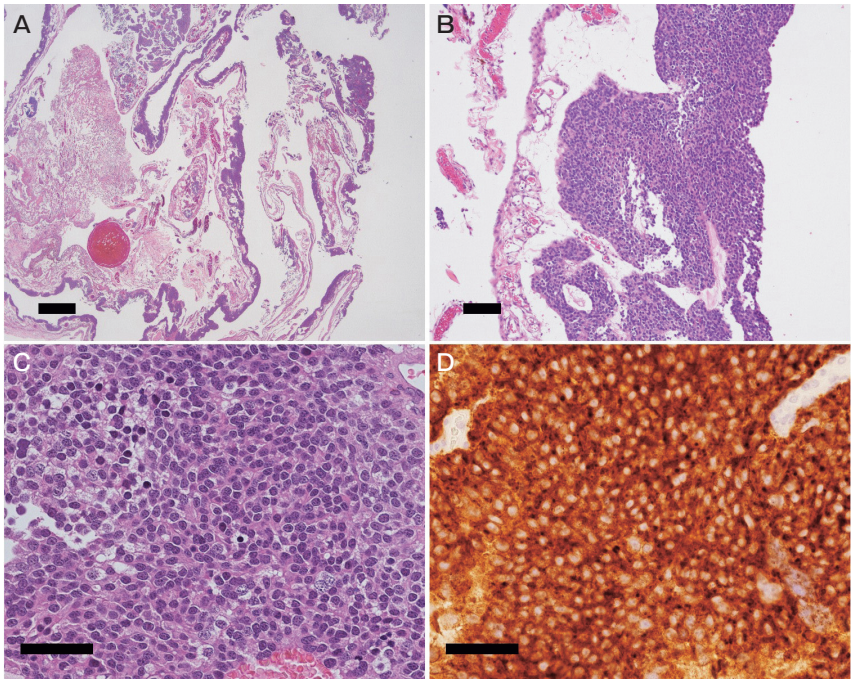

Fig. 4 Pathological findings of the specimen at the second surgical resection. **A**, H&E staining (scale bar = 1,000 μm) showing dense tumor cells located in the wall of the cystic lesion; **B**, H&E staining (scale bar = 100 μm) showing dense tumor cells on the inner side of the wall; **C**, H&E staining (scale bar = 50 μm) showing tumor cells with round nuclei resembling the specimen at the first surgery; **D**, Immunohistochemical staining of the synaptophysin (scale bar = 50 μm) showing positive staining in tumor cells, just as in the specimen obtained in the first surgery.

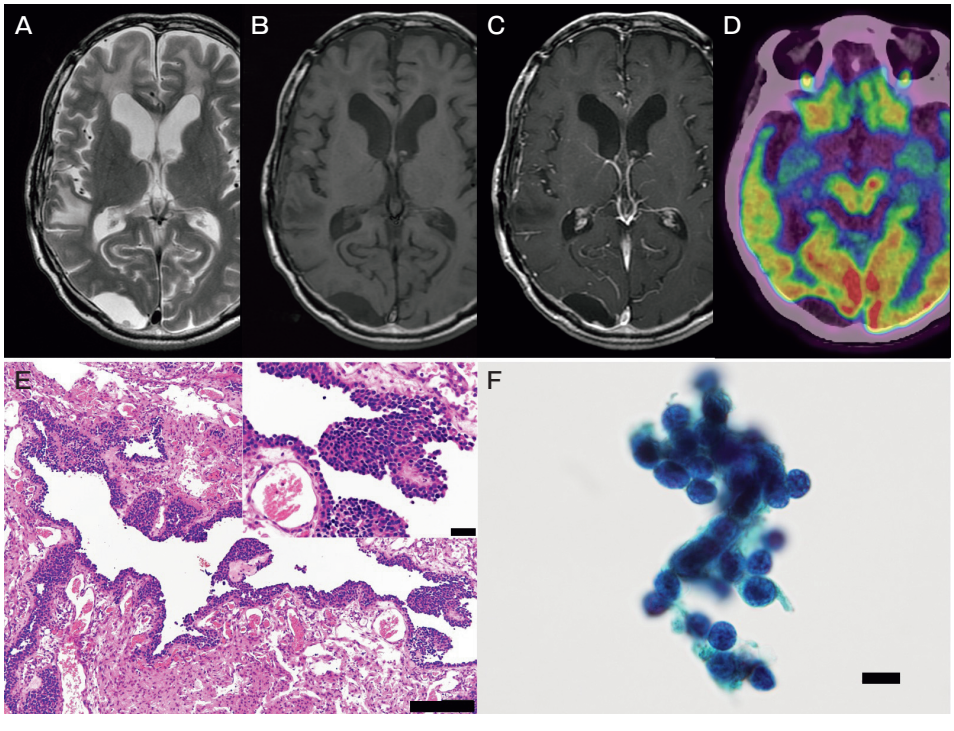

Fig. 5 Radiological and pathological findings at the third surgery. **A**, T2WI of MRI showing a high-intensity lesion in the subdural space of the right occipital lobe. A nodule-like lesion is also observed in the cystic lesion; **B**, T1WI of MRI showing the cystic lesion as low intensity; **C**, Gd-T1WI of MRI showing enhancement in the wall of the cystic lesion, while the inside of the lesion was not enhanced; **D**, FDG-PET showing negative accumulation at the cystic lesion; **E**, H&E staining (scale bar = 200 μm; inset, scale bar = 80 μm) showing tumor cells similar to the previous recurrence accumulating with a multilayered structure; **F**, Cytological diagnosis of the fluid content of the cystic lesion (scale bar = 20 μm) showing the presence of tumor cells.

a lack of accumulation (Fig. 5D). Because the radiological findings were similar to those for the previous recurrence, the patient underwent resection surgery with suspicion of ONB recurrence. Pathological examination showed tumor cells similar to the specimen obtained at the previous intracranial recurrence (Fig. 5E). Moreover, for the first time, the patient underwent cytological diagnosis of the fluid content of the lesion, and tumor cells were found to be present (Fig. 5F). The patient underwent additional focal irradiation (50 Gy) for the tumor bed with a diagnosis of intracranial recurrence of ONB.

Discussion and Conclusions

Some cases of subdural hematoma associated with dural metastasis of malignant neoplasms have been reported [12-25]. Although the radiological findings in the present case appeared similar to CSDH, they differed from the findings described in previous reports. Subdural recurrence of ONB has also been reported [9, 10], but in these previous cases the tumor presented as a solid mass on MRI, which differed from our case. To the best of our knowledge, no case with cystic intracranial recurrence of extracranial malignancies, including ONB, has been previously reported. We initially misdiagnosed the recurrent lesion in this case as CSDH, although the content of the lesion was xanthochromic fluid and not old hematoma, which is generally observed in CSDH. Because such subdural lesions present atypical radiological findings mimicking CSDH, it is important to recognize the presence of cystic intracranial recurrence of ONB. As shown in the second recurrence in this case, cytological diagnosis can be helpful in predicting malignant characteristics and should have been considered during the first drainage surgery. It is unknown whether this intracranial recurrence is specific to ONB, as no other cases of such recurrence have been reported.

Although the mechanism of intracranial recurrence in this case was uncertain, two possible causes were considered: hematogenous metastasis to the dura mater and arachnoid dissemination. Among these possible mechanisms, dural metastasis was considered less likely because the intraoperative findings showed intact dura mater that was easily detached from the lesion. However, the intraoperative and histopathological findings did not suggest a definite mechanism of recurrence. Although the resection stump was pathologically confirmed as negative for tumor cells, the olfactory bulb or surrounding dura mater would be considered possible sites of origin for the recurrence because the initial lesion had pathologically extended to the olfactory bulb. However, MRI and operative findings did not reveal any apparent attachment between the recurrent lesion and olfactory bulb.

Previous studies have indicated a 75-77.7% positive rate for ONB on FDG-PET [3, 4], and 75% of recurrent tumors have been reported to be positive on FDG-PET [4]. While a subset of ONB cases are negative on FDG-PET, such cases would likely be misjudged in the postoperative course. Previous reports suggested that ONBs that have a negative result on FDG-PET are low-grade, well-differentiated malignancies [3] or are false negatives due to the high physiologic glucose metabolism rate in normal brain tissue in cases with intracranial metastasis [4]. In the present case, although the FDG-PET findings for the initial tumor were not available, we consider that FDG-PET was unable to detect FDG intake in the tumor cells because the content of the lesion was liquid and the tumor cells existed only in the lesion membrane; in addition, there was high FDG uptake in the surrounding brain. A similar phenomenon was noted in a case of cutaneous angiosarcoma with a metastatic pulmonary cystic lesion without hypermetabolic findings on FDG-PET [26]. While cystic intracranial recurrence of ONB is extremely rare, such cases would be difficult to diagnose as recurrences on FDG-PET. Fujioka *et al*. have reported a case with intracranial recurrence of ONB with a negative FDG-PET result [4], but MRI showed a massive enhanced lesion. The incidence of cystic intracranial recurrences like this is unknown. To accurately diagnose recurrence in the follow-up of ONB cases, pathological confirmation should be considered in cases with atypical radiological findings.

In conclusion, cystic intracranial recurrence of ONB is a rare presentation, and it is difficult to diagnose due to the lack of accumulation on FDG-PET. Pathological confirmation should be considered in cases with atypical radiological findings, even if they have negative FDG-PET results.

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References

1. WHO Classification Head and Neck Tumours, Wenig BM, Dulguerov P, Fanburg-Smith JC, Kapadia SB, Thompson LDR: International Agency for Research on Cancer, Lyon (2005) pp 66–70.
2. Nakao K, Watanabe K, Fujishiro Y, Ebihara Y, Asakage T, Goto A and Kawahara N: Olfactory neuroblastoma: long-term clinical outcome at a single institute between 1979 and 2003. Acta Otolaryngol Suppl (2007): 113–117.
3. Wu HB, Wang QS, Zhong JM, Zhou WL, Li HS and Qiao-yu W: Preliminary study on the evaluation of olfactory neuroblastoma using PET/CT. Clin Nucl Med (2011) 36: 894–898.
4. Fujioka T, Toriihara A, Kubota K, Machida Y, Nakamura S, Kishimoto S, Ohashi I and Shibuya H: Long-term follow-up using 18F-FDG PET/CT for postoperative olfactory neuroblastoma. Nucl Med Commun (2014) 35: 857–863.
5. de Gabory L, Abdulkhaleq HM, Darrouzet V, Bebear JP and Stoll D: Long-term results of 28 esthesioneuroblastomas managed over 35 years. Head Neck (2011) 33: 82–86.
6. Kim YS, Jung S, Jang WY, Lee KH, Moon KS and Kim IY: Recurrent Olfactory Neuroblastoma in Remote Leptomeninges, Mimicking Intracranial Meningioma. World Neurosurg (2016) 96: 612 e619–612 e614.
7. Tamase A, Nakada M, Hasegawa M, Shima H and Yamashita J: Recurrent intracranial esthesioneuroblastoma outside the initial field of radiation with progressive dural and intra-orbital invasion. Acta Neurochir (Wien) (2004) 146: 179–182.
8. Dinca EB, Radatz MW, Rowe J and Kemeny AA: Gamma Knife(R) radiosurgery for recurrent intracranial olfactory neuroblastoma (esthesioneuroblastoma): a case report. J Med Case Rep (2012) 6: 240.
9. Capelle L and Krawitz H: Esthesioneuroblastoma: a case report of diffuse subdural recurrence and review of recently published studies. J Med Imaging Radiat Oncol (2008) 52: 85–90.
10. Murakami M, Kakita K, Kimura S and Hosokawa Y: Subdural extension of recurrent olfactory neuroblastoma. Case report. Neurol Med Chir (Tokyo) (2005) 45: 596–599.
11. Kadish S, Goodman M and Wang CC: Olfactory neuroblastoma. A clinical analysis of 17 cases. Cancer (1976) 37: 1571–1576.
12. Ashish K, Das K, Mehrotra A, Jaiswal A, Jaiswal S, Sahu R and Srivastav A: Intracranial dural metastasis presenting as chronic subdural hematoma: a case report and review of literature. Turk Neurosurg (2014) 24: 992–995.
13. Boukas A, Sunderland GJ and Ross N: Prostate dural metastasis presenting as chronic subdural hematoma. A case report and review of the literature. Surg Neurol Int (2015) 6: 30.
14. Comanescu A, Rosca E, Bota M and Ninulescu G: Chronic subdural hematoma in a patient with acute myeloid leukemia and dural metastatic infiltration. Rom J Morphol Embryol (2008) 49: 259–262.
15. D'Angelo V, Bizzozero L, Fontana RA, Colombo N and Minola E: Chronic subdural hematoma associated with dural metastasis from mammary carcinoma. Case report and review of the literature. Acta Neurol (Napoli) (1988) 10: 206–212.
16. Fukino K, Terao T, Kojima T, Adachi K and Teramoto A: Chronic subdural hematoma following dural metastasis of gastric cancer: measurement of pre- and postoperative cerebral blood flow with N-isopropyl-p-[123I]iodoamphetamine--case report. Neurol Med Chir (Tokyo) (2004) 44: 646–649.
17. Ishii N, Yokosuka K, Sekihara Y, Hirano K, Suzuki Y and Ishii R: [A case of subdural hematoma associated with dural metastasis of lung cancer]. No Shinkei Geka (2007) 35: 511–513.
18. Katsube T, Kikuchi T, Konnno S, Murayama M, Kobayashi R, Kuhara K, Yoshimatsu K, Shiozawa S, Shimakawa T, Naritaka Y, Ogawa K, Hagiwara S and Aiba M: Subdural hematoma associated with dural metastasis of gastric carcinoma: report of two cases. Anticancer Res (2007) 27: 4339–4344.
19. Kamiya K, Inagawa T and Nagasako R: [Chronic subdural hematoma due to dural metastasis: demonstration of adenocarcinoma cell nests in the fluid. Case report]. Neurol Med Chir (Tokyo) (1987) 27: 892–898.
20. Kunii N, Morita A, Yoshikawa G and Kirino T: Subdural hematoma associated with dural metastasis--case report. Neurol Med Chir (Tokyo) (2005) 45: 519–522.
21. Leech RW, Welch FT and Ojemann GA: Subdural hematoma secondary to metastatic dural carcinomatosis. Case report. J Neurosurg (1974) 41: 610–613.
22. Nagayama I, Katoh H, Sakumoto M, Itoh M and Yoshida K: Subdural hematoma associated with dural metastasis from paranasal sinus cancer: a case report and review of the literature. ORL J Otorhinolaryngol Relat Spec (1993) 55: 240–243.
23. Tseng SH, Liao CC, Lin SM, Chen Y and Shun CT: Dural metastasis in patients with malignant neoplasm and chronic subdural hematoma. Acta Neurol Scand (2003) 108: 43–46.
24. Yuan X, Zhao H, Zhao C, Xiao H, Sun G, Bai Y and Niu J: Chronic subdural hematoma due to dural metastasis of gastric adenocarcinoma progressing rapidly with uncal herniation. J Craniofac Surg (2014) 25: 2270–2272.
25. Kuan-Yin T, Dueng-Yuan H and Hsin IM: Subdural hematoma associated with skull and dural metastasis of gastric carcinoma: a case report. Turk Neurosurg (2013) 23: 796–799.
26. Andersen KF, Albrecht-Beste E, Berthelsen AK and Loft A: Angiosarcoma of the Scalp: Metastatic Pulmonary Cystic Lesions Initially Misinterpreted as Benign Findings on 18F-FDG PET/CT. Diagnostics (Basel) (2015) 6.