Neurology Asia 2020; 25(4) : 619 – 621

Cervical spinal ependymoma in a child with Down syndrome: A case report and review of the literature

Thitiporn Fangsaad

Department of Pediatrics, Bhumibol Adulyadej Hospital, Bangkok, Thailand

Abstract

Down syndrome is one of the most common chromosomal abnormalities. They have an increased risk of leukemia and other hematologic malignancies due to 3 oncogenes on chromosome 21. However, solid tumors seem to be underrepresented in Down syndrome. Central nervous system (CNS) tumors are even less common, although, there is no antioncogene for glial tumors on chromosome 21. Down syndrome with ependymoma is a rare association. We report a case of Down syndrome with cervical spinal ependymoma who presented with torticollis and left arm weakness. MRI was compatible with ependymoma and pathology confirmed ependymoma grade II. The patient underwent tumor removal surgery and local radiation therapy. Follow-up MRIs in one year showed resolution of the enhancing lesion, with remarkable improvement of motor power.

Keywords: Spinal ependymoma; Down syndrome; oncogene

INTRODUCTION

Down syndrome is one of the most common chromosomal abnormalities. It is often caused by trisomy 21 (94%), Robertsonian translocation (5%) and mosaic (1%). Down syndrome occurs in about 1 per 1,000 babies born per year. Down syndrome patient have an increased risk of leukemia and other hematologic malignancies. However, solid tumors seem to be underrepresented in Down syndrome. Central nervous system (CNS) tumors are even less common. Down syndrome with ependymoma is a rare association. There were only 2 cases reported in the literature in 2002 and 2010. We report a case of Down syndrome with ependymoma.

CASE REPORT

A 4-year-old boy, with a known case of trisomy 21-Down syndrome, presented to the orthopedic department in our hospital with torticollis for 2 weeks. He was a normal full-term child. Developmental milestones were all delayed. He had no history of injury, fever, cardiac or thyroid diseases, and was on physical therapy. He was able to run and use his hands and arms as normal. Physical examination showed his head tilted to the right side and his chin deviated to the left side. A CT scan of the cervical spine (C-spine) with C1-C2 3D reconstruction was done. C1-C2 rotatory subluxation was diagnosed. He underwent cervical traction followed by a cervical collar. His mother reported that he seemed to be better but still had torticollis. Five months later, he presented with progressive torticollis and left arm weakness. He could not run, but could walk. He was referred to the pediatric department. Physical examination showed normal consciousness, all cranial nerves were intact, power grade 5 except left arm grade 1 and left leg grade 4; pin prick sensation intact, hypotonia, hyperreflexia, Babinski sign present bilaterally, clonus negative, no cerebellar signs such as nystagmus or truncal ataxia. Because he had torticollis and left arm weakness, localization was most likely at the intramedullary level of the C-spine. His clinical course progressed and therefore tumor was suspected.

Magnetic resonance imaging (MRI) of the cervical spine revealed an intramedullary, enhancing mass at the C2-T1 cord level and syringomyelia associated with the tumor from the medulla to the T4 cord level (Figure 1). He subsequently underwent a laminectomy with tumor removal from C2-T1. Pathologic examination revealed ependymoma grade II (Figure 2). He received local radiation therapy. Follow-up MRIs in one year showed resolution of the enhancing lesion. He has had remarkable

Address correspondence to: Thitiporn Fangsaad, M.D., Pediatric department, Bhumibol Adulyadej Hospital, 171 Phahonyothin Rd, SaiMai, Bangkok, 10220, Thailand. E-mail: fthitiporn@gmail.com

Date of Submission: 13 April 2020; Date of Acceptance: 29 April 2020

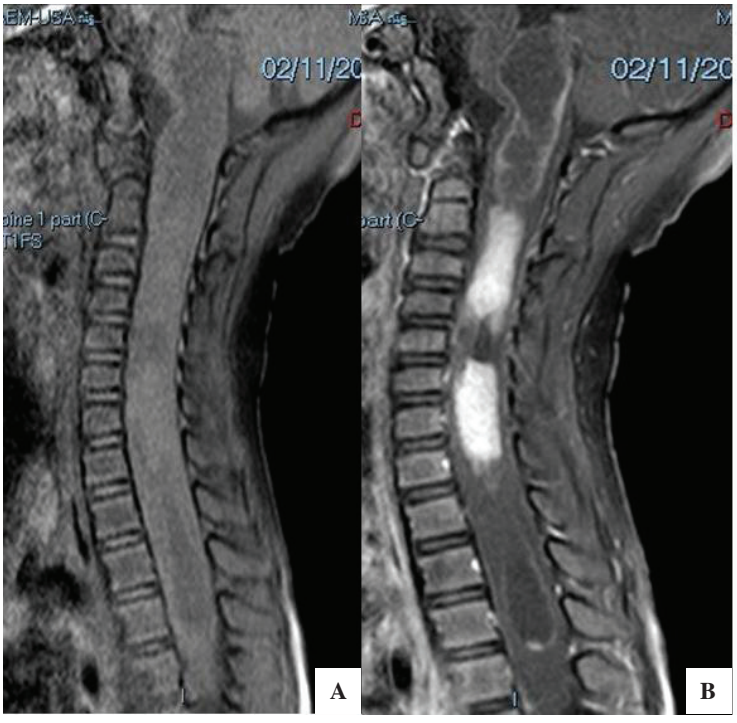

Figure 1. MRI showed a mixed solid-cystic intramedullary lesion involving the medulla, entire cervical to T4 spinal cord associated with cord expansion. The solid portion was at the C2-T1 cord level. There were peripheral enhancing cystic portions and syringomyelia associated with the tumor mass.

improvement of motor power which is grade 4+ in the left extremities.

DISCUSSION

Down syndrome (DS) is the most common chromosomal abnormality with trisomy of chromosome 21. Out of 223 genes mapping to chromosome 21, 127 have already been identified. Among them, 3 oncogenes, AML, ERG, and ETS2 have been implicated in leukemogenesis.[1] Therefore children with Down syndrome have an increased risk of leukemia approximately 10-20 times higher than children without Down syndrome.

Solid tumors seem to be underrepresented in those with Down syndrome. Central nervous system (CNS) tumors are even less common. There are a total of 39 CNS tumors with Down syndrome reported and they are primarily gliomas, germ cell tumors and meningiomas.[2-3] There were only 2 ependymomas reported, 1 was found incidentally during autopsy in a 19-week fetus at the medulla oblongata[4] and the other was found in a 13-year female at the lumbar region.[5] Although,

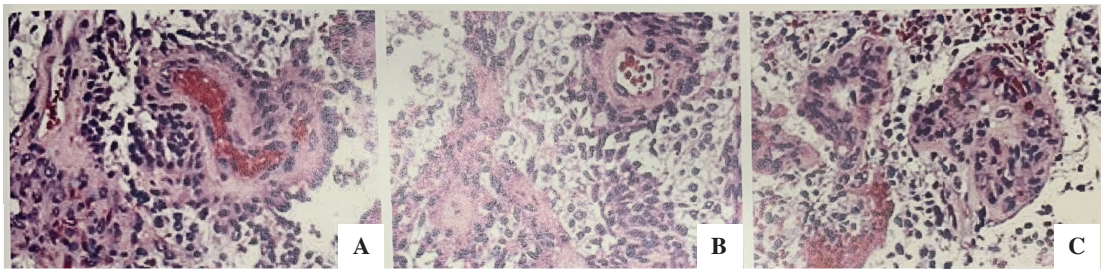

Figure 2. Microscopic examination: Sections show segments of tumor. Perivascular pattern is occasionally noted (A). Tumor cells have variable features; oval, spindle, and round cells with clear cytoplasm (B) are appreciated. Although occasional foci of endothelial proliferation are detected (C), mitoses are rarely found (0-1/10 HPFs). No necrosis is seen.

CNS tumors in Down syndrome are rare, there are 2 studies on allelotype analysis which did not suggest antioncogene for glial tumors on chromosome 21.[6-7] So chromosome 21 is not associated with ependymoma, but may reflect a chance phenomenon rather than an increased risk.[9] Instead, for nerve tissue tumors, gene ANA (from Abundant in Neuroepithelium Area) that impairs cell cycle progression[10] and S100[11] beta that induces neural differentiation may play a possible role.

Ependymoma itself accounts for 3-6% of all CNS tumors and 15% of spinal cord tumors. Spinal ependymoma is more common in adult than pediatric patients, whereas the reverse is true with intracranial ependymoma. Lumbosacral and filum terminale regions are found in half of spinal ependymoma cases and the other half are found in the cervical or thoracic regions. There are 2 previous studies showing that 1 ependymoma had gain of chromosome 21 by using cytogenic screening method of comparative genome hybridization among 15 intracranial germ cell tumors and 26 ependymomas.[8-9] In addition, a recent genetic and molecular review of spinal ependymoma reported that a common genetic mutation associated with ependymoma is neurofibromatosis 2 on chromosome 22. Otherwise, this review showed no association with Down syndrome or chromosome 21 in terms of chromosomal gain or loss. These findings confirm that chromosome 21 does not increase the risk of ependymoma. Since the report of ependymoma with Down syndrome is so rare, the prognosis for ependymoma in Down syndrome patients is assumed to be no different from that of the general population. One literature review suggested a new therapeutic option for spinal ependymoma based on genomic and molecular features, but was limited by not having uncovered a promising target.

In conclusion, this is a rare case of Down syndrome with cervical spinal ependymoma who presented with torticollis and left arm weakness. He had a good recovery following tumor removal surgery and local radiation therapy. Our literature review suggests that the ependymoma is likely a chance occurrence and no related to the underlying chromosomal abnormality.

ACKNOWLEDGEMENTS

The author would like to express her sincere gratitude to Assist. Prof. Nattaporntira Phalakornkul, M.D. and Nuttapon Lertkankasuk, M.D. for being part of care taking team; to Utcharee Intusoma, M.D., Ph.D. for her advice on publication; and to Ms. Christine Gordon and Michael J. Feinstein M.D. for English editing of the manuscript.

DISCLOSURE

Conflict of interest: None

REFERENCES

1. Savasan S, Taub JW, Ravindranath Y. Down syndrome and leukemia-an overview of cytogenetic and molecular events. *Turk J Pediatr* 1997;39:519-31.
2. Jaber AJ, Alkhani AM. Thoracic spinal meningioma in a child with Down syndrome: A case report and review of the literature. *Int J Pediatr Adol Med* 2014;1:93-6.
3. Satge D, Monteil P, Sasco AJ, *et al*. Aspects of intracranial and spinal tumore in patients with Down syndrome and report of a rapidly progressing grade 2 astrocytoma. *Cancer* 2001;91:1458-66.
4. Rickert CH, Gocke H, Paulus W. Fetal ependymoma associated with Down's syndrome. *Acta Neuropathol* 2002;103:78-81.
5. Biswas A, Puri T, Goyal S, *et al*. Spinal myxopapaillary ependymoma with Down syndrome: exploring an unusual association. *J Pediatr Hematol Oncol* 2010;32:e38-e41.
6. Fults D, Pedone CA, Thomas GA, White R. Allelotype of human malignant astrocytoma. *Cancer Res* 1990;50:5784-9.
7. Von Deimling A, Fimmers R, Schmidt MC, *et al*. Comprehensive alllelotype and genetic analysis of 466 human nervous system tumors. *J Neuropathol Exp Neurol* 2000;59(6):544-58.
8. Scheil S, Bruderlein S, Eicker M, *et al*. Low frequency of chromosomal imbalances in anaplastic ependymomas as detected by comparative genomic hybridization. *Brain Pathol* 2001;11(2):133-43.
9. Yoshida Y, Matsuda S, Ikematsu N, *et al*. ANA, a novel member of Tob/BTG1 family, is expressed in the ventricular zone of the developing central nervous system. *Oncogene* 1998;16:2687-93.
10. Satge D. A decreased incidence of neuroblastomas in Down's syndrome and overproduction of S-100 B protein. *Med Hypotheses* 1996;46:393-9.