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Case Report

Posterior fossa immature teratoma in an infant with trisomy 21: A case report and review of the literature

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Abstract

Background: Intracranial teratoma associated with Down syndrome is rare. With only three previously reported cases, our case is the first one presenting an immature component.

Case Description: A 2-month-old boy with trisomy 21 presented with lethargy and head enlargement. A magnetic resonance imaging (MRI) study showed an obstructive hydrocephalus with 0.5 cm posterior fossa tumor compressing the cerebellum. The tumor revealed a mixed intensity on T1- and T2-weighted MRI images and was surrounded by peritumoral cysts. It was heterogeneously enhancing and showed multinodular mass. The tumor was gross totally removed *via* suboccipital craniotomy and histologically diagnosed as immature teratoma. Four cycles of chemotherapy consisting of cisplatin and etoposide followed the surgery. The radiotherapy was withheld due to infancy. Recurrent lesions in the tumor bed were noted 10 months later. They were removed in the second surgery and histologically identified as mature teratoma.

Conclusion: Maturation of immature teratoma may be a result of natural conversion of multipotent embryonal cells into mature tissues and following chemotherapy.

Key words: Down syndrome, immature teratoma, maturation, posterior fossa tumor

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INTRODUCTION

Teratomas, neoplasms which are composed of tissues derived from three germ cell layers, constitute approximately 0.2% of all intracranial tumors.[17] They mostly occur in children during the first decade and grow frequently in the midline region including the pineal gland.[3,17] Here, we report a rare case of posterior fossa immature teratoma in an infant with Down syndrome.

CASE REPORT

A 2-month-old boy with known Down syndrome (trisomy 21) was referred to our department with presentation of rapid head enlargement. He was born as a full-term baby to a 30-year-old mother by normal delivery without perinatal complications.

On examination, the boy was lethargic and found to have variable waveforms of nystagmus (congenital nystagmus). The head circumference was 39 cm with bulging of the anterior fontanel. Computed tomography (CT) [Figure 1a] of the brain showed a large heterogeneously dense midline posterior fossa tumor, 5 cm in diameter, involving the cerebellum. Small speckles of calcification were also seen. Severe hydrocephalus with periventricular lucency was present. The tumor was of mixed intensity on T1- and T2-weighted magnetic resonance images (MRI) and consisted of various sized cysts [Figure 1b and c]. The tumor strongly enhanced with gadolinium and was multiloculated [Figure 1d-f]. Serum α-fetoprotein (AFP) was elevated to 2.91×10^6 UI/L. Serum levels of human chorionic gonadotropin (HCG) and β-HCG were normal, 1.1 and 0.2 mlU/ml, respectively.

Midline suboccipital craniotomy exposed a highly vascularized tumor with variable consistency; cystic, solid, and elastic hard. Gross total removal was achieved in a piecemeal fashion. The tumor capsule was easily detached from the cerebellar hemisphere, but not from the cerebellar vermis. An intact pineal gland was seen in the supracerebellar cistern after tumor removal. Postoperative MRI showed the total removal of the tumor [Figure 2a–c].

Histopathologically, the tumor was composed of incompletely differentiated components resembling fetal tissues. The most immature elements were primitive embryonal mesenchymal tissue or neuroectodermal tissue with canalicular structure resembling a developing neural tube or neuroepithelial rosettes [Figure 3a]. This tumor showed a positive reaction to AFP immunostaining [Figure 3b]. Neuroepithelial rosettes reacted positively to β-tubulin 3 and MAP2 [Figure 3c and d]. Glial fibrillary acidic protein (GFAP) immunostaining was negative [Figure 3e]. The MIB-1 index was approximately 10% [Figure 3f].

Four cycles of chemotherapy with regimens comprised

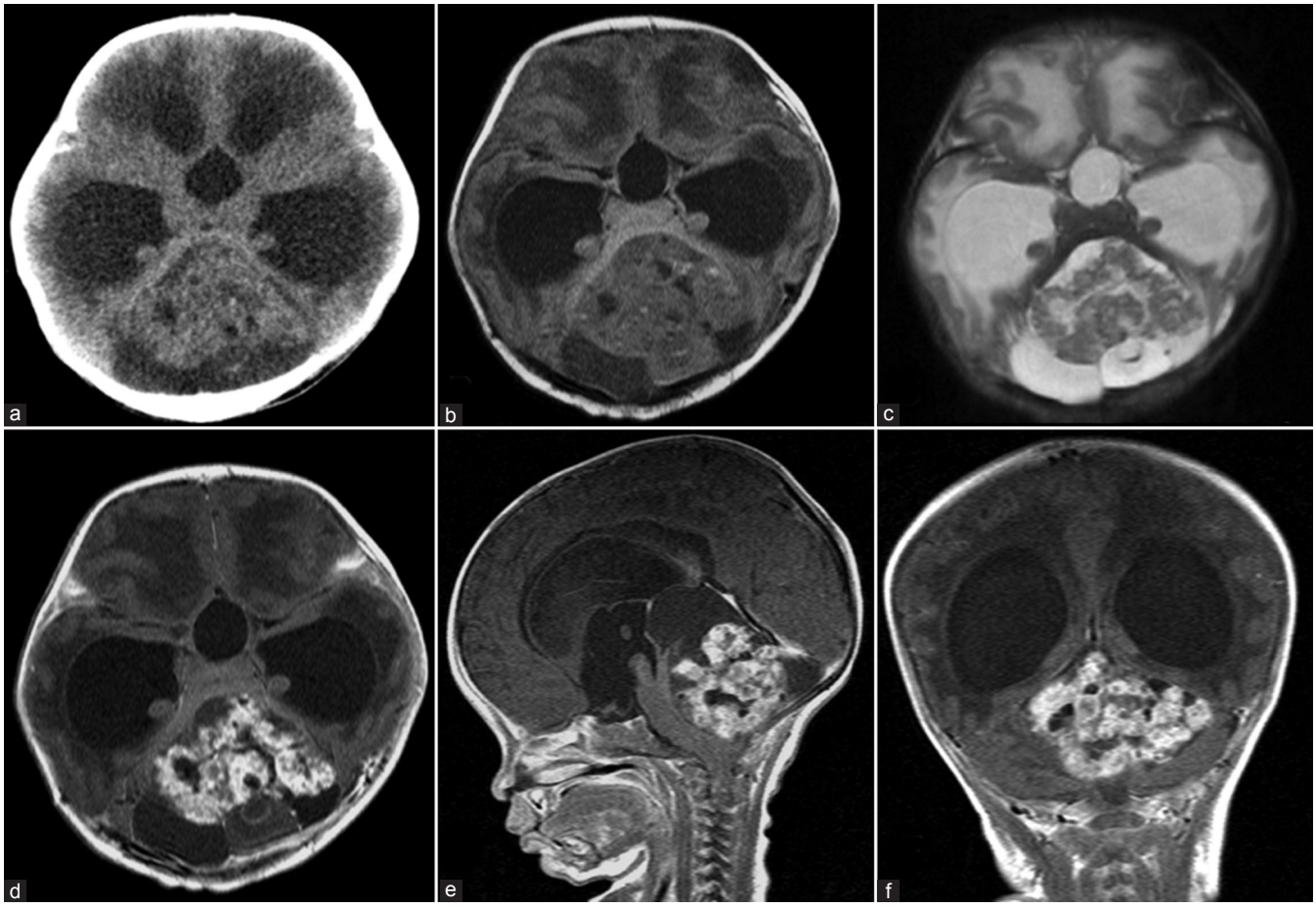

Figure 1: Preoperative computed tomography (CT) (a) showed a large tumor with inhomogeneous density compressing cerebellum. Hydrocephalus was present with periventricular lucency. It is also inhomogeneous and multiloculated on T1-weighted (b) and T2-weighted (c) magnetic resonance images (MRIs). Gadolinium enhanced MRI (d-f) showed heterogeneous enhancement effect

of cisplatin and etoposide followed the surgery. The AFP serum level decreased to 2.74 × 10^4 UI/L after chemotherapy. In addition, it had dropped to 1.25 × 10^4 UI/L when two recurrent lesions were detected in the cerebellar vermis and tentorium on MRI [Figure 4a-c], performed 10 months after the first surgery. The second operation was done via the same approach, and histological diagnosis of the recurrent tumor was mature teratoma. No additional treatment has been given since then. The AFP serum level has remained normal in the range 2.06 × 10^3 to 2.31 × 10^3 UI/L since the second operation. The latest MRI studied 3 years after the second surgery [Figure 4d-f] showed no recurrences. The patient is now 4-year-old and has been living in the nursing house with minimum assistance.

DISCUSSION

Teratomas represents 0.2% of all intracranial tumors[17] and 1.2–5% of intracranial tumors in children.[11,17] In cases of Down syndrome, the proportion of germ cell tumors is quite high reaching to 61% of all intracranial tumors associated with this disease.[13] However, association of teratoma with Down syndrome is quite rare. We only

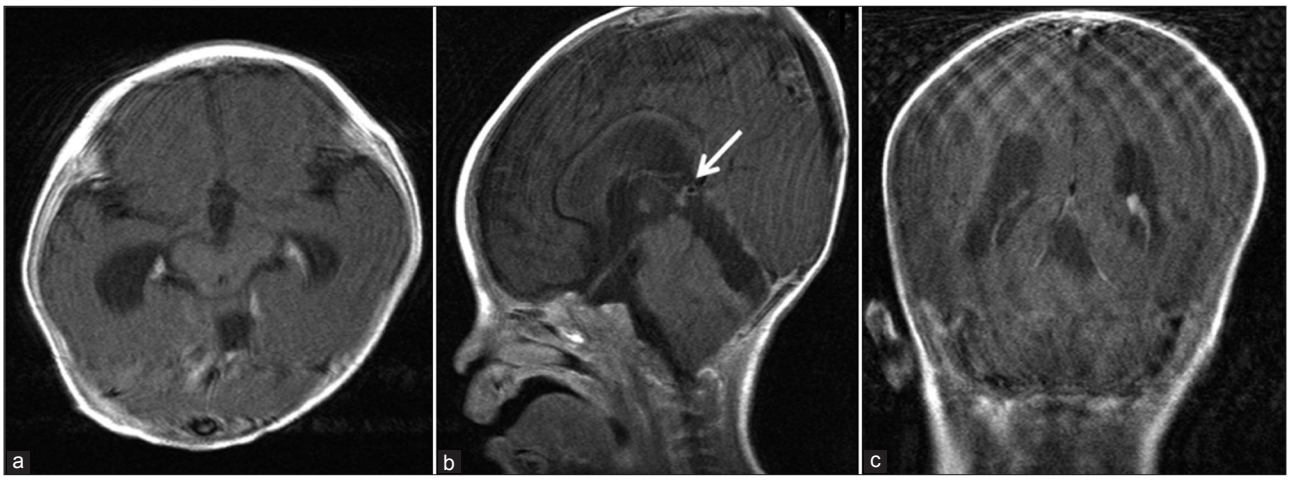

Figure 2: Postoperative axial (a), sagital (b), and coronal (c) MRIs revealed the total resection of tumor with improvement of the hydrocephalus state. Note pineal gland remained intact (arrow)

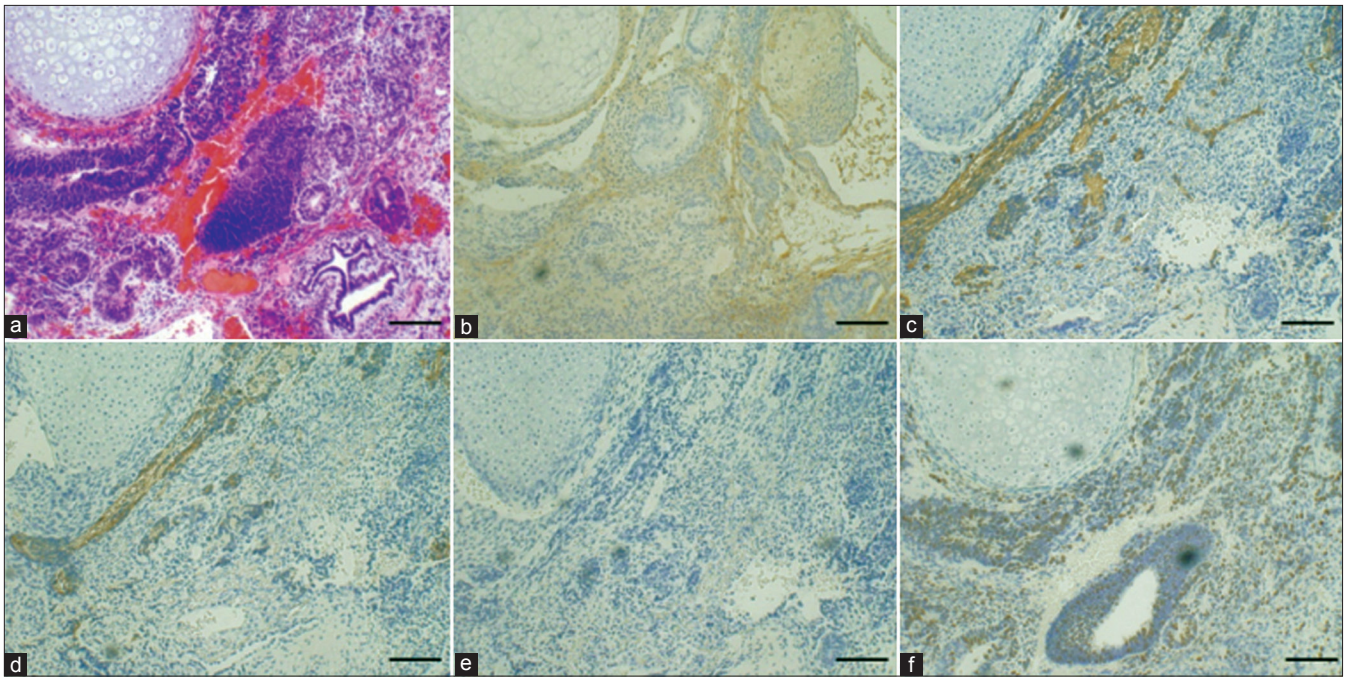

Figure 3: Histological patterns showed canalicullar structure resembling a developing neural tube or neuroephitelial rosettes (a). These patterns showed positive reaction with α-fetoprotein (AFP) immunostaining (B). Neuroepithelial rosettes react positively with β-tubulin 3 (c), and MAP2 (d). GFAP immunostaining was negative (e). The MIB 1 index was approximately 10% (f). (a) H and E, ×100; (b–f) ×100 (original magnification). Barr showed 100 μm

found four cases of this type including ours, three of them being Japanese [Table 1].[7,12,18] There was no gender preponderance. Symptoms at the diagnosis included weight loss, lethargy, strabismus, and head enlargement. The age at diagnosis ranged from newborn to 7 years, with three infants. Subtle neurologic manifestation by intracranial-occupying lesion in already retarded development of Down syndrome may result in delayed diagnosis.[1] In this case, signs of hydrocephalus expedited early diagnosis.

The midline part of brain is a location frequently harboring misplacements of embryonal tissues.[3] For intracranial teratomas, the pineal gland is the most frequent site.[2,8] Interestingly, the predilection of intracranial germ cell tumors in Down syndrome seems to be exceptional; it usually arises in places other than the pineal gland.[3,16] Of the four cases reported, only one case arose from the pineal region [Table 1]. Pathogenesis of intracranial germ cell tumors in Down

Table 1: Reported cases of teratoma in Down's syndrome

Authors (year)	Age/Sex	Site	Histology	Symptoms	Treatment	Follow-up period	Outcome
Nakato *et al*. (1982)	7 years/M	Third ventricle	Mature teratoma	Loss of appetite	VP shunt, 38 Gy radiation	2 months	Dead
Yamasaki *et al*. (1985)	4 months/F	Posterior fossa, basal ganglia	Teratoma	Head enlargement	VP shunt	3 months	Dead
Robson *et al*. (1997)	Newborn/F	Pineal region	Mature teratoma	Strabismus, lethargic	Total removal	n.d.	Alive
Present Case	2 months/M	Cerebellar vermis	Immature teratoma	Head enlargement	VP shunt, gross total removal, chemotherapy	3 years	Alive

n.d: not described, VP: Ventriculo-peritoneal

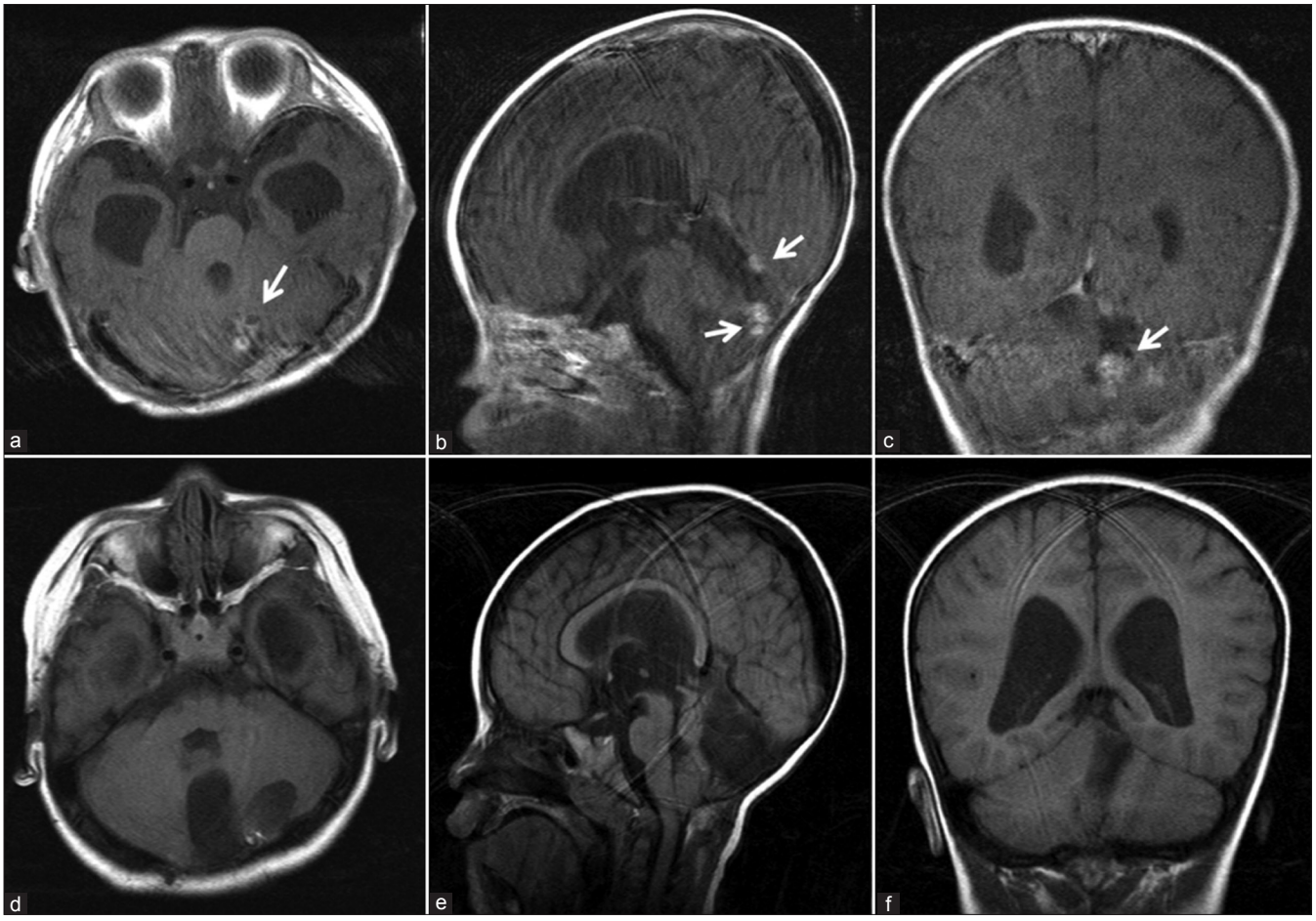

Figure 4: Two recurrent tumors (arrows) were found on axial (a), sagital (b), and coronal (c) MRIs obtained 10 months after the first surgery. The latest axial (d), sagital (e), and coronal (f) MRIs studied 3 years after the second operation showed no recurrence

syndrome is still unclear. Some authors suggest an excess of luteinizing hormone and follicle-stimulating gonadotropin caused by cryptorchidism[14] or inherent genetic changes associated with this disease relate to the tumorigenesis.[1,13]

In infancy and early childhood, 45% of brain tumors arise in infratentorial space,[11,17] the common pathologies being astrocytoma in 36%, medulloblastoma in 30%, ependymoma in 23%, followed by mixed neural-glial tumor and atypical teratoid/rhabdoid tumor. In our case, known Down syndrome, elevated AFP, and MRI findings such as heterogeneity of the tumor intensity, multiple cysts, and cauliflower-like multinodular appearance fortunately led to correct preoperative diagnosis.

We generally treat immature teratoma with carboplatin–etoposide combination chemotherapy followed by radiation according to the protocol for intracranial germ cell tumors proposed by The Japanese Pediatric Brain Tumor Study Group.[5] In this case, however, radiation therapy was precluded due to the fear of damaging developing brain at this young age, so we adopted the more potent cisplatin–etoposide chemotherapeutic regimen. We encountered two recurrent lesions after four cycles of chemotherapy. The resected recurrent tumors were histologically mature, and further recurrence has not been detected for the last 3 years.

Maturation of immature teratoma may be a result of natural conversion of multipotent embryonal cells into mature tissues as seen in fetal development. In the case of extracranial immature teratomas, most of recurrent lesions after the chemotherapy showed features of maturation, whereas the majority that did not receive chemotherapy had recurrent lesions with initial immature features.[4] Clinical and experimental observation suggest that this apparent maturation results from destruction of the less-differentiated elements of the tumor by chemotherapy.[6,9,10] However, the role of chemotherapy in intracranial immature teratoma maturation is still not explicitly clear, because of the rarity of such cases, with only two cases previously reported by Shaffrey *et al*.[15]

CONCLUSIONS

We reported a rare immature teratoma in an infant with Down syndrome which has been controlled with two surgeries and cisplatin-based chemotherapy at a 4-year follow-up. The biomechanism of the maturation process of intracranial immature teratoma cases have yet to be elucidated. Although a persistently normal AFP serum level and proof of histologic maturation on the second look surgery may serve as predictors of good outcome, regular MRI follow-up including the spinal column would be mandatory for the early detection of the development of any recurrent disease.

REFERENCES

1. Chik K, Li C, Shing MM, Leung T, Yuen PM. Intracranial germ cell tumours in children with and without Down syndrome. J Pediatr Hematol Oncol;1999:21:149-51.
2. HuangX, Zhang R, ZhouL F. Diagnosis and treatment of intracranial immature teratoma. Pediatr Neurosurg 2009;45:354-60.
3. Jennings MT, Gelman R, Hochberg F. Intracranial germ-cell tumours: Natural history and pathogenesis. J Neurosurg1985;63:155-67.
4. Lian LJ, Tang MY, Liu TH. Retroconversion of ovarian immature teratoma malignancy. Chin Med J (Engl)1980;93:24-30.
5. Matsutani M, UshioY, Abe H, Yamashita J, Shibui S, Fujimaki T, *et al*. Combined chemotherapy and radiation therapy for central nervous system germ cell tumours: Preliminary results of a Phase II study of the Japanese Pediatric Brain Tumor Study Group. Neurosurg Focus 1998;5:e7.
6. McCartney AC, Paradinas FJ, Newlands ES. Significance of the'maturation' of metastases from germ cell tumours after intensive chemotherapy. Histopathology1984;8:457-67.
7. Nakato H, Kuwabara S, Maesako N, Inomata H, Ishimoto F, Hashida K, *et al*. A case of Down's syndrome complicated by teratoma of the third ventricle of the brain (author's transl) No To Shinkei1982;34:145-50.
8. Ogawa K, Toita T, Nakamura K, Uno T, Onishi H, Itami J, *et al*. Treatment and prognosis of patients with intracranial nongerminomatous malignant germ cell tumours: Amultiinstitutional retrospective analysis of 41 patients. Cancer2003;98:369-76.
9. Oosterhuis JW, Damjanov I. Treatment of primary embryo-derived teratocarcinomas in mice with cis-diamminedichloroplatinum. Eur J Cancer ClinOncol1983;19:695-9.
10. Oosterhuis JW, Suurmeyer AJ, Sleyfer DT, Koops HS, Oldhoff J, Fleuren G. Effects of multiple-drug chemotherapy (cis-diammine-dichloroplatinum, bleomycin, and vinblastine) on the maturation of retroperitoneal lymph node metastases of nonseminomatous germ cell tumors of the testis. No evidence for De Novo induction of differentiation. Cancer1983;51:408-16.
11. Rickert CH, Probst-Cousin S, Gullotta F. Primary intracranial neoplasms of infancy and early childhood. Childs NervSyst1997;13:507-13.
12. Robson CD, Price DL, Barnes PD, Taylor GA. Radiologic-pathologic conference of Children's Hospital Boston: Pineal region mass in a neonate. Pediatr Radiol1997;27:829-31.
13. Satgé D, Monteil P, Sasco AJ, Vital A, Ohgaki H, Geneix A, *et al*. Aspects of intracranial and spinal tumours in patients with Down syndrome and report of a rapidly progressing Grade 2 astrocytoma. Cancer2001;91:1458-66.
14. Satgé D, Sasco AJ, Curé H, Leduc B, Sommelet D, Vekemans MJ. An excess of testicular germ cell tumours in Down's syndrome: Three case report and a review of the literature. Cancer1997;80:929-35.
15. Shaffrey ME, Lanzino G, Lopes MB, Hessler RB, Kassell NF, Vanden Berg SR. Maturation of intracranial immature teratomas. Report of two cases. J Neurosurg1996;85:672-6.
16. Tanabe M, Mizushima M, Anno Y, Kondou S, Dejima S, Hirao DJ, *et al*. Intracranial germinoma with Down's syndrome: A case report and review of the literature. SurgNeurol1997;47:28-31.
17. The Committee of Brain Tumor Registry of Japan. Report of brain tumour registry of Japan (1984–2000). Neurol Med Chir (Tokyo) 2009;49Suppl:S5-15.
18. Yamasaki S, Hamasaki Y, A case of cerebellar tumour associated with Down's syndrome. Arch JpnChir1985;54:305-13.