Therapeutic Courses of Presumed Intracranial Immature Teratoma Diagnosed Based on Increased Alpha-fetoprotein

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Abstract

Intracranial immature teratoma (ImT) is one of the non-germinomatous germ cell tumors, and elevated serum alpha-fetoprotein (AFP) value is a crucial clinical diagnostic indicator of ImT. In this retrospective study conducted among patients diagnosed with intracranial ImT, diagnostic procedures, therapeutic courses, histopathological diagnosis, and prognosis were reviewed. Among 106 patients with intracranial germ cell tumors, 11 were diagnosed with ImT and treated since 2000. ImT was diagnosed via biopsy or based on mild or moderate serum AFP elevation of 10–500 ng/mL. Complete remission via chemoradiotherapy was achieved in only two (18%) patients; five (45%) patients suffered from growing disease during treatment; and seven patients required salvage tumor resection. The 10-year progression-free and overall survival rates were 76.2% and 87.5%, respectively. The therapeutic courses of ImT varied. Notably, cases in which treatment was applied considering ImT were highly prone to experience growing disease during treatment.

Keywords: alpha-fetoprotein, growing teratoma syndrome, immature teratoma, intracranial germ cell tumor, teratoma

Introduction

Teratoma is an intracranial germ cell tumor (IGCT) subtype. Pure mature teratomas (MTs) are curable by only surgical resection,[1] whereas germ cell tumors (GCTs) with immature teratoma (ImT) components were categorized into non-germinomatous GCTs (NGGCTs) and treated via high-intensity chemoradiotherapy in Western countries.[2] In Japan, ImT exhibited a favorable prognosis than other NGGCTs, including yolk sac tumor (YST), choriocarcinoma (CC), and embryonal carcinoma (EC).[3, 4] Thus, ImT is traditionally categorized as independent "intermediate prognosis" group, and treatment intensity for ImT differs from that for germinomas or other malignant NGGCTs.[5]

The definitive diagnosis of ImT is difficult and ambiguous. Several previous studies have indicated that the mild or moderate elevation of alpha-fetoprotein (AFP) value, which is a representative tumor marker of IGCTs, from 10 ng/mL to 500–1000 ng/mL, is associated with the presence of ImT components.[6-8]

The clinical courses of ImT are complicated and sometimes unpredictable.[9, 10] Growing teratoma syndrome (GTS) is a rare but well-known clinical phenomenon during adjuvant treatment for IGCTs, especially ImT.[11, 12] GTS is characterized by 1) elevated tumor marker normalization, 2) tumor enlargement after chemotherapy, and 3) resected tissue consisting of only mature teratoma without malignancy.[13, 14] Moreover, some cases that demonstrate growing lesions during or after adjuvant treatment do not match the classical definition of GTS.[12, 15] In this retrospective study, we reviewed the therapeutic courses of patients with presumed ImT diagnosed based on elevated AFP. Moreover, this study aimed to comprehend the clinical characteristics of these tumors and the labyrinth of therapeutic courses for ImT.

Materials and Methods

The local Institutional Review Board at Hokkaido University Hospital approved this retrospective study. We retrospectively reviewed the medical records of patients with IGCTs treated at our institution from January 2000 to January 2024. We identified 106 patients with primary IGCT for whom AFP and β-human chorionic gonadotropin (β-hCG) levels were measured at diagnosis. At our institution, the patients with ImT were diagnosed based on following criteria: 1) serum or cerebrospinal fluid (CSF) AFP of 10–500 ng/mL and β-hCG of <1000 mIU/mL and 2) absence of malignant GCT components, including YST, CC, and EC, in patients who had undergone surgical biopsy before adjuvant therapy. The patients who had not undergone surgical biopsy were presumed to have ImT based on only the AFP and β-hCG values. The patients diagnosed with ImT, regardless of germinoma components, were treated using a specific treatment protocol.

The presence of germinoma components was speculated via histopathology or β-hCG elevation. However, the treatment protocol was similar regardless of the presence of germinoma.

Basic treatment strategy for "presumed" ImTs and ImT with germinoma components

We applied the four-week cycle of ICE regimen, including ifosfamide (900 mg/m^2 days 1–5), cisplatin (20 mg/m^2, days 1–5), and etoposide (60 mg/m^2, days 1–5), as induction chemotherapy before 2009 or CARE regimen, including carboplatin (550 mg/m^2, day 1) and etoposide (100 mg/m^2, day 1–3), after 2010.[5, 16] Induction chemotherapy was applied before radiotherapy. The cycles of induction chemotherapy were based on the therapeutic response. Salvage resection of the tumor was performed before radiotherapy, or subsequent radiotherapy was applied if the tumor demonstrated poor treatment response to induction chemotherapy. If the tumor showed no increase in size during induction chemotherapy, radiotherapy was administered within 4 weeks after completing 3–6 cycles of chemotherapy.

In radiotherapy, a dose of 23.4–25.2 Gy at 1.8 Gy per fraction was delivered to the whole ventricle for pineal or neurohypophyseal lesion and to the whole brain for basal ganglia lesion. Thereafter, boost irradiation up to 50.4 Gy was delivered to the local tumor site. After 2014, proton beam therapies were adopted instead of conventional radiotherapy, with an equivalent radiation dose administered. Spinal irradiation was not applied as the primary treatment.

Salvage resection was performed if the lesion was resectable in case the residual lesion remained observed after completing radiotherapy. Additional three or four chemotherapy cycles using an ICE regimen were applied as consolidation treatment after residual tumor resection.

Assessment of treatment response and prognosis

Recently, the European Society for Paediatric Oncology Brain Tumour Group and North American Childrens's Oncology Group (SIOPE/COG) proposed a new standard for the imaging response assessment of central nervous system GCTs.[17] The effects of treatment after completing primary treatment for this series were retrospectively evaluated using this new assessment protocol. However, this method has not been clearly described in terms of how to evaluate the course of treatment for NGGCTs. Therefore, the effects of induction chemoradiotherapy were also retrospectively evaluated using RECIST version 1.1 criteria.[18] Progression-free survival (PFS) and overall survival (OS) were measured from the first treatment intervention day (surgery or chemotherapy) to the day of

recurrence or death. Growing lesions during chemoradiotherapy were not considered as recurrence events in this study.

Results

Patient characteristics and diagnostic procedure of immature teratoma

Among 106 patients with IGCTs, 20 (18.9%) had an elevated serum AFP level of >10 ng/mL. No patients showed AFP elevation in only the CSF. Pre-treatment biopsy specimens of 86 patients with negative serum AFP (<10 ng/mL) showed no ImT components. Figure 1A describes these 20 cases in detail. Among 14 patients that had undergone surgical biopsy, 7 had malignant GCT components, 4 were diagnosed with ImT, 1 was diagnosed with ImT with germinoma, and 2 were diagnosed with germinoma alone. One patient with histological ImT was considered to have a malignant GCT due to their extremely elevated serum AFP level (6085 ng/mL) and treated accordingly. The remaining six patients had undergone induction chemotherapy without a histological diagnosis. Five patients were diagnosed with ImT or ImT with germinoma, and one patient was diagnosed with malignant GCT due to a serum AFP level of >500 ng/mL. In summary, 11 out of 20 patients with IGCTs with AFP elevation were presumed to have ImT, including ImT with germinoma components. Table 1 summarizes the characteristics of these 11 patients. We further investigated the therapeutic courses of these 11 "presumed" ImT cases, including 9 males and 2 females.

The median age of these patients was 14 years (range: 3–20 years). The primary tumor sites were neurohypophysea (N = 5), pinea (N = 4), and basal ganglia (N = 2). Subependymal infiltration in the lateral ventricle occurred in one neurohypophyseal case (case #1). The median serum AFP value before treatment was 28.7 ng/mL (range: 11.1–486.1 ng/mL). Serum AFP values were higher than CSF AFP values in eight out of nine patients that showed AFP in both serum and CSF (Fig. 1B)

Treatment response to induction chemoradiotherapy

Figure 2A illustrates the effects of chemoradiotherapy, and Table 1 shows the detailed information of each patient. As induction chemotherapy, the ICE regimen was administered in four patients and CARE regimen was administered in 7 patients. Induction chemotherapies were applied for 1–6 cycles. Figure 2B shows the sequential change in serum AFP values. Except in one case (case #9), serum AFP values decreased following treatment. Overall, complete remission was achieved in only 2 (18%) of 11 patients. Moreover, partial response and stable disease (SD) were achieved in two patients each. Six patients (patients #6–#11) discontinued induction chemotherapy

within two cycles due to poor response. Two patients (patients #6 and #10) were administered subsequent radiotherapy, and the remaining four patients (patients #7, #8, #9, and #11) had undergone surgical tumor resection. Two patients with SD (patients #5 and #6) had undergone salvage resection after radiotherapy, and histopathological diagnoses of these residual lesions were MT. In both cases, additional chemotherapy using the ICE regimen was applied as consolidation therapy.

Growing lesions during chemotherapy or chemoradiotherapy

Five (45%) of 11 patients exhibited growing lesions during chemoradiotherapy. Among them, four (patients #7, #8, #9, and #11) had undergone salvage resection before radiotherapy. One patient (patient #10) had undergone salvage resection after chemoradiotherapy (as described in detail in Figure 7). In particular, three patients (patients #7, #8, and #10) fulfilled the classical GTS criteria, but two patients did not fulfill the criteria. In patient #9 (Fig. 3), the tumor increased in size following induction chemotherapy, accompanied by elevated serum AFP value, but the histological diagnosis of the tissue obtained via salvage resection was only extensive fibrosis. In patient #11 (Fig. 4), his consciousness rapidly deteriorated immediately after primary induction chemotherapy due to increasing tumor size, and he required emergency craniotomy 4 days after treatment initiation. The histopathological diagnosis of this case was ImT.

Subsequent radiotherapy was administered in four patients who had undergone salvage resection before radiotherapy. After completing radiotherapy, two patients (#8 and #9) had undergone further chemotherapy using the ICE regimen because of the residual lesions. Additional ICE chemotherapy was administered in one patient (#10) who had undergone salvage resection after chemoradiotherapy.

Prognosis

After primary treatment, six patients achieved complete response according to the SIOPE/COG assessment protocol; these six patients included two patients who showed complete remission following chemotherapy and four patients in whom complete resection was performed via salvage surgery. Furthermore, five patients, including containing two without salvage resection and three with incomplete resection via salvage surgery, showed partial response (PR). Figure 4 shows Kaplan–Meyer curves. The median follow-up period was 67.2 months. Furthermore, 10-year PFS and OS were 76.2% and 87.5%, respectively. Two patients, patients #4 (Fig. 6) and #10 (Fig. 7), experienced recurrence and died due to the tumor (case #10). Both recurrence cases belonged to the non-NED group. Recurrence had occurred within 2 years of primary diagnosis. Serum

AFP values at diagnosis of one deceased patient were highest in this series (486.1 ng/mL).

Among five patients who showed PR, the residual lesion gradually decreased in size in three patients (#3, #8, and #9). Radiological remission of residual disease was observed in one patient (#9) 2 years after treatment.

Discussion

Here, we summarized the complexity of therapeutic courses for patients with ImT, regardless of germinoma components. We previously revealed the treatment results of "presumed" germinoma at onset.[19] We also previously reported that serum or CSF AFP values of ≤10 ng/mL can aid in the diagnosis of germinoma. All "presumed" germinomas were observed to decrease in size following chemoradiotherapy.[19] In addition, the residual lesion after chemoradiotherapy completion was observed at 43.5%, but most residual lesions spontaneously regressed in size during follow-up periods.[19] Conversely, in patients with ImT with serum AFP value elevation of >10 ng/mL, most tumors could not achieve complete remission following adjuvant chemoradiotherapy. Moreover, approximately half of these patients showed an increase in tumor size during treatment induction and did not always fulfill the classical GTS definition. Serum AFP values at diagnosis are a strong indicator of the difference in therapeutic response to chemoradiotherapy according to our previous report[19] and this investigation.

Elevated AFP concentration is a strong predictor of NGGCTs.[1, 20] Patients with AFP values of >1000 ng/mL at diagnosis show a poor prognosis.[2] Recently, Hong et al. revealed that the prognosis of MT and ImT is not significantly different.[21] Their series indicated that AFP values are equally increased for patients with a pathological diagnosis of pure MT and ImT. Therefore, diagnosis based on histological results may be inaccurate. Sugiyama et al. indicated that diagnosis based on tumor marker levels was superior to that based on morphological evaluation of biopsy specimens, and the patients with serum AFP levels ranging from 10.0 to 999 ng/mL were considered to have teratoma or mixed GCTs containing large teratoma components.[6] Takami et al. investigated the correlation between tumor markers and histopathological diagnosis in 124 Japanese patients with IGCTs.[7] They revealed that most of the cases in which tumor markers exhibited severe serum AFP elevation of >250 ng/mL were malignant GCTs, and the majority of ImT cases demonstrated moderate serum AFP elevation of 25–250 ng/mL.[7] Takami et al. indicated a trend of poor prognosis in patients with ImT with high AFP levels compared with those with low AFP levels.[8] Our series demonstrated that the deceased patient (patient #10) was the only patient in whom serum AFP was >250 ng/mL. Patients with ImT with highly elevated AFP, i.e., >250 ng/mL, should be treated as

having malignant GCT even in the absence of malignant components.

Qaddoumi et al. revealed that CSF and serum AFP values were strongly correlated, and AFP values were higher in the serum than in the CSF of patients with NGGCTs.[22] Takami et al. reported a similar result.[8] In addition, we revealed that the serum AFP values in 9 out of 10 patients with ImT were higher than the CSF AFP values. Moreover, no patients demonstrated isolated CSF AFP elevation in all our GCT cohorts (data not shown), indicating that serum AFP value may be a reliable and sufficient tumor marker.

GTS is a well-known therapeutic phenomenon in NGGCT treatment.[10-12, 14] GTS is generally defined as an enlarged tumor mass consisting of only mature teratoma during/after adjuvant therapy with tumor marker normalization.[13] The frequency of GTS was 6.5%–11.5% in the IGCT series, and all GTS cases originated from NGGCTs.[10, 11] The predictive factor for GTS occurrence was determined only in the presence of the ImT component. In our series, the frequency of GTS was 45%, which was much higher than that reported in previous studies,[10-12] indicating that GTS may be a much more predominant therapeutic phenomenon in patients with ImT than we have recognized. Notably, only three out of five patients fulfilled the classical GTS definition in our series. Kanamori et al. revealed that three out of five tumors with progressive disease during or after chemoradiotherapy did not fulfill the criteria for GTS.[15] Tsuyuguchi et al. indicated that the factor of histopathological appearance of obtained tissue via salvage resection should be excluded from the GTS definition.[12] Their case series and literature review revealed that the MT or ImT component of the tissue specimen obtained via salvage surgery of GTS depends on salvage surgery timing. Histological diagnosis of ImT was dominant at the earlier treatment stage compared with that of mature teratoma.[12] Notably, ImT increases during chemoradiotherapy and sometimes does not necessarily follow the classical definition of GTS.

The growth of teratoma, particularly during GCT treatment, remains uncertain. One powerful hypothesis is that chemotherapy may promote the conversion of immature tissue to mature tissue and then cause mature tissue to flourish.[23] Tsuyuguchi et al. considered that cystic change of ImT during MT conversion induced by chemotherapy may be a primary causative factor of GTS.[12] However, it remains unknown which type of teratoma is prone to growth following chemotherapy. The frequency of growing lesions during induction chemotherapy was relatively high in our series; hence, we should recognize that GCTs presenting with ImT components and elevated AFP are particularly likely to occur growing lesion during induction chemotherapy.

Salvage (second-look) resection for residual lesion during or after adjuvant

therapy should be considered in NGGCTs.[2, 15, 24-26] The SIOP-CNS-GCT-96 trial revealed that patients with malignant NGGCTs who had residual lesion after protocol treatment demonstrated significantly worse survival; thus, residual lesion resection is strongly recommended.[2] Several reports have emphasized that salvage surgery of residual lesions is important for improving their prognosis in intracranial teratomas.[9, 27] We should strive for "no" end-of-treatment residual disease in patients with ImT because two out of five patients with PR showed early relapse in our series.

The requirement for additional chemotherapy for residual tumors after salvage surgery or radiotherapy is controversial. The optimum goal is to obtain a complete remission before initiating radiotherapy; therefore, additional radical surgery is considered, followed by radiotherapy as a consolidation treatment.[28] So far, no studies have reported the efficacy of additional chemotherapy after radiotherapy for NGGCTs, including ImT. In our series, one (20%) out of five patients who had received additional chemotherapy experienced recurrence, whereas one (50%) out of two patients who had not received additional chemotherapy despite residual lesion experienced recurrence. Additional chemotherapy after salvage resection or radiotherapy may help prevent the re-growth of residual lesions in patients with ImT.

This study had several limitations. First, this was a single-insititution retrospective review and the number of patients was limited. Second, the definitive diagnosis of ImT was ambiguous. Patients with IGCTs had undergone only surgical biopsy; thus, a definitive diagnosis was impossible because of intratumoral heterogeneity. Surgical specimens do not represent a whole tumor.[7] In addition, in this series, 5 of 11 patients were diagnosed based only on the elevated AFP levels without surgical biopsy. Therefore, it is difficult to definitively conclude the presence of ImT in every patient.

Conclusion

We summarized the therapeutic courses of patients with ImT with elevated AFP. When ImT was diagnosed based on serum AFP values, there was a higher probability of the occurrence of GTS. This suggests that the diagnosis of ImT based on serum AFP values may be adequate. The overall prognosis of patients with ImT was relatively good with standard chemotherapy and whole ventricle-based irradiation that were equivalent to those for patients with germinoma. However, one patient, in whom serum AFP was >250 ng/mL, had a poor prognosis. A tumor with a serum AFP level of >250 ng/mL may be considered a malignant GCT, even in the absence of a malignant component in the biopsy specimen. The clinical courses of ImT may be highly variable and unpredictable, and variation in treatment process should be considered while developing a treatment

strategy or clinical trial for ImT.

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Author Contributions

Shiegru Yamaguchi was responsible for preparation of the manuscript and data collection and analysis. All authors reviewed and approved the final version of the manuscript.

Declaration of Conflict Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Approval

The Health Science Research Ethics Board at Hokkaido University Hospital (018-0363) approved this study and waived the requirement for informed consent.

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Figure Legends

Fig 1.

(A) Summary of 20 germ cell tumor cases with alpha-fetoprotein elevation according to the surgical biopsy. The patients labeled with the white box were diagnosed with immature teratoma or immature teratoma with germinoma component, and the patients labeled with the gray box were diagnosed with malignant germ cell tumors. (B) Scatter plots of alpha-fetoprotein (AFP) values before treatment in serum sample (x-axis) and cerebrospinal fluid (CSF) sample (y-axis) in patients with immature teratoma. Areas with a blue background indicate patients in whom the serum AFP values were higher than the CSF AFP values. Serum AFP values were higher than CSF AFP values in eight out of nine patients.

Fig 2

(A) Pie chart illustrating treatment response to induction chemoradiotherapy for patients with immature teratoma. (B) Sequential changes in the serum alpha-fetoprotein (AFP) value. Except in one patient (patient #9), serum AFP values decreased following treatment regardless of changes in tumor size.

Fig 3

The case shows a growing lesion during chemotherapy accompanied by serum alpha-fetoprotein (AFP) elevation (patient #9, 12-year-old man). T1-weighted MR imaging with gadolinium (A, C). He presented with visual disorder with diabetes insipidus. The tumor was observed in the neurohypophyseal region (A). Serum AFP was elevated at 12.1 ng/mL, and the biopsy specimen revealed only a germinoma component (B). He had undergone induction chemotherapy using carboplatin and etoposide, but the tumor increased in size gradually with visual function deterioration. Additionally, the serum AFP value was elevated to 75.0 ng/mL. He had undergone salvage resection via craniotomy and the tumor was subtotally resected. The histopathological appearance of resected tissue revealed extensive fibrosis without germinoma and teratoma component (D) (B: hematoxylin and eosin stain, original magnification ×400, D: hematoxylin and eosin stain, original magnification ×200).

Fig 4

The case demonstrates early tumor enlargement immediately after induction chemotherapy (patient #11, 13-year-old man). T1-weighted MR imaging with gadolinium before treatment (A). He was diagnosed with immature teratoma originating from left

basal ganglia without biopsy since serum alpha-fetoprotein was elevated at 38.4 ng/mL. He had undergone induction chemotherapy using carboplatin and etoposide. Four days after chemotherapy initiation, his consciousness rapidly worsened, and CT revealed a growing tumor (B). He underwent an emergency craniotomy and the tumor was removed. The pathological appearance was immature teratoma (C). Hypercellular immature mesenchyme and chondroid matrix were observed (hematoxylin and eosin stain, original magnification ×200).

Fig 5

Progression-free survival (PFS) and overall survival (OS) of patients with immature teratoma (A). PFS and OS according to the presence of residual lesions at the end of primary treatment (B and C, respectively).

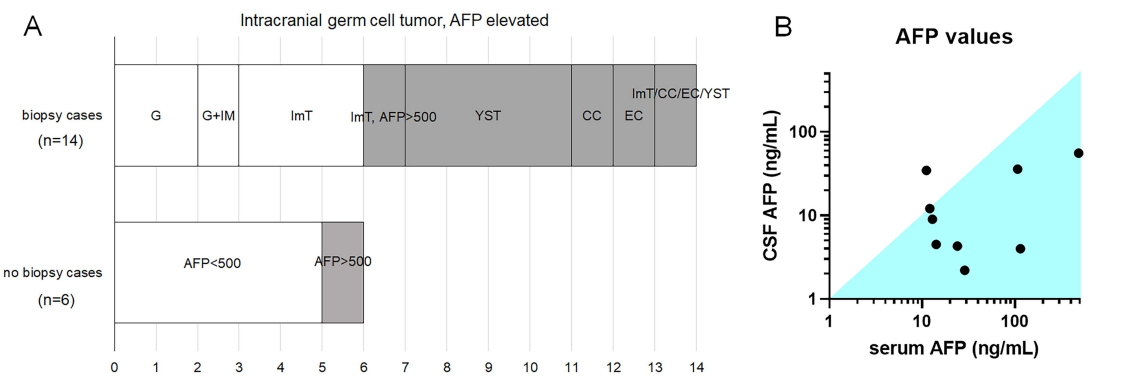
Fig 6

One recurrence case of this series (patient #4, 19-year-old man). T1-weight MR imaging with gadolinium (A-C). A large tumor was observed in the neurohypophyseal region before treatment (A). Serum AFP and ß-hCG were elevated at 11.1 ng/mL and 26.3 mIU/mL, respectively, and the patient had undergone chemoradiotherapy without histological confirmation presumed as neurohypophyseal immature teratoma with germinoma. A small residual lesion was observed at the end of primary treatment (B). Local recurrence was confirmed approximately 14 months after the completion of primary treatment (C). He underwent tumor resection via trans-sphenoidal surgery. The histopathological diagnosis of the resected lesion was mature teratoma (D). Small glands resembled a central canal in the background of scar-like fibrous tissue (hematoxylin and eosin stain, original magnification ×400).

Fig 7

The deceased case of this series (patient #10, 16-year-old man). T1-weighted MR imaging with gadolinium (A-C, E). At the onset, the enhanced tumor was observed in the pineal region (A). He was diagnosed with immature teratoma with germinoma via surgical biopsy. The tumor was stable in size following first induction chemotherapy using the ifosfamide, cisplatin, and etoposide (ICE) regimen. Hence, he underwent subsequent radiotherapy. After completing radiotherapy, additional ICE chemotherapy was applied for residual disease, but the tumor was growing (B). He underwent salvage surgery, which achieved subtotal resection (C). Glandular structures lined by columnar epithelium are seen in the histopathological appearance of resected tissue (hematoxylin

and eosin stain, original magnification ×100) (D). The histopathological diagnosis was mature teratoma, which was consistent with growing teratoma syndrome. He underwent two courses of further additional ICE chemotherapy. However, the local recurrence was observed 12.7 months after the presentation (E), and he died due to the tumor 17 months after diagnosis.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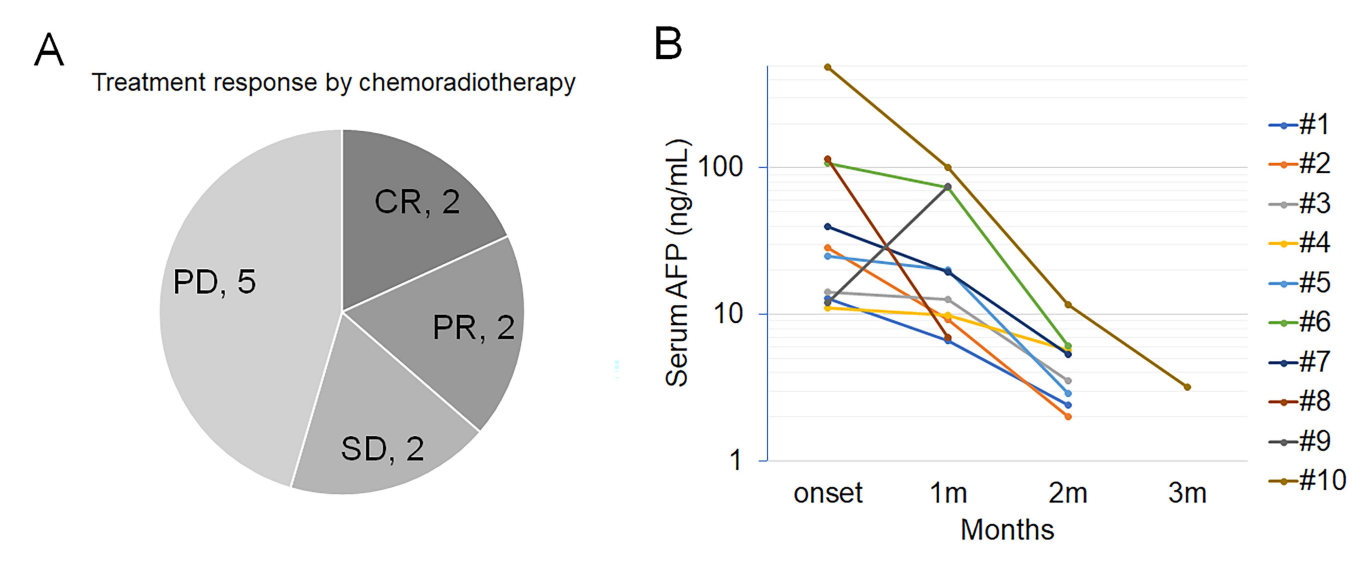
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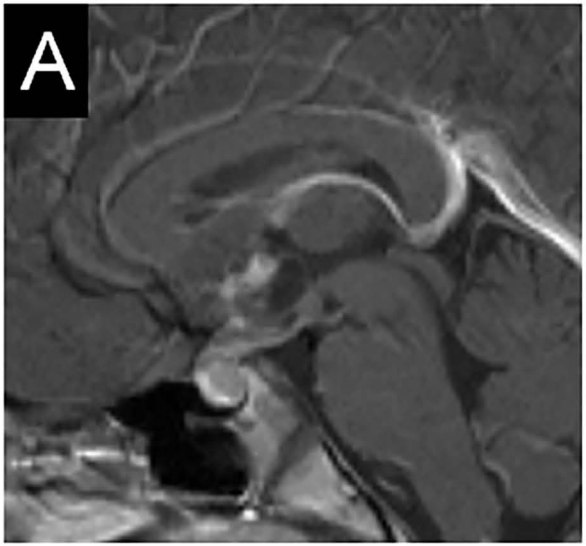
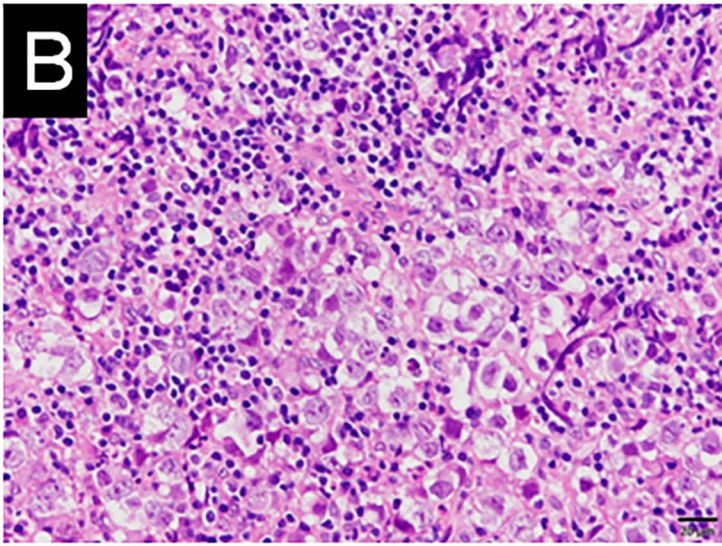
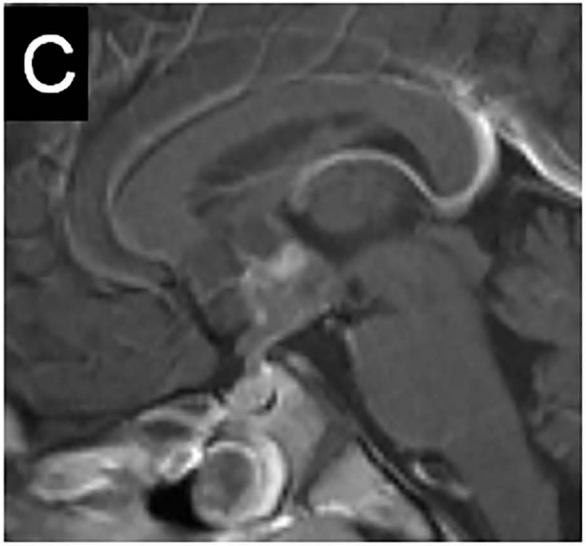
#10


A


B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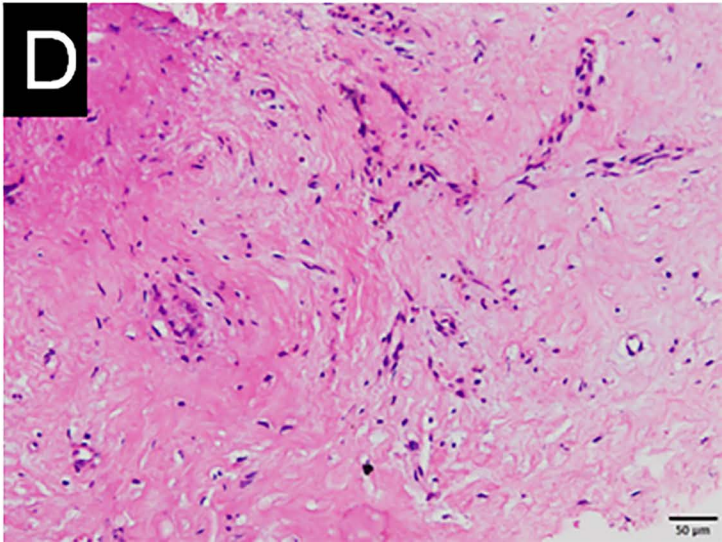
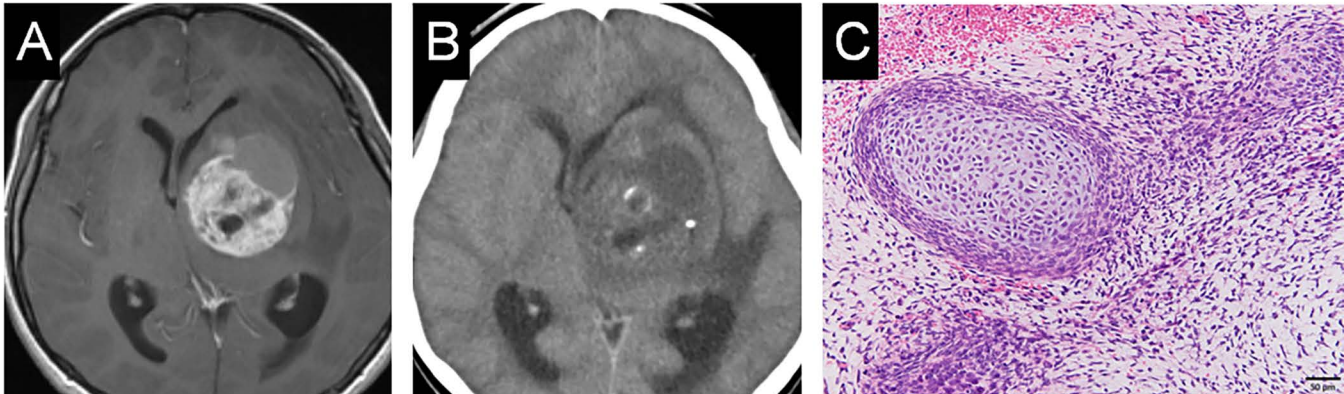
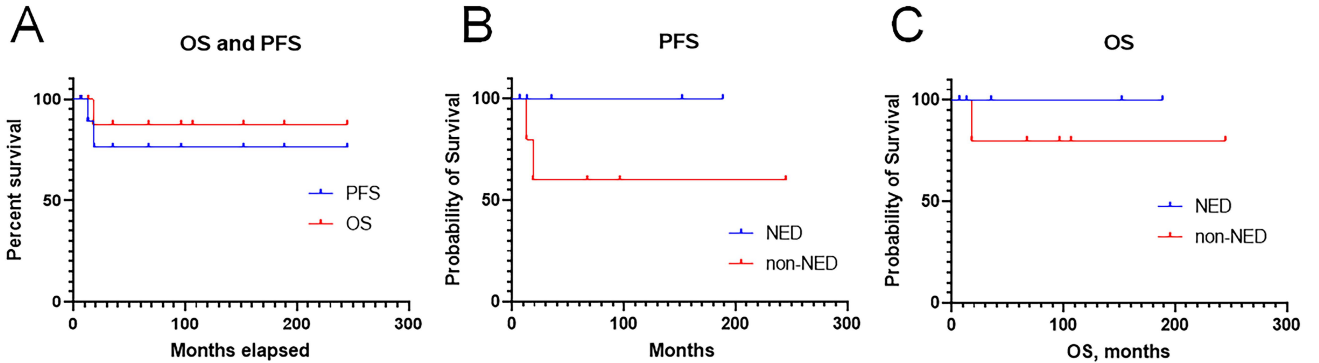
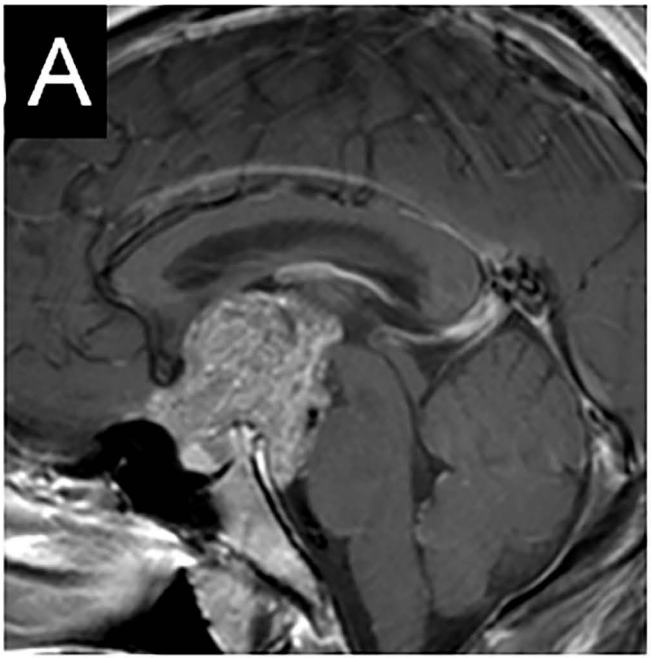
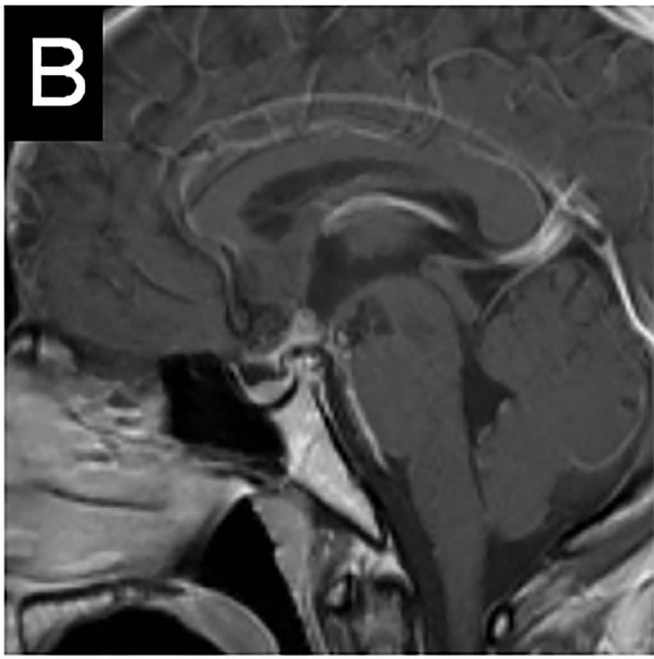
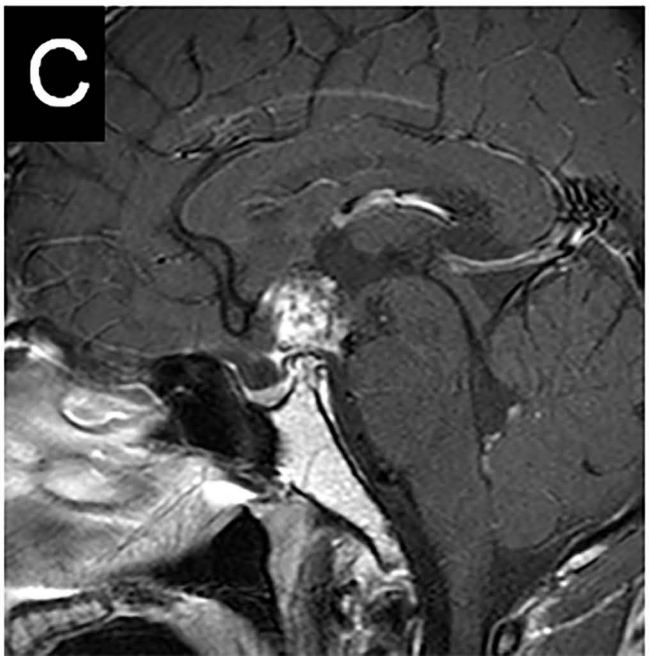

D
50 µm

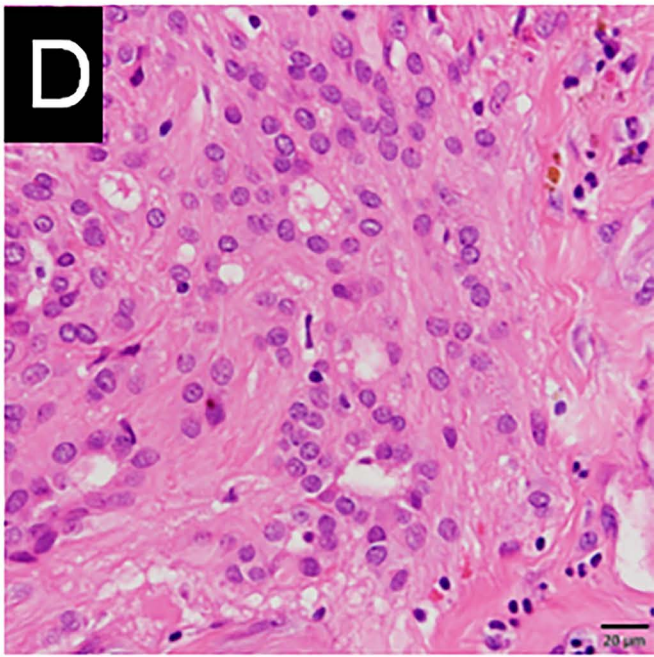

A
B
C
50 μm

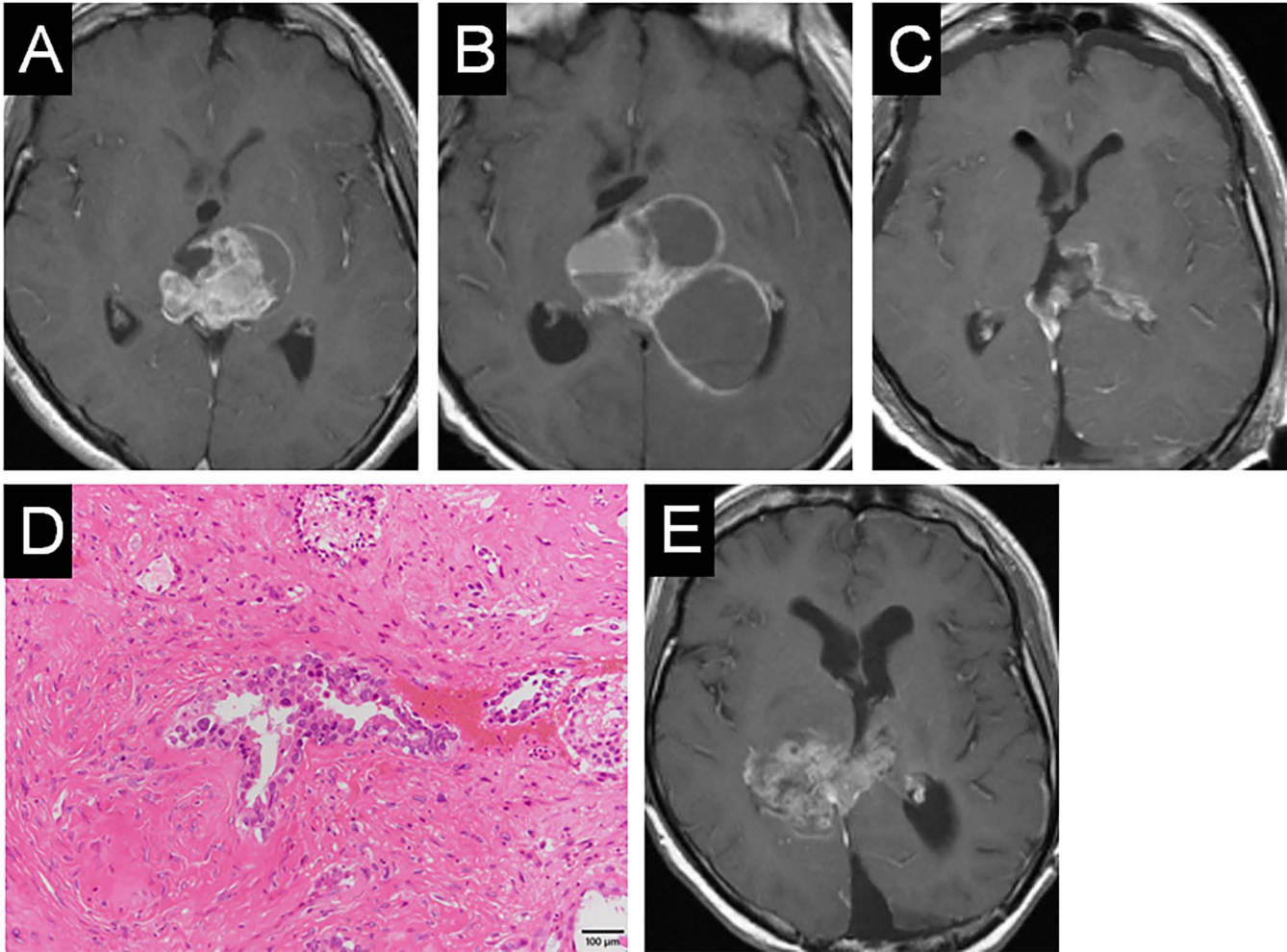

A
OS and PFS
Percent survival
100
50
0
0
100
200
300
Months elapsed
PFS
OS
B
PFS
Probability of Survival
100
50
0
0
100
200
300
Months
NED
non-NED
C
OS
Probability of Survival
100
50
0
0
100
200
300
OS, months
NED
non-NED


A


B


C


D
20 µm


A
B
C
D
100 µm
E

Summary of clinical characteristics of immature teratomas with AFP elevation

Case No	Age/ Sex	location	Biopsy prior to Cx	Serum AFP	Serum ß-hCG	Primary Cx regimen	Cycle of Cx	Treatment response by CRT	Pathology of salvage surgery	The day of salvage surgery	Additional Cx (ICE)	Assessment after treatment	Recurrence (months)	Follow up (months)	Status
#1	16/ M	NH	G	12.9	0.6	ICE	4	CR	-	-	No	NED	none	35.2	Alive, NED
#2	10/ M	BG	N/A	28.7	6.4	CARE	3	CR	-	-	No	NED	none	6.7	Alive, NED
#3	10/F	NH	N/A	14.2	<0.5	ICE	6	PR	-	-	No	Non-NED	none	245	Alive, w/D
#4	19/ M	NH	N/A	11.1	26.3	CARE	4	PR	-	-	No	Non-NED	18.5	106	Alive, NED
#5	16/ M	P	G+ImT	24	<0.3	CARE	3	SD	MT	141	Yes	NED	none	8	Alive, NED
#6	14/ M	P	N/A	107	5.4	ICE	1	SD	MT	69	Yes	NED	none	188	Alive, NED
#7	20/ M	P	N/A	39.5	1.5	CARE	2	PD	MT	75	No	NED	none	13.3	Alive, NED
#8	3/F	NH	ImT	114.8	<0.5	CARE	1	PD	MT	35	Yes	Non-NED	none	96.4	Alive, w/D
#9	12/ M	NH	G	12.1	1.4	CARE	1	PD	fibrosis	48	Yes	Non-NED	none	67	Alive, NED

#10	16/M	P	ImT	486.1	0.7	ICE	1	PD	MT	225	Yes	Non-NED	12.7	17	Dead
#11	13/M	BG	ImT	38.4	21.2	CARE	1	PD	ImT	4	No	NED	none	152	Alive, NED

NH; neurohypophyseal, P; pineal, BG; basal ganglia, G; germinoma, ImT; immature teratoma, MT; mature teratoma, Cx; chemotherapy, ICE; Ifosfamide + Cisplatin + Etoposide, CARE: Carboplatin + Etoposide, CRT: chemoradiotherapy, NED; non evidence of disease, w/D; with disease