Child's Nervous System
https://doi.org/10.1007/s00381-021-05172-1

CASE REPORT

Spontaneous regression of congenital brain tumors: a report of two cases

Ghazaleh Kheiri [1] · Zohreh Habibi [1] · Farideh Nejat [1]

Received: 16 February 2021 / Accepted: 15 April 2021

Abstract

Background Vanishing brain tumor is defined as spontaneously disappearing or decreasing of the initial brain mass volume to ≤ 70% before establishing the definitive diagnosis. The condition is rare and can be attributed to different factors. The exact mechanism is under debate, but the increasing rate and accuracy of neuroimaging studies and occurrence of similar scenario in other pathologies rather than brain tumors can be of particular importance in finding vanishing brain lesions.

Case report We present two unusual cases of congenital brain masses which underwent spontaneous shrinkage within the first months of life.

Conclusion The condition is scarcely observed in congenital brain masses. As congenital brain lesions are distinct entities with peculiar characteristics, this rare phenomenon may reflect different aspects in this age group.

Keywords Congenital · Brain tumors · Regression · Mass lesion · Vanishing

Introduction

Vanishing tumors are defined as space-occupying lesions, presenting radiologic features of tumors, which spontaneously resolve during radiologic follow-up [1]. It occurs in 1 out of 60,000–100,000 patients [2, 3]. Only few cases of vanishing brain tumors have been reported.

As congenital brain lesions are distinct entities with peculiar characteristics, this rare phenomenon may reflect different aspects in this age group. Herein, we present two unusual cases of congenital brain masses which underwent spontaneous shrinkage in magnetic resonance imaging (MRI) follow-up during the first months after birth.

✉ Zohreh Habibi
z-habibi@sina.tums.ac.ir

[1] Department of Pediatric Neurosurgery, Children's Medical Center Hospital, Tehran University of Medical Sciences, Tehran 1419733151, Iran

Case presentation

Case 1

A 2-month infant was evaluated because of increased head circumference and a suspicious abnormal shadow observed in trans-fontanelle ultrasonography. She had uneventful delivery and perinatal medical records. Brain MRI revealed a 16 × 11-mm enhancing mass at quadrigeminal plate, and a mild ventriculomegaly without periventricular edema. The lesion was isosignal to hypersignal in T2-weighted and hyposignal in T1-weighted images, with avid gadolinium enhancement (Fig. 1a). The baby had a soft fontanelle, with no sign of increased intracranial pressure (ICP). She was prescribed oral acetazolamide and underwent close surveillance. After 2 months, follow-up MRI showed a significant decrease in the mass, estimated about 8 × 5 mm (Fig. 1b). The third MRI, at 8 months, demonstrated a 5 × 3 enhancing mass without hydrocephalus (Fig. 1c). At 18 months, only a small enhancing spot could be seen on the right side of tectal plate (Fig. 1d). The patients never needed CSF diversion, and her developmental milestones were compatible with age.

Published online: 01 May 2021

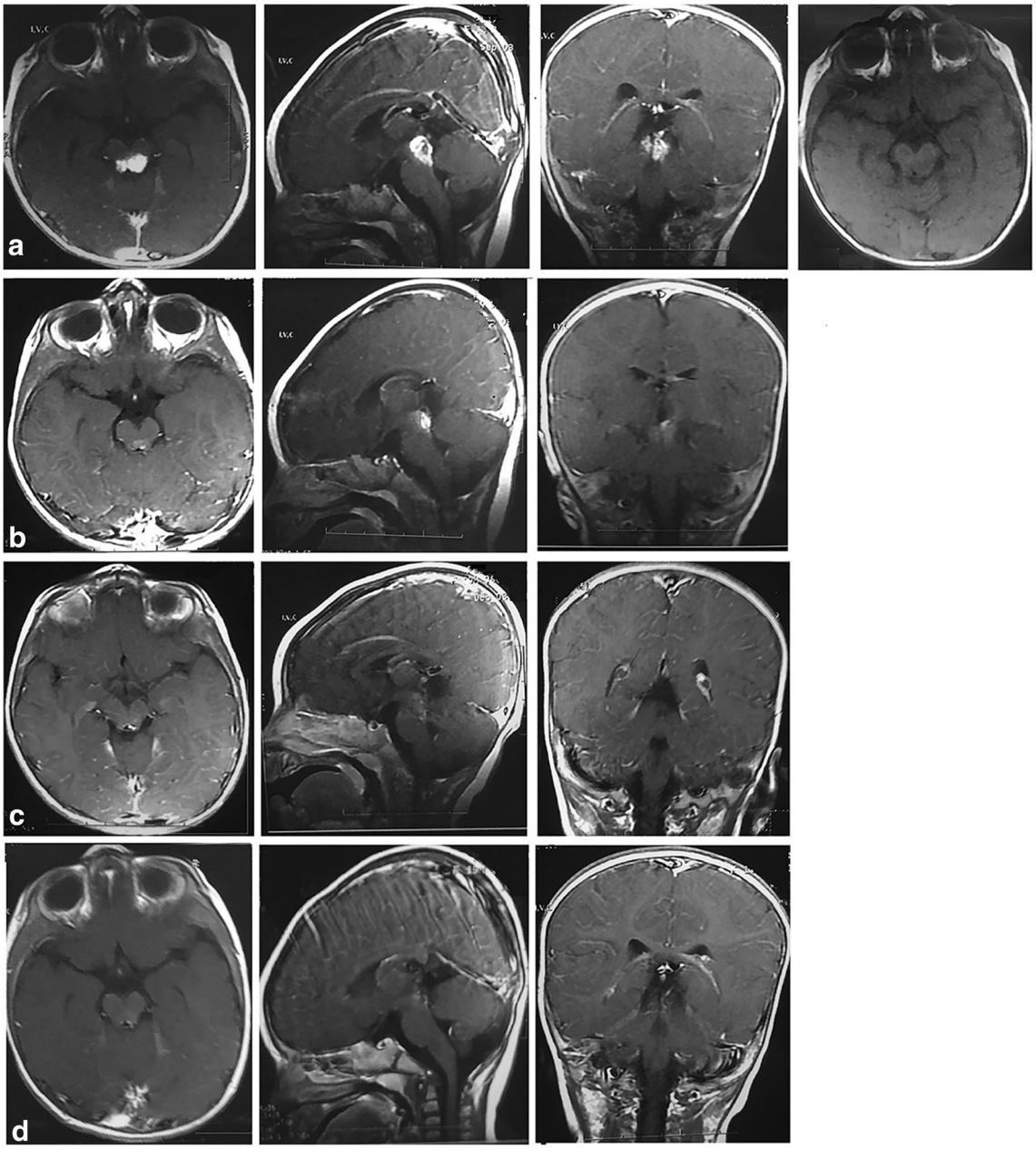

Fig. 1 Axial, sagittal, and coronal MRI images of the tectal plate mass at the age of 2 months (**a**), 4 months (**b**), 8 months (**c**), and 18 months (**d**) showing decease in the size and enhancement of the lesion. In the top right, the most lateral panel of the first row (**a**) demonstrates hyposignal mass on MRI without gadolinium which can help excluding hemorrhagic events

Case 2

A neonate was referred from an obstetric unit with prenatal diagnosis of hydrocephalus and a suspicious supratentorial mass, found by ultrasound in the last weeks of gestation. Physical examination revealed full fontanel. Brain MRI confirmed huge enhancing multiloculated cystic solid mass in left frontal area (Fig. 2a and b). Due to low weight, approach to mass lesion was postponed, and he underwent cystoperitoneal shunting followed by close surveillance. The fluid displayed negative cytology, but tissue sampling was not attempted at this step as the patient had been planned for a tumor surgery after he put on weight in the following weeks. Head circumference and developmental milestones remained in normal ranges. Follow-up MRI at 3 months revealed significant shrinkage in the size and enhancement of solid part. In close radiological follow-up, the enhancing part of lesion showed gradual decrease and disappeared at 18 months (Fig. 2c). The patient was readmitted at the age of 21 months, with distal catheter extrusion from the tiny skin of umbilicus. The proximal site was not functional and the shunt was totally

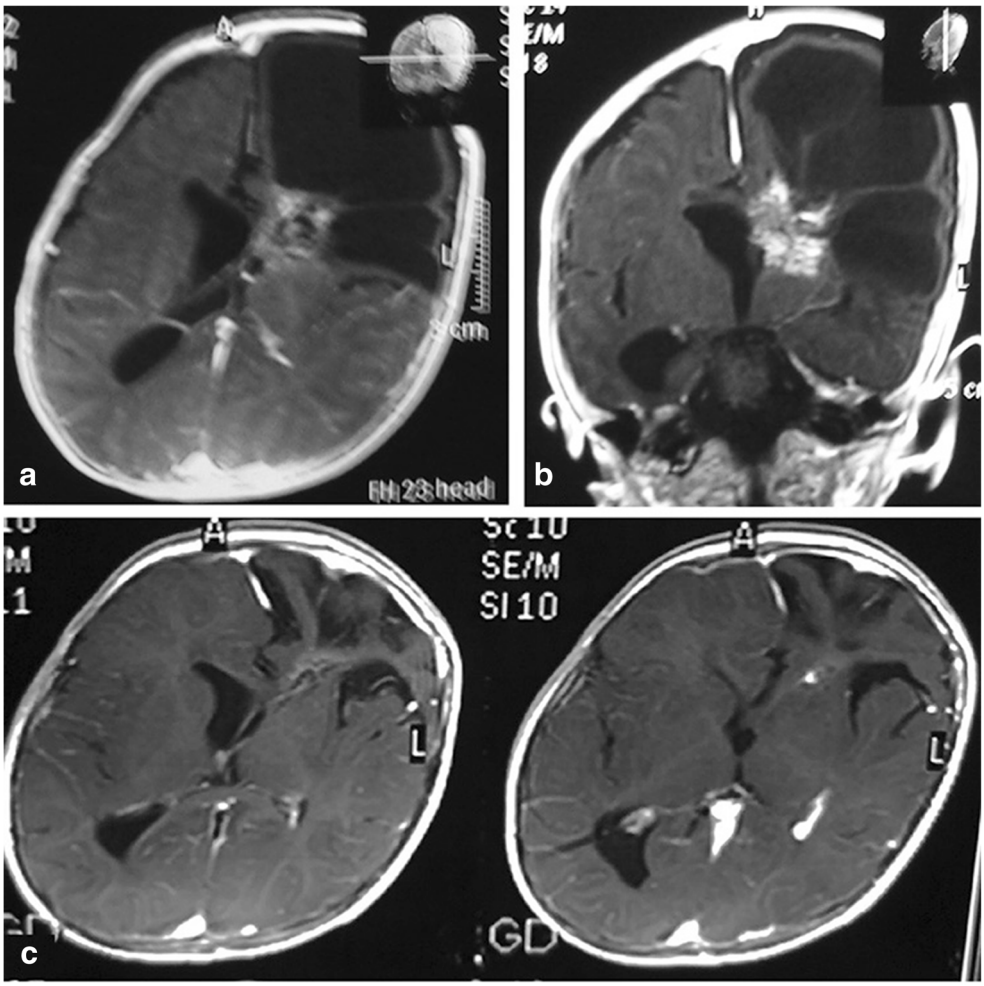

Fig. 2 **a** and **b** Brain MRI, performed in neonatal period, demonstrated huge enhancing multiloculated cystic solid mass in the left frontal area. **c** The enhancing part of lesion showed gradual decrease and disappeared at the age of 18 months

removed. He developed no new symptoms in postoperative period and 1 year afterward.

No genetic investigation was performed for none of the patients. Institutional ethical approval and informed consents were taken.

Discussion

Spontaneous regression of malignant tumors is an unusual phenomenon which have been observed in malignant melanomas, renal cell carcinomas, neuroblastomas, testes germ cell tumors, and brain tumors [4, 5]. Spontaneously disappearing or decreasing of the initial brain mass volume to ≤ 70% before establishing the definitive diagnosis, observed by MRI or computed tomography (CT), is defined as vanishing tumor, tumor regression, ghost tumor, or burned-out tumor [4–9]. Primary CNS lymphoma (PCNSL) is the commonest pathology in vanishing brain tumors [10–12].

The increasing rate and accuracy of neuroimaging studies should be considered a factor in finding brain tumors regression. The possibility of observing atypical findings that were not visualized by previous techniques has increased [1].

Apart from the higher rate of neuroimaging, several hypotheses have been suggested for the mechanism of tumor regression, such as hydration effects of CSF, spontaneous apoptosis, immunological responses, effects of corticosteroid therapy, and small dose of radiation for diagnosis purposes. Infection and fever have also been suggested as possible stimuli [13]. Even though, the exact mechanism has still remained unclear [7, 8].

One other proposed explanation is that many other CNS lesions may display similar scenario. Hayashi et al. reported four cases of demyelinating disease presented as masses with progressive regression [14]. Hamed et al. suggested differential diagnosis of the vanishing masses in children, including (1) tumors; (2) tumor-like demyelinating lesions or tumefactive multiple sclerosis; and (3) intracranial infection/granulomas, hematoma, or tuberculoma [15]. These alternative diagnoses usually have indistinguishable features in history and physical exam, nonspecific CSF pattern, and similar MRIs. New imaging techniques like MR spectroscopy, iron nanoparticle imaging studies, perfusion MRI, and SPECT can

help differentiating between neoplastic and inflammatory lesions. General workup to rule out hematologic diseases and lymphoma can be of help [16, 17]. In some occasions, tissue biopsy may be the only diagnostic alternative.

In cases of vanishing brain lesions, even after the disappearance of the mass, follow-up MRIs should be routinely done for at least 3–5 years [18].

In the present cases, regression occurred with no intervention. In both cases, the characteristics of the first MRIs could exclude the possibility of intracerebral hemorrhage which is one of the most important differential diagnoses of spontaneously vanishing lesions of brain. Surveillance for raised ICP and treatment of hydrocephalus were the top priorities in the management of these cases. The first patient harbored a tectal plate lesion. Most lesions in this area are benign gliomas, with only a small percentage being malignant [19–21]. Considering the high rate of benign pathology, favorable outcomes can be achieved with conservative management [22, 23]. The literature suggestions for this entity remain controversial between conservative management, biopsy and adjuvant therapy, and resection, with all achieving similar outcomes [24]. The current congenital case underwent conservative management which ended up in tumor regression. The second patient had prenatal diagnosis of a supratentorial mass. He underwent cystoperitoneal shunting to gain weight before major tumor surgery. The lesion showed spontaneous regression and he remained shunt free after tumor vanishing.

Overall, congenital tumors should be managed with caution. Considering low body mass and small amount of circulating blood volume, neonates and young infants are not good candidates for aggressive tumor resection. In selected cases, conservative treatment and ICP management via CSF diversion may save time until the child gains weight and can tolerate craniotomy. In rare occasions, the lesion may spontaneously regress during surveillance, as happened for the current cases.

It can be hypothesized that postnatal changes in the physiological state and cellular microenvironment would have triggered tumor regression. Tumor cells may stop cycling or start apoptosis due to potential alterations in microenvironment and cerebrovascular hemodynamic. Besides, the tumoral cells of congenital neoplasms may mature after birth owing to these microenvironmental changes. Vascular events, either with hemorrhagic or ischemic mechanism, may play a role in tumor apoplexy and disappearance [25]. This condition has been particularly recorded for tumors of pineal region, and can be used to justify the event in case 1. Moreover, CSF diversion surgeries are proposed to trigger spontaneous tumor regression, and cases of vanishing tumors after shunting and endoscopic third ventriculostomy (ETV) have been reported [8, 13, 26]. It is hypothesized that surgical trauma may activate the host's immunological responses, leading to tumor disappearance [8]. Changes in the cerebral hydrodynamics following CSF diversion may also alter cerebrovascular flow and vascular supply of the lesion, and subsequently induce tumor regression. Through the same mechanism, cystoperitoneal shunting in case 2 may have triggered spontaneous regression of the lesion.

Regardless of the mentioned hypotheses, a wait-and-watch policy should be considered in neonates with congenital brain mass whenever indicated.

Declarations

Conflict of interest The authors report no conflict of interest and no funding or financial support.

References

1. Frassanito P, Tamburrini G, Massimi L, Caldarelli M, Di Rocco C (2015) Ghost tumors of the central nervous system: definition, clinical implications, and proposal of classification. World Neurosurg 84(3):663–670. https://doi.org/10.1016/j.wneu.2015.03.063
2. Sutherland CS, Kelly JJ, Morrish W, Sutherland GR (2010) Identification of disappearing brain lesions with intraoperative magnetic resonance imaging prevents surgery. Neurosurgery 67(4):1061–1065. https://doi.org/10.1227/NEU.0b013e3181ee4303
3. Cole WH (1981) Efforts to explain spontaneous regression of cancer. *J Surg Oncol* 17(3):201–209
4. Bromberg JE, Siemers MD, Taphoorn MJ (2002) Is a "vanishing tumor" always a lymphoma? Neurology 59(5):762–764. https://doi.org/10.1212/wnl.59.5.762
5. Mosillo C, Scagnoli S, Pomati G, Caponnetto S, Mancini ML, Bezzi M, Cortesi E, Gelibter A (2017) Burned-out testicular cancer: really a different history. Case Rep Oncol 10(3):846–850. https://doi.org/10.1159/000480493
6. Takekawa H, Hozumi A, Hirata K, Yamazaki K (2008) A spontaneously vanishing primary cerebral lymphoma "ghost tumour". Neurol Neurosurg Psychiatry 79(10):1159. https://doi.org/10.1136/jnnp.2007.132282
7. Fujimaki T, Mishima K, Asai A, Suzuki I, Kirino T (1999) Spontaneous regression of a residual pineal tumor after resection of a cerebellar vermian germinoma. J Neuro-Oncol 41(1):65–70. https://doi.org/10.1023/a:1006155120191
8. Murai Y, Kobayashi S, Mizunari T, Ohaki Y, Adachi K, Teramoto A (2009) Spontaneous regression of a germinoma in the pineal body after placement of a ventriculoperitoneal shunt. *J Neurosurg* 93(5):884–886. https://doi.org/10.3171/jns.2000.93.5.0884
9. Ono H, Shin M, Takai K, Oya S, Mukasa A, Saito N (2011) Spontaneous regression of germinoma in the pineal region before endoscopic surgery: a pitfall of modern strategy for pineal germ cell tumors. J Neuro-Oncol 103(3):755–758. https://doi.org/10.1007/s11060-010-0432-1 Epub 2010 Oct 15
10. Weingarten KL, Zimmerman RD, Leeds NE (1983) Spontaneous regression of intracerebral lymphoma. Radiology 149(3):721–724
11. Okita Y, Narita Y, Miyakita Y, Ohno M, Fukushima S, Maeshima A, Kayama T, Shibui S (2012) Long-term follow-up of vanishing tumors in the brain: How should a lesion mimicking primary CNS

lymphoma be managed? Clin Neurol Neurosurg 114(9):1217–1221. https://doi.org/10.1016/j.clineuro.2012.02.053
12. Al-Yamany M, Lozano A, Nag S, Laperriere N, Bernstein M (1999) Spontaneous remission of primary central nervous system lymphoma: report of 3 cases and discussion of pathophysiology. J Neuro-Oncol 42(2):151–159. https://doi.org/10.1023/a:1006162615774
13. Ide M, Jimbo M, Yamamoto M, Hagiwara S, Aiba M, Kubo O (1997) Spontaneous regression of primary intracranial germinoma. Cancer 79(3):558–563. https://doi.org/10.1002/(sici)1097-0142(19970201)79:3<558::aid-cncr19>3.0.co;2-2
14. Hayashi T, Kumabe T, Jokura H, Fujihara K, Shiga Y, Watanabe M, Higano S, Shirane R (2003) Inflammatory demyelinating disease mimicking malignant glioma. J Nucl Med 44(4):565–569
15. Hamed SA, Mekkawy MA, Abozaid H (2015) Differential diagnosis of a vanishing brain space occupying lesion in a child. World J Clin Cases 3(11):956–964. https://doi.org/10.12998/wjcc.v3.i11.956
16. Weller M, Stevens A, Sommer N, Schabet M, Wiethölter H (1992) Humoral CSF parameters in the differential diagnosis of hematologic CNS neoplasia. Acta Neurol Scand 86(2):129–133. https://doi.org/10.1111/j.1600-0404.1992.tb05053.x
17. Hunt MA, Jahnke K, Murillo TP, Neuwelt EA (2006) Distinguishing primary central nervous system lymphoma from other central nervous system diseases: a neurosurgical perspective on diagnostic dilemmas and approaches. Neurosurg Focus 21(5):E3. https://doi.org/10.3171/foc.2006.21.5.4
18. Krogh-Jensen M, D'Amore F, Jensen MK, Jensen MK, Christensen BE, Thorling K, Pedersen M, Johansen P, Boesen AM, Andersen E (1995) Clinicopathological features, survival and prognostic factors of primary central nervous system lymphomas: trends in incidence of primary central nervous system lymphomas and primary malignant brain tumors in a well-defined geographical area. Population-based data from the Danish Lymphoma Registry, LYFO, and the Danish Cancer Registry. Leuk Lymphoma 19(3-4):223–233. https://doi.org/10.3109/10428199509107892
19. Oka K, Kin Y, Go Y, Ueno Y, Hirakawa K, Tomonaga M, Inoue T, Yoshioka S (1999) Neuroendoscopic approach to tectal tumors: a consecutive series. J Neurosurg 91(6):964–970. https://doi.org/10.3171/jns.1999.91.6.0964
20. Lapras C, Bognar L, Turjman F, Villanyi E, Mottolese C, Fischer C, Jouvet A, Guyotat J (1994) Tectal plate gliomas. Part I: microsurgery of the tectal plate gliomas. Acta Neurochir 126(2-4):76–83. https://doi.org/10.1007/BF01476414
21. Kaku Y, Yonekawa Y, Taub E (1999) Transcollicular approach to intrinsic tectal lesions. Neurosurgery 44(2):338–343. https://doi.org/10.1097/00006123-199902000-00052
22. May PL, Blaser SI, Hoffman HJ, Humphreys RP, Harwood-Nash DC (1991) Benign intrinsic tectal "tumors" in children. J Neurosurg 74(6):867–871. https://doi.org/10.3171/jns.1991.74.6.0867
23. Stroink AR, Hoffman HJ, Hendrick EB, Humphreys RP (1986) Diagnosis and management of pediatric brain-stem gliomas. J Neurosurg 65(6):745–750. https://doi.org/10.3171/jns.1986.65.6.0745
24. Ternier J, Wray A, Puget S, Bodaert N, Zerah M, Sainte-Rose C (2006) Tectal plate lesions in children. J Neurosurg 104(6 Suppl):369–376. https://doi.org/10.3171/ped.2006.104.6.369
25. Mattogno PP, Frassanito P, Massimi L, Tamburrini G, Novello M, Lauriola L, Caldarelli M (2016) Spontaneous regression of pineal lesions: ghost tumor or pineal apoplexy? World Neurosurg 88:64–69
26. Alkhani AM, Boop FA, Rutka JT (1999) Involution of enhancing intrinsic tectal tumors after endoscopic third ventriculostomy. Report of two cases. J Neurosurg 91(5):863–866