Spinal cord involvement in two children with posterior reversible encephalopathy syndrome

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Spinal cord involvement (SCI) is a rare feature of posterior reversible encephalopathy syndrome (PRES), especially in children. SCI is generally symptomatic, and may have a different outcome compared with encephalic localization of PRES. We reported about two cases of SCI in pediatric patients with PRES, after multimodal anticancer therapies, including radiotherapy, chemotherapy and targeted agents.

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Practice points

- Posterior reversible encephalopathy syndrome with spinal cord involvement (SCI) is a rare clinical manifestation.
- SCI is generally symptomatic.
- SCI may be irreversible.
- Outcome of spinal and encephalic localization of posterior reversible encephalopathy syndrome could be different.
- Subsequent multimodal anticancer treatments may have unexpected cumulative toxicities.

Posterior reversible encephalopathy syndrome (PRES) is a clinical–radiological entity due to vasogenic edema [1]. Pathogenesis of the edema seems to be related to hypertension, described in 67–80% of cases and to disruption/deregulation of the blood–brain barrier [3,4].

The intensity and severity of clinical manifestations vary and may require intensive care unit admission. Imaging findings, mainly characterized as areas of hyperintensity in T2-weighted MR images, also vary in severity. Thorough familiarity with the imaging criteria is crucial to the diagnosis. The combination of suggestive clinical manifestations and radiological criteria establishes the diagnosis of PRES.

Spinal cord involvement (SCI) has been reported only in adults with PRES [2]. We report herein two children who after completion of high-dose chemotherapy, craniospinal irradiation and bevacizumab for metastatic medulloblastoma developed PRES with SCI. In the two cases, craniospinal irradiation and high-dose chemotherapy were completed from more than 6 months. Bevacizumab was the latest therapy. In both clinical presentations included headache, vision loss, hypertension and progressive consciousness impairment. One patient also experienced generalized seizures and respiratory failure.

An 11-year-old boy (Figure 1) had baseline MR images showing no brain or spinal cord signal changes (Figure 1A). Axial FLAIR and sagittal T2-weighted MR images (Figure 1B) obtained 72 h since clinical onset of PRES show bilateral and symmetric cortical hyperintense areas in posterior parietal and temporal lobes according to a dominant

Figure 1. 11-year-old boy. (A) Baseline MR images showing no brain or spinal cord signal changes. (B) Axial FLAIR and sagittal T2-weighted MR images (B) obtained 72 h since clinical onset of PRES show bilateral and symmetric cortical hyperintense areas in posterior parietal and temporal lobes according to a dominant parietal-occipital PRES pattern [3] and an extensive hyperintensity of the spinal cord from C3 to the conus medullaris. (C) Axial FLAIR and sagittal T2-weighted MR images obtained 3 months later show complete resolution of the cortical brain abnormalities and a residual signal hyperintensity from D1 to the conus medullaris. FLAIR: Fluid attenuated inversion recovery; MR: Magnetic resonance; PRES: Posterior reversible encephalopathy syndrome.

parietal-occipital PRES pattern [3] and an extensive hyperintensity of the spinal cord from C3 to the conus medullaris (Figure 1B). Axial FLAIR and sagittal T2-weighted MR images obtained 3 months later show complete resolution of the cortical brain abnormalities and a residual signal hyperintensity from D1 to the conus medullaris (Figure 1C).

The other case, a 13-year-old girl (Figure 2), had a baseline axial FLAIR and sagittal T2-weighted MR images showing a focal hyperintensity in the right frontal lobe and bilateral hyperintensity of the paravermian portion of the cerebellar hemispheres surrounding a dilated IV ventricle (Figure 2A). Axial FLAIR and sagittal T2-weighted MR images obtained 72 h since clinical onset of PRES show cortical hyperintense areas in the left frontal and parietal lobes according to a holohemispheric watershed PRES pattern [3] and bilateral hyperintensity of the cerebellum and central hyperintensity of the spinal cord from medulla to C4 (Figure 2B). Axial FLAIR and sagittal T2-weighted MR images obtained 3 months later show partial resolution of brain signal abnormalities and a residual hyperintensity of the central spinal cord from medulla to C3 (Figure 2C).

In both cases, T1 contrast-enhanced sequences did not show metastases. Cerebrospinal fluids obtained with lumbar puncture were negative for tumor cells.

Both patients were treated in an intensive care unit for supporting respiratory function and for adequate monitoring of all vital signs. The goal of specific treatment was the achievement of blood pressure control, through β -blockers, calcium channel blockers and ACE inhibitors. Furthermore, dexamethasone was also administered to reduce edema, after solving hypertension.

Clinical outcome was characterized in both patients by paraplegia with sphincters failure in one. Encephalic features underwent to complete resolution.

Discussion, conclusion & future perspective

In pediatric oncology, PRES is a rare effect described mainly with intrathecal chemotherapy. Furthermore, SCI with PRES is an even rarer event, today described only in adults with different etiologies [3]. In children with brain malignancy, improvement in survival due to modern multimodal anticancer treatments including surgery, radiotherapy, chemotherapy and targeted agents may increase risk of cumulative toxicities, with rare events, as well as described cases. Contribution of single treatments to PRES' pathophysiology based on hypertension and blood–brain barrier dysfunction [1] is unknown.

Figure 2. 13-year-old girl. (A) Baseline axial FLAIR and sagittal T2-weighted MR images showing a focal hyperintensity in the right frontal lobe and bilateral hyperintensity of the paravermian portion of the cerebellar hemispheres surrounding a dilated IV ventricle. No signal change is present in the spinal cord. (B) Axial FLAIR and sagittal T2-weighted MR images obtained 72 h since clinical onset of PRES show cortical hyperintense areas in the left frontal and parietal lobes according to a holohemispheric watershed PRES pattern [3] and bilateral hyperintensity of the cerebellum and central hyperintensity of the spinal cord from medulla to C4. (C) Axial FLAIR and sagittal T2-weighted MR images obtained 3 months later show partial resolution of brain signal abnormalities and a residual hyperintensity of the central spinal cord from medulla to C3. FLAIR: Fluid attenuated inversion recovery; MR: Magnetic resonance; PRES: Posterior reversible encephalopathy syndrome.

Prediction of so rare adverse events is very difficult. Clinical multicentric surveys for cumulative long-term toxicities may help to understand if predictive factors are available.

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Ethical conduct of research

Clinical activity described in this report has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All details that might disclose the identity of the patient have been omitted.

Informed consent disclosure

The authors state that they have obtained verbal and written informed consent from the patient/patients for the inclusion of their medical and treatment history within this case report.

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