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CASE REPORT

Diffuse intrinsic pontine glioma ventricular peritoneal shunt metastasis: a case report and literature review

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Abstract

Dissemination of diffuse intrinsic pontine glioma (DIPG) outside the central nervous system is exceptional. Here, we present a child diagnosed with DIPG who developed seeding along the track of the ventriculoperitoneal shunt and review the literature on this unusual occurrence.

Keywords Diffuse intrinsic pontine glioma · Ventriculo-peritoneal shunt · Extracranial metastasis

Diffuse intrinsic pontine glioma (DIPG) represents one of the most aggressive tumors of the central nervous system in children, and despite numerous clinical trials of radiotherapy, chemotherapy, and biological treatments, efforts to improve outcomes have been unsuccessful [1]. The pattern of progression of DIPG is primarily local, and patients usually present with recurrence of brainstem symptoms within a few months after completion of radiotherapy. Recent reports have identified cases of leptomeningeal dissemination, essentially diagnosed on imaging studies, and symptomatic cases are rare [2, 3]. Even more unusual is the dissemination of this tumor outside the central nervous system. Here, we describe case of DIPG metastasis along the ventriculo-peritoneal shunt (VPS) track.

Case report

A 4-year 9-month-old previously healthy female presented with a week's history of headache, vomit, decreased energy, uncoordinated gait, and left facial weakness. MRI revealed a large pontine lesion (Fig. 1) with hydrocephalus. She underwent VPS insertion. Due to typical clinical and MRI DIPG characteristics, no biopsy was performed.

She underwent focal irradiation (54 Gy in 30 fractions). Her clinical status improved, and there was improvement on her post-radiation MRI scan. She eventually attended school on daily basis and enjoyed normal daily activities.

Seven months from the time of diagnosis, she started to show symptoms of tumor progression. MRI reported tumor progression. She underwent focal re-irradiation (21.6 Gy in 12 fractions). Re-irradiation was uneventful and again provided good clinical benefit with improvement of her symptoms. Subsequent slight neurological deterioration and radiological progression were noted 3 months from re-irradiation. At this point, her parents noted three firm nodules overlying her shunt tubing (Fig. 2). One of the lesions was biopsied and pathology report described high-grade glioma. She was started oral temozolomide in attempt to improve symptoms of progression. Despite this treatment, she continued to slowly decline, with progressive neurological deterioration. She did not show further evidence of extracranial dissemination during this period. She died 17 months from presentation. Parents consented for a brain autopsy as well as biopsy of VPS nodules.

At autopsy, the brain weighted 1322 g (expected for age). Transverse sections of the brainstem and cerebellum showed a mass centered in the pons, diffusely expanding the brainstem at all levels, with focal areas of hemorrhage and areas of myxoid degeneration. At the supratentorial level, the hemispheric leptomeninges showed diffuse tumor infiltration. At the abdominal level, there were subcutaneous nodules surrounding the shunt tract. Microscopically, these abdominal mass lesions showed a fibrillary neoplasm similar of that seen

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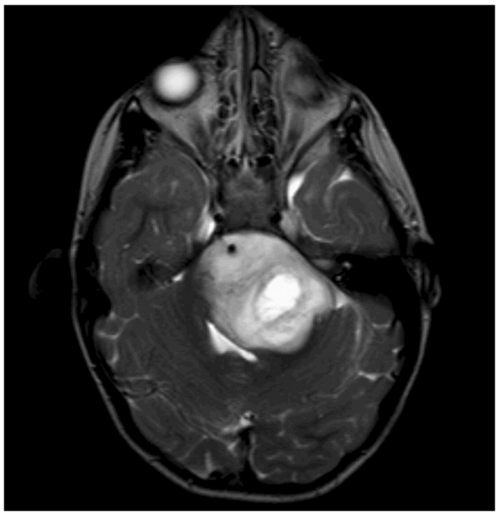

Fig. 1 Initial MRI showed a right-sided pontine lesion with some cystic-necrotic component. At follow-up, there was a cystic necrotic right-sided pontine lesion

on previous surgical biopsy. Both primary neoplasm and its extracranial metastatic deposits harbored the K27 M H3.3 mutation (Fig. 3).

Discussion

This observation adds to the literature on the metastatic potential of DIPG. In this observation, since the clinical and radiological presentation was typical, there was no initial biopsy performed. The biopsy of the subcutaneous nodule was the first evidence of high-grade glial tumor. DIPG diagnosis was subsequently confirmed at autopsy.

The initial course of our patient was classical. The 7-month period until progression is in agreement with previous reports on DIPG [1, 4]. Our patient underwent a second course of radiation, a treatment modality that is increasingly used [5–7]. Leptomeningeal dissemination in DIPG has been reported and is estimated to occur in up to 30% of patients [2, 3]. This is likely an underestimation, as only few DIPG patients undergo autopsy, and data on leptomeningeal dissemination are essentially based on MRI studies performed at the time of progression. It is speculated that glioma cells either disseminate via the cerebrospinal fluid or migrate via the axonal route to reach the leptomeninges and then disseminate along the ependymal lining [2]. The mechanisms involved in extraneural dissemination are less clear. A number of reports have documented peritoneal seeding from brain tumors through a VPS [8, 9], including 4 reports in astrocytic brainstem tumors [10–13]. All 4 patients presented with ascites that was the initial symptom of peritoneal dissemination. An additional report described a patient with a malignant brainstem tumor who developed a large pleural effusion following the insertion of a ventriculopleural shunt [14]. In our patient, there was no ascites, and the metastatic nodules developed along the shunt track, suggesting another modality of dissemination. The shunt was inserted at the time of initial diagnosis and the nodules were identified only 1 year later. At no point during the course of the disease did the patient show any evidence of peritoneal dissemination or further extraneural dissemination. There is no clear explanation for the occurrence of this complication.

We could only find two occurrences of subcutaneous seeding along VPS tracks, both observations concerning adult patients. The first was a patient with normal pressure hydrocephalus treated with a VP shunt who presented with a subcutaneous mass along the VPS catheter. Investigations led to the diagnosis of pancreatic carcinoma [15]. The second case occurred in patient with primary central nervous system lymphoma who underwent a VPS insertion and subsequently developed tumor-like masses in the right neck and periumbilical areas, along the route of the subcutaneous tunnel of the VP shunt [16].

While it is likely that the VP shunt is the pathway of spread of tumor cells in the context of malignant ascites, the pathogenesis of malignant cell extravasating along the catheter remains poorly understood. One can argue in our case that the extended survival span of the patient secondary to the re-irradiation treatment may explain the occurrence of this unusual complication. However, the long interval (12 months) between the shunt insertion and the subcutaneous spread suggests that dissemination was more likely secondary to tumor recurrence/progression. From a histological standpoint, the

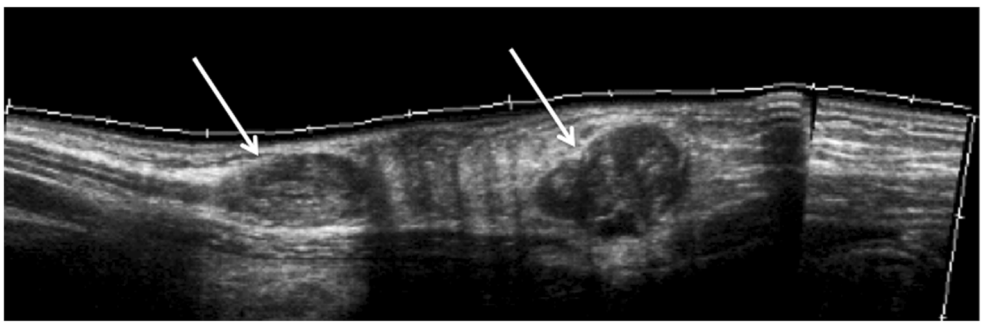

Fig. 2 Ultrasound of the VPS masses showed nodules (arrows) related to the VP shunt in the lower chest. These nodules are solid and heterogeneous in echogenicity, and they are well defined. The shunt passes through part of each nodule

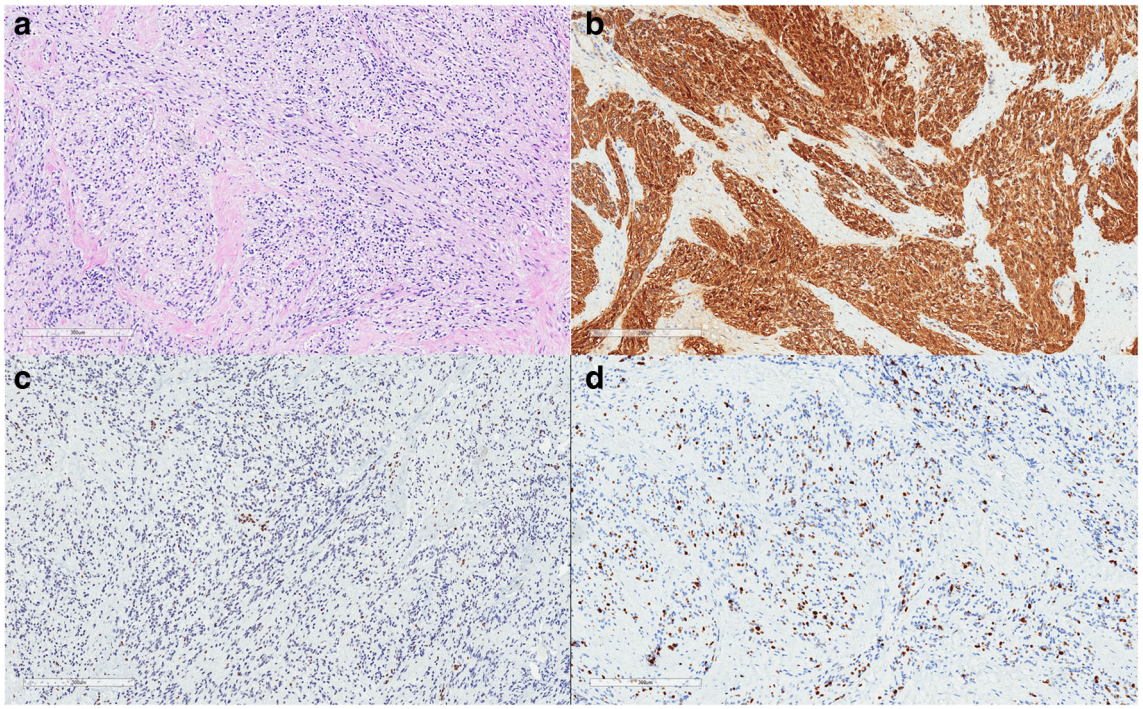

Fig. 3 Morphological features of the abdominal nodule showing a cellular neoplasm separated by bands of collagen (**a**, H&E). The tumor cells are immunopositive for GFAP (**b**) and have lost expression of H3K27me3 (**c**). The MIB-1 proliferative index is ~20% (**d**). Scale bars represent 300 μm

characteristics of the subcutaneous nodules were similar to that of the primary tumor at autopsy. It is remarkable that both nodules and primary tumor harbored the K27 M-H3.3 mutation.

In conclusion, we describe here an unusual occurrence of subcutaneous spread of a DIPG along the shunt track, which appears different from classical VP shunt seeding previously reported, as illustrated by the absence of ascites in our patient. As new treatment strategies are currently investigated, one should keep in mind the metastatic potential of DIPG.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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References

1. Hargrave D, Bartels U, Bouffet E (2006) Diffuse brainstem glioma in children: critical review of clinical trials. Lancet Oncol 7:241–248
2. Gururangan S, McLaughlin CA, Brashears J, Watral MA, Provenzale J et al (2006) Incidence and patterns of neuraxis metastases in children with diffuse pontine glioma. J Neuro-Oncol 77:207–212
3. Sethi R, Allen J, Donahue B, Karajannis M, Gardner S, Wisoff J, Kunnakkat S, Mathew J, Zagzag D, Newman K, Narayana A (2011) Prospective neuraxis MRI surveillance reveals a high risk of leptomeningeal dissemination in diffuse intrinsic pontine glioma. J Neuro-Oncol 102:121–127
4. Vanan MI, Eisenstat DD (2015) DIPG in children - what can we learn from the past? Front Oncol 5:237
5. Janssens GO, Gandola L, Bolle S, Mandeville H, Ramos-Albiac M, van Beek K, Benghiat H, Hoeben B, Morales la Madrid A, Kortmann RD, Hargrave D, Menten J, Pecori E, Biassoni V, von Bueren AO, van Vuurden DG, Massimino M, Sturm D, Peters M, Kramm CM (2017) Survival benefit for patients with diffuse intrinsic pontine glioma (DIPG) undergoing re-irradiation at first progression: a matched-cohort analysis on behalf of the SIOP-E-HGG/DIPG working group. Eur J Cancer 73:38–47
6. Morales La Madrid A, Santa-Maria V, Cruz Martinez O, Mora J, Puerta Roldan P et al (2017) Second re-irradiation for DIPG progression, re-considering "old strategies" with new approaches. Child's Nerv Syst 33:849–852
7. Lassaletta A, Strother D, Laperriere N, Hukin J, Vanan MI, Goddard K, Lafay-Cousin L, Johnston DL, Zelcer S, Zapotocky M, Rajagopal R, Ramaswamy V, Hawkins C, Tabori U, Huang A, Bartels U, Bouffet E (2018) Reirradiation in patients with diffuse intrinsic pontine gliomas: the Canadian experience. Pediatr Blood Cancer 65:e26988
8. Rickert CH (2003) Extraneural metastases of paediatric brain tumours. Acta Neuropathol 105:309–327
9. Rickert CH (1998) Abdominal metastases of pediatric brain tumors via ventriculo-peritoneal shunts. Child's Nerv Syst 14:10–14
10. Barajas RF Jr, Phelps A, Foster HC, Courtier J, Buelow BD et al (2015) Metastatic diffuse intrinsic pontine glioma to the peritoneal cavity via ventriculoperitoneal shunt: case report and literature review. J Neurol Surg Rep 76:e91–e96

11. Newton HB, Rosenblum MK, Walker RW (1992) Extraneural metastases of infratentorial glioblastoma multiforme to the peritoneal cavity. Cancer 69:2149–2153
12. Mosca L, Baldini M (1976) Early glial tumor metastases through a ventriculo-atrial shunt. Tumori 62:47–54
13. Jacques TS, Miller K, Rampling D, Gatscher S, Harding B (2008) Peritoneal dissemination of a malignant glioma. Cytopathology 19:264–266
14. Wakamatsu T, Matsuo T, Kawano S, Teramoto S, Matsumura H (1971) Glioblastoma with extracranial metastasis through ventriculopleural shunt. Case report. J Neurosurg 34:697–701
15. Nawashiro H, Otani N, Katoh H, Ohnuki A, Ogata S, Shima K (2002) Subcutaneous seeding of pancreatic carcinoma along a VP shunt catheter. The Lancet. Oncology 3:683
16. Ko JH, Lu PH, Tang TC, Hsu YH (2011) Metastasis of primary CNS lymphoma along a ventriculoperitoneal shunt. J Clin Oncol 29:e823–e824