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Primary Intracranial Yolk Sac Tumor in the Posterior Fossa: Case Report of a Child with Down Syndrome

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Introduction

Down syndrome (DS) has an increased risk of leukemia and a decreased incidence of solid tumors [1]. However, Asian patients with DS do not have a lower risk of brain tumors, especially germ cell tumors [2]. Satge et al. summarized 38 central nervous system tumors in DS and reported that 14 (61%) of 23 cases under age 15 were germ cell tumors [3]. All reported cases were Asian, and yolk sac tumors (YST) had the highest occurrence. Recently, the association between germ cell tumors and DS has been reported. We report a case of intracranial YST originating from the posterior fossa dura mater. Although DS related intracranial GCTs tend to occur in atypical sites such as the basal ganglia, origination in the posterior fossa dura is extremely rare.

Case report

A two and a half year old boy diagnosed with DS by newborn chromosomal screening was referred to our institution with vomiting and severe truncal ataxia. Magnetic resonance (MR) images demonstrated a mass measuring 40×26 mm in the right posterior fossa. T2 weighted image revealed a mass with high intensity, a cerebrospinal fluid cleft and marked perifocal edema that resulted in tonsillar herniation and obstructive hydrocephalus. Postcontrast 3-dimensional magnetization prepared rapid gradient echo imaging (MPRAGE) depicted an enhancing mass with wide attachment to the thickened posterior fossa dura (Fig. 1). Constructive interference in steady state (CISS) images clearly showed that the mass compressed and displaced cerebellar cortex. Spinal MR images showed no mass or dissemination. Diagnoses of peripheral PNET or AT/RT were considered preoperatively. Emergent surgery via the lateral suboccipital route was performed on the day of admission. A reddish-gray mass was noted on the surface of the cerebellum and adherent to the thickened posterior fossa dura mater. This operative finding suggested that this tumor originated from the posterior fossa dura mater around the transverse-sigmoid sinus junction. The hypervascular and friable mass was removed totally. The posterior fossa dura mater was excised as much as possible. Postoperative MR images confirmed no residual tumor (Fig. 2).

Histopathological findings revealed that the tumor consisted of proliferating tubules and solid sheets of tumor cells in loose reticular stroma. A Schiller-Duval body and hyaline droplets were sparsely seen. The tumor cells obviously existed among the dura mater. Immunohistochemical staining revealed strong positivity for α fetoprotein (AFP), AE1/AE3 and INI1 whereas human chorionic gonadotropin (HCG), epithelial membrane antigen, glial fibrillary acidic protein, Olig2, NeuN, CD30 and oct3/4 were negative (Fig. 3). No other GCT components were recognized. The MIB-1 labeling index was as high as 60%. Further images showed no evidence of primary extra-gonadal disease including the thorax, abdomen and pelvis. The final diagnosis was primary intracranial pure YST originating from posterior fossa dura mater.

Systemic chemotherapy was initiated with three cycles of VBP (VP16 120 mg/m² on day 1-3, bleomycin 15 mg/m² on day 2, and CDDP 20 mg/m² on day 1-5). At the end of chemotherapy, his serum AFP level decreased from 3746.9 to 1.5 ng/ml (normal range: 1.0-10.0 ng/ml). The HCG level remained

normal. We did not administer radiotherapy after tumor resection because his parents refused radiotherapy due to the risk of further deterioration of his cognitive function. Cytological examination of cerebrospinal fluid (CSF) remained negative.

Five months after surgery, his serum AFP level increased to 173.0 ng/ml, and MR images confirmed small local recurrence. After removal of the recurrent tumor, another five cycles of BEP was administered, and local irradiation of 54Gy/30fr was conducted with parental consent.

No tumor recurrence on follow up MR imaging or elevation of serum AFP have been seen in one and half years.

Discussion

There is a 10-30 fold increased risk of acute leukemia in patients with DS [1]. Although several brain tumors, such as GCT, glioblastoma, angioma, rhabdomyosarcoma, are thought to be related to DS, a distinct risk remains unclear. Twenty cases of primary intracranial GCTs associated with DS have been reported, and five of these were YSTs. Ehara et al. reported two germ cell tumors based on 1514 autopsied cases with DS in Japan [2]. Even in consideration of their higher incidence, Japanese and Asian patients with DS do not have a lower risk of germ cell tumors. The ratio (25%; 5/20 cases) of YST is also quite high in patients with DS compared to those without DS (less than 5%) in Japan [4]. Primary intracranial GCTs usually arise from midline structures, i.e. pineal, suprasellar, and third ventricular region; however, in DS patients, the basal ganglia was the most affected site of this rare entity. Regarding YSTs, the affected sites are amorphous, i.e. cerebellar hemisphere, cerebello-pontine angle, pineal body and basal ganglia. The posterior fossa dura mater is an extremely rare site for YST.

YSTs might arise either from primordial germ cells that have migrated improperly during embryonic development or from undifferentiated pluripotent embryonic or extraembryonic cells that have escaped the influence of primary developmental factors. Although recent molecular biological and genetic surveillance suggest an extra chromosome 21 may activate oncogenes or inactivate tumor suppressor genes, resulting in development of GCT, this hypothesis remains controversial [3]. Additionally, certain chromosomal abnormalities (particularly chromosomes 1, 3, and 6) also have been suggested to participate in YST development.

Pathohistologically, pure intracranial YST is quite rare, as they often possess other components of GCTs. An endodermal sinus-like structure is called a Schiller-Duval body and is pathognomonic of YSTs; however, Schiller-Duval bodies are present in 50-70% of YSTs [5]. Immunohistochemical studies are useful because YST cells are positive for AFP. However, AFP is not specific for YSTs, as primitive neuroepithelial elements of immature teratoma may also be positive for AFP. Embryonal carcinoma, although positive for CD30, is negative for AFP.

The prognosis of YST is quite dismal. Matsutani et al. described 5-year survival of 27% for YSTs,

embryonal carcinomas, choriocarcinomas, and immature teratomas after partial resection and radiotherapy [5]. It also reported that YST exhibited the worst prognosis with 25% survival at 5 years and 0% at 10 years in four patients of a 111 GCT patient series. Platinum-based chemotherapy combined with radiotherapy is standard treatment for intracranial GCTs. Robertson et al. reported the multimodal “sandwich” therapy, a course of PE (cisplatin and etoposide) therapy before radiation therapy and JEB protocol (etoposide, carboplatin, bleomycin) after radiation therapy, to malignant GCTs resulted in 4-year actuarial event-free and total survival rates of 67 and 74%, respectively. Lu et al. successfully treated pineal YST using a combination of PVB (etoposide, bleomycin, and cisplatin) and methotrexate. For gonadal malignant GCTs, combination chemotherapeutic regimens such as VAC (vinblastine, adriamycin, and cytoxan) or VBP (etoposide, bleomycin, and cisplatin) are highly effective. The sensitivity to chemotherapy is generally high among patients with DS. Dose-reduction multidrug chemotherapy is the standard therapy for acute myeloid leukemia in DS.

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Figure legends

Figure 1 MRI demonstrates a large extra-axial mass with marked perifocal edema. The tumor compresses and displaces the cerebellar cortex. The extra-axial mass showed a so-called cerebrospinal fluid cleft (arrow). Postcontrast 3-dimensional magnetization prepared rapid gradient echo imaging (MPRAGE) depicted an enhancing mass with wide attachment to the thickened posterior fossa dura. a. T2 weighted image, b. Gadolinium-enhanced MPRAGE axial image, c. Gadolinium-enhanced MPRAGE coronal image, d. Constructive interference in steady state image

Figure 2 a. A well-circumscribed tumor was seen (asterisk) via the right lateral suboccipital approach. The tumor was reddish-gray, hypervascular and friable. b. Immediately after the initial surgery, MRI revealed no residual tumor.

Figure 3 a. The tumor consists of proliferating tubules and solid sheets of tumor cells in loose reticular stroma (HE; magnification $\times 200$). b. A Schiller-Duval body and hyaline droplets are sparsely seen (HE; magnification $\times 200$). c. The tumor cells exist among the dura mater (HE: magnification $\times 100$). d. Immunohistochemical staining reveals a strong positivity for α fetoprotein (AFP).

Figure1a



Figure1b

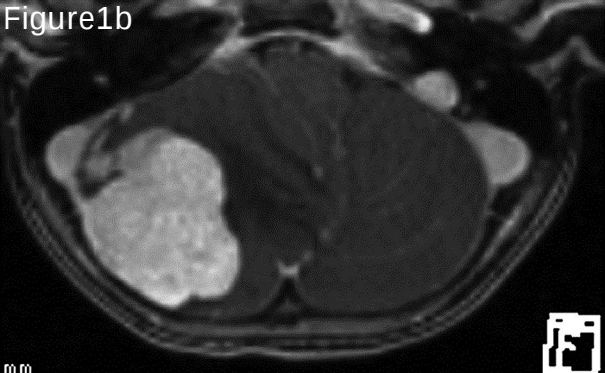


Figure1c

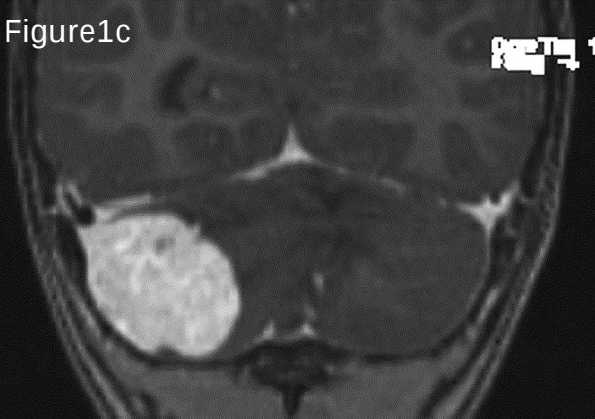


Figure1d

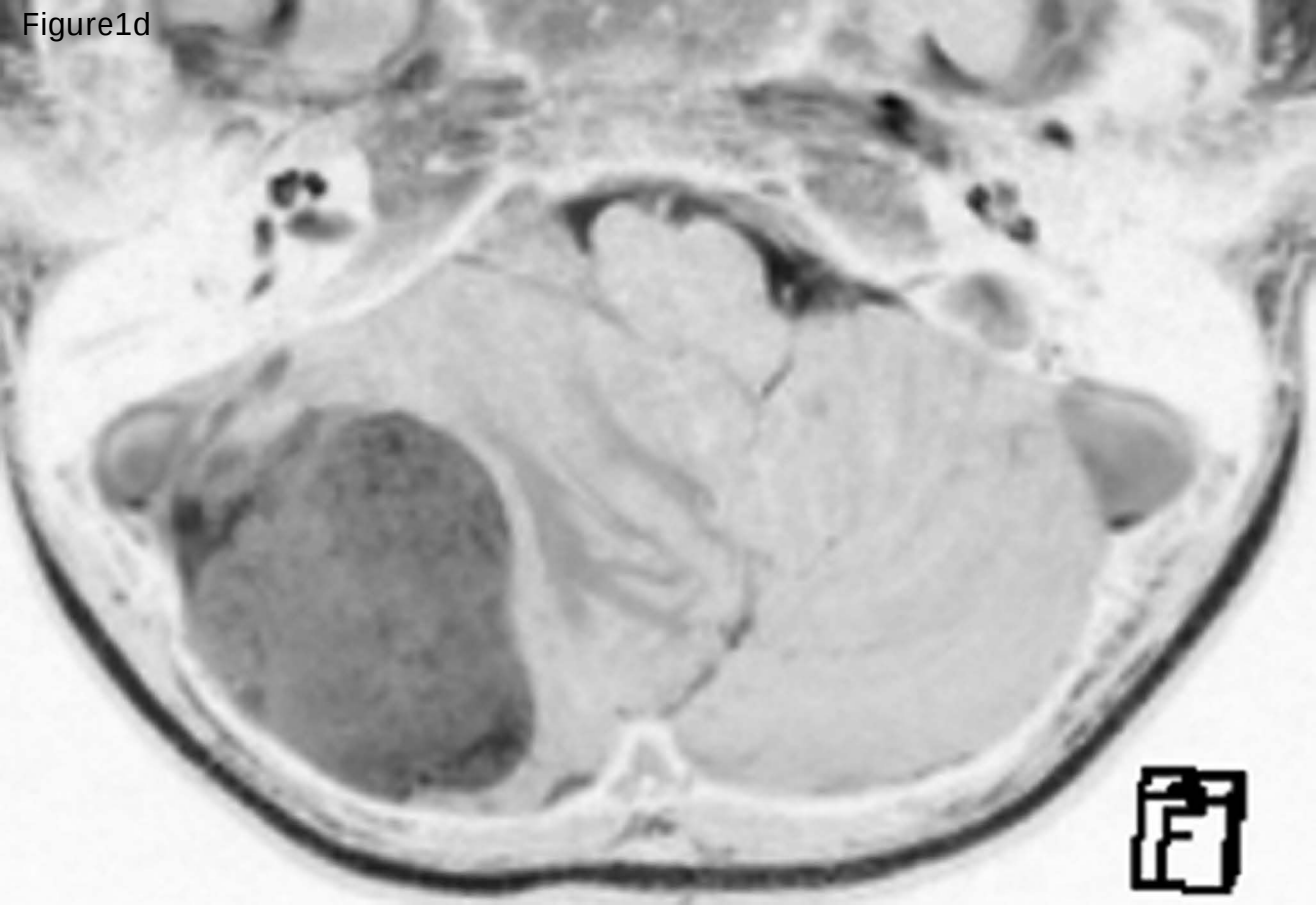
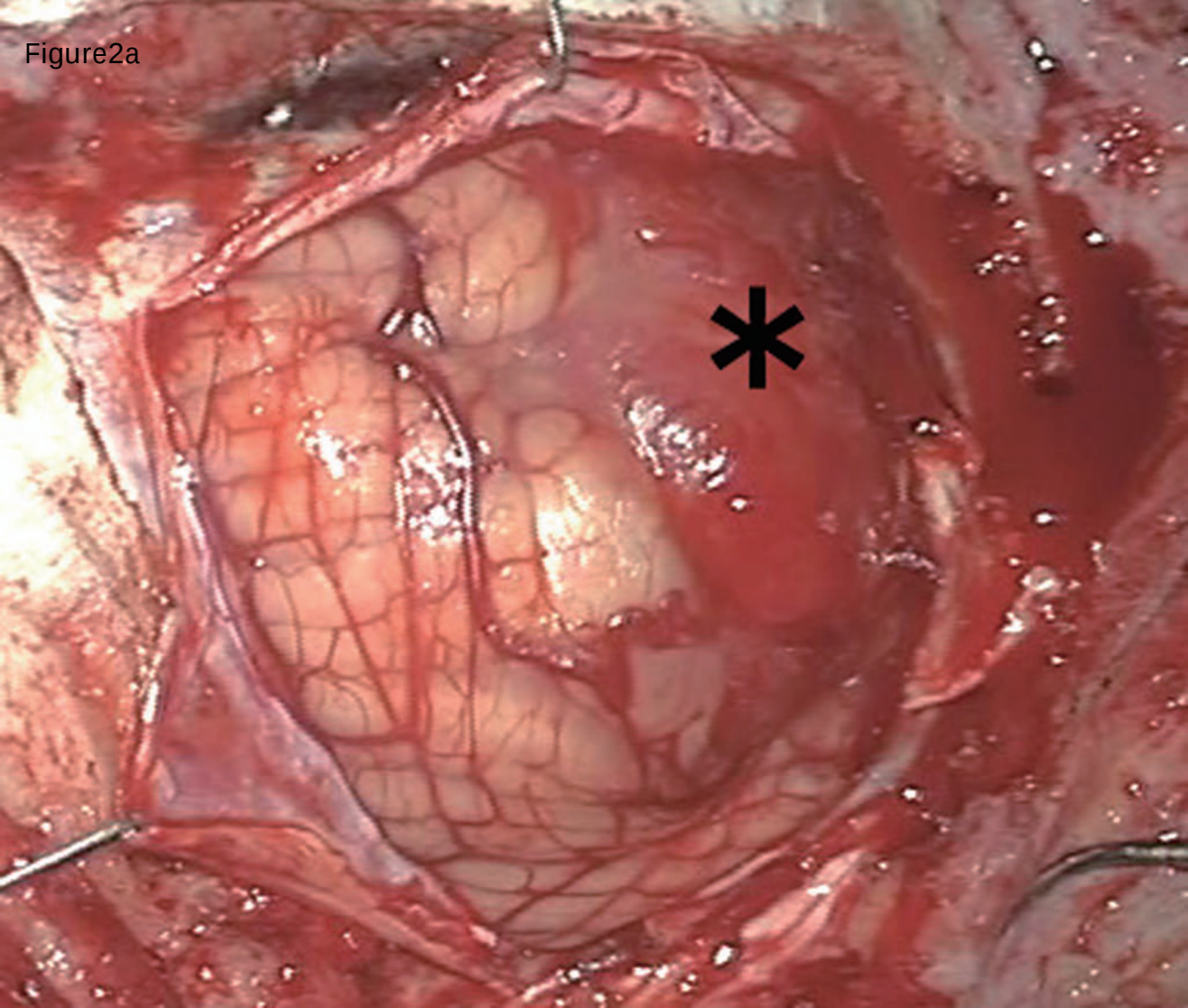


Figure2a



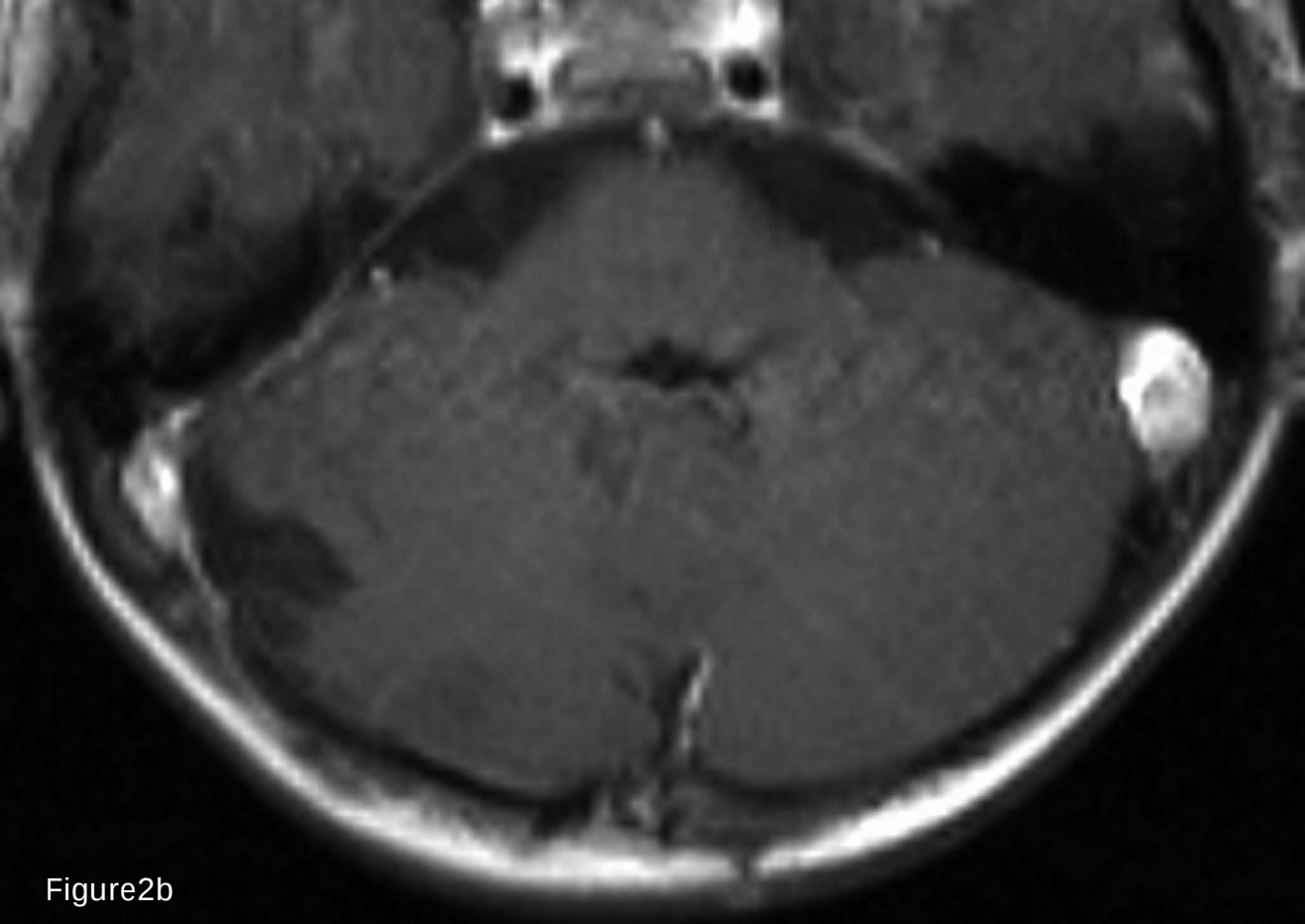
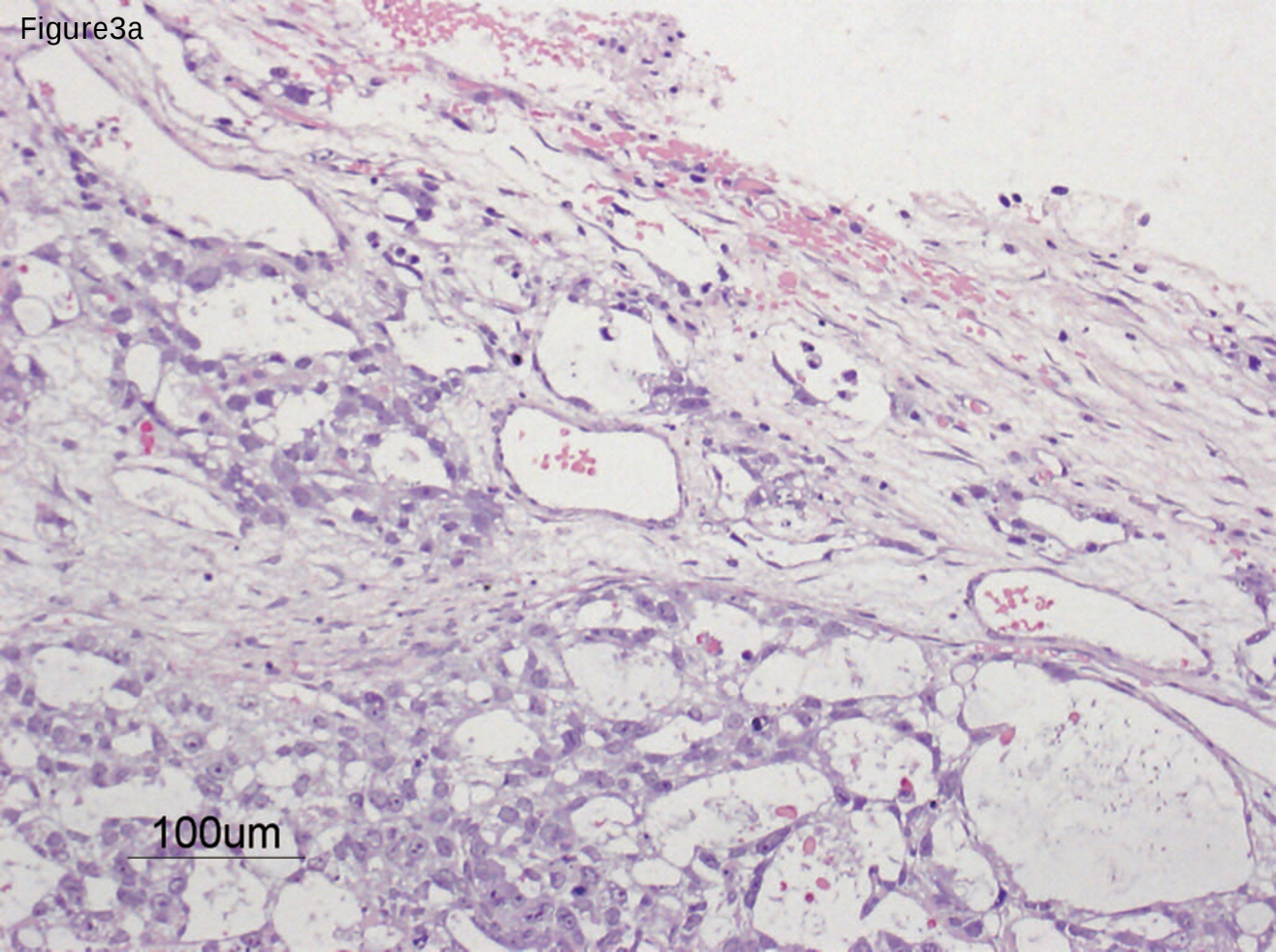
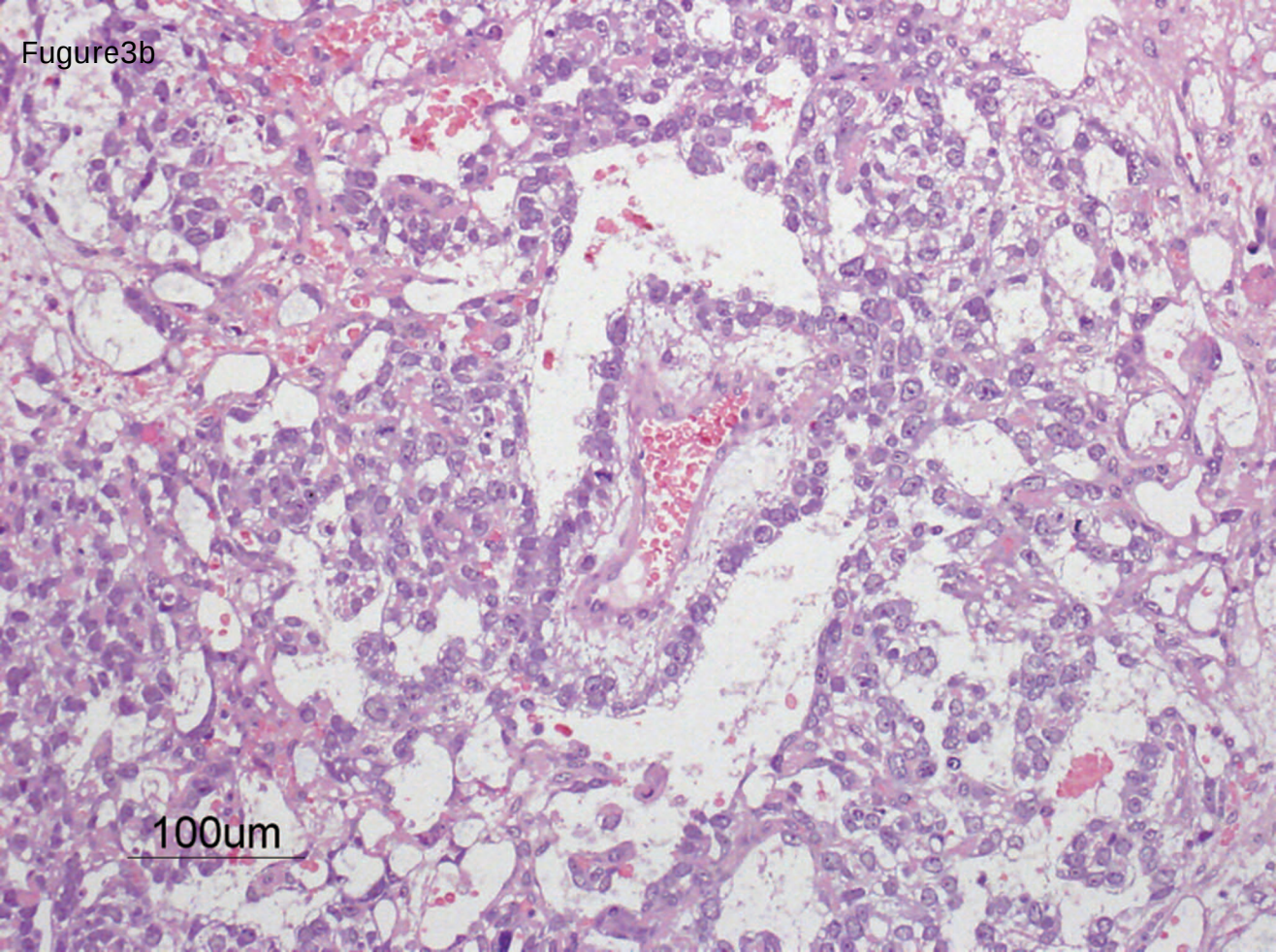


Figure2b

Figure3a



Fugure3b



100µm

Figure3c

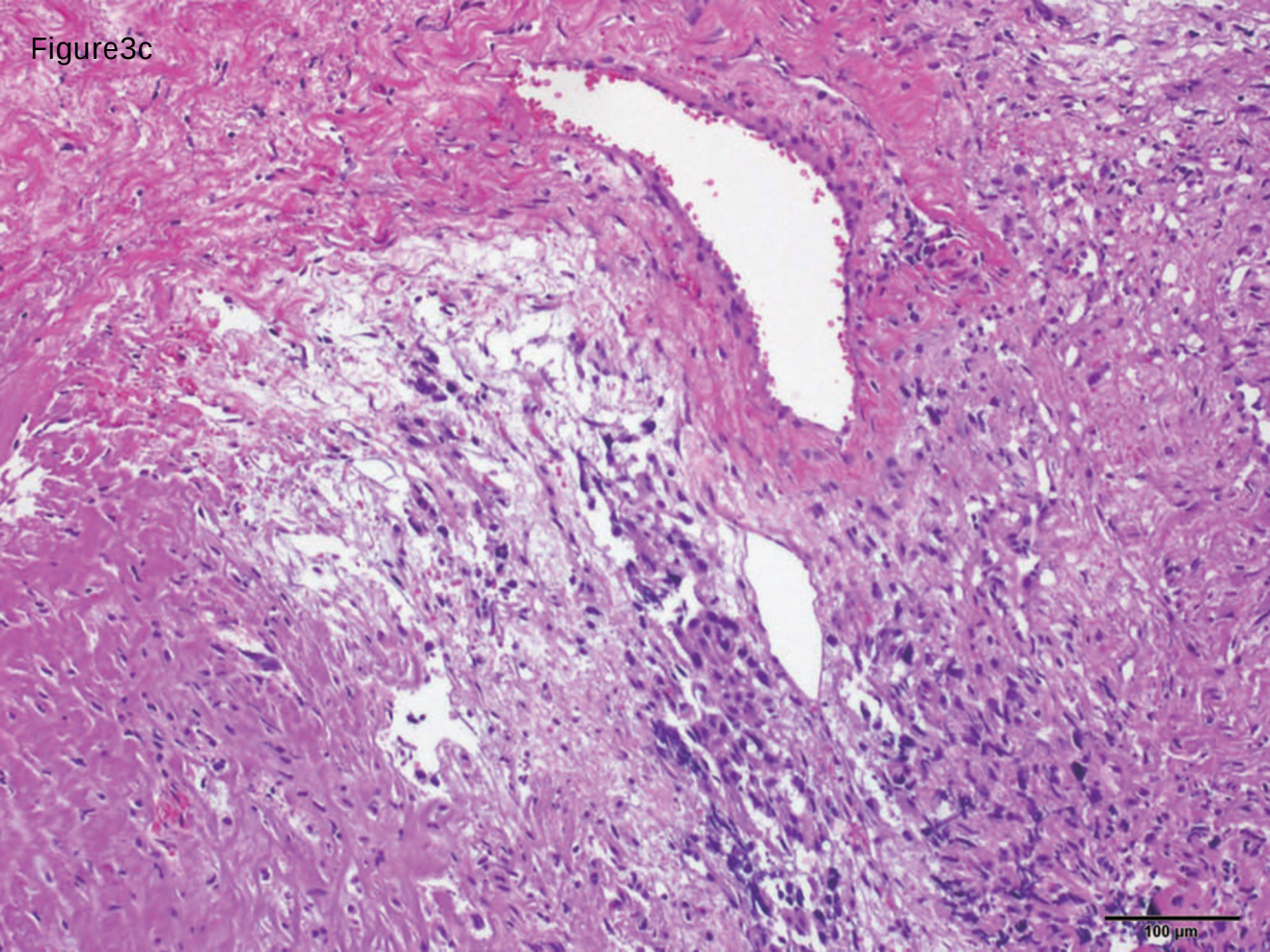
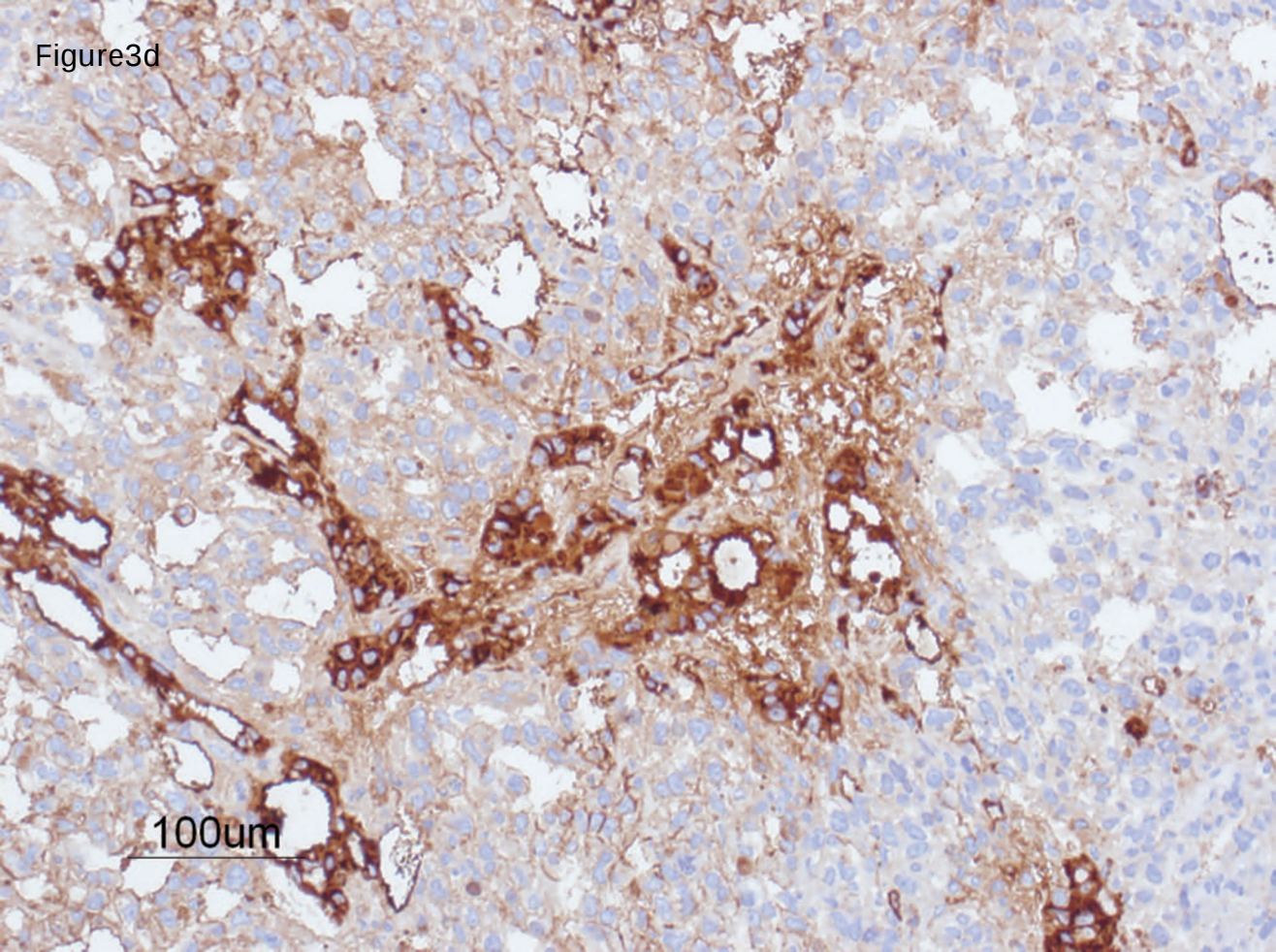


Figure3d



100um