Case Report

Slit-like hypertensive hydrocephalus: Report of a late, complex, and multifactorial complication in an oncologic patient

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Received: 31 March 2020
Accepted: 07 July 2020
Published: 01 August 2020

DOI: 10.25259/SNI_145_2020

ABSTRACT

Background: Several sophisticated techniques and many chemotherapy drugs have improved life expectancy of oncologic patients allowing us to observe late complications which present many years after the initial treatment.

Case Description: We present a unique case of a patient affected by acute lymphoblastic leukemia at the age of 6 years, treated with whole brain radiotherapy and intrathecal chemotherapy, developing meningiomatosis and leptomeningeal alterations as late complications and the interaction of these two entities caused a peculiar form of hydrocephalus without ventricular dilation. The diagnosis of pseudotumor cerebri was excluded due the postradio/chemotherapy development of meningiomatosis, not present in a previously head magnetic resonance imaging, that exerted compression to the Sylvian aqueduct causing intracranial hypertension with papillary stasis without ventricles enlargement due to brain stiffness. Moreover, a peculiar intraoperative rubbery consistency of brain parenchyma was detected strengthening this complex diagnosis.

Conclusion: At the best of our knowledge, this is the first report of obstructive hydrocephalus without ventricles dilation caused by brain stiffness related to late alterations of oncologic treatments. This report could be a guide for further complex patients diagnoses and for improving treatments efficacy.

Keywords: Hydrocephalus, Intrathecal chemotherapy, Meningiomatosis, Radiotherapy, Slit ventricle

INTRODUCTION

Life expectancy of oncologic patients, both adults and pediatric, has progressively improved with the development of modern treatments and diagnostics. Several sophisticated techniques and many chemotherapy drugs fit with the single patient’s needs. A positive consequence of these improvements is the emergence of long-term survivors. This has led to very long follow-ups that can teach us important lessons, as now we have the chance to observe late
complications which present many years after the initial treatment.

We present a unique case of a patient affected by acute lymphoblastic leukemia at the age of 6 years, treated with whole brain radiotherapy (WBRT) and intrathecal chemotherapy, who developed cerebral meningiomatosis and leptomeningeal alterations as late complications, and the interaction of these two entities caused a peculiar form of hydrocephalus without ventricular dilation.

CASE DESCRIPTION

Clinical presentation

A 35-year-old female was admitted to our institution because she had been suffering from progressive headaches for about 10 years – referred as debilitating in the past 6 months – which worsen with emotions like rage or concern, associated with blurred vision and tinnitus. Mini-mental state examination (MMSE) gave a score of 23.

Medical history

Her clinical history was positive for acute lymphoblastic leukemia, diagnosed in 1990 and treated with AIEOP 8703 protocol (cobalt radiotherapy [RT] in pediatric age and intrathecal chemotherapy with IV vincristine, IV daunorubicin, prednisone, methotrexate intrathecal, and IM L-asparaginase). In 1995, she was declared in complete remission. A right oophorectomy at the age of 9, caused by ovarian torsion, was also reported. In 2000, she underwent brain magnetic resonance imaging (MRI) that did not find pathological alterations. In 2011, she underwent *in vitro* fertilization, which unfortunately failed.

Preoperative imaging and instrumental assessment

The patient underwent in-depth investigation that documented cerebral meningiomatosis, characterized by 5 meningiomas, <3 cm each, located at the right cerebral middle fossa, at the border of the right tentorium, at the torcula, at the middle third of the superior sagittal sinus (SSS), and at the left Sylvian fissure; a T2-weighted brain MRI sequence documented a typical bilateral enlargement of optic nerve sheath, related to intracranial hypertension; of notice, ventricles were not enlarged, but they presented slit-like aspect [Figure 1]. Considering that the tentorial meningioma was compressing the Sylvian aqueduct, an MRI with cerebrospinal fluid (CSF) flowmetry was performed revealing an irregular pattern at the level of Sylvian aqueduct [Figure 2]; cerebral MR venography showed normal venous flow at the level of the SSS, due to the fact that the meningiomas were of little size and in T1-weighted gadolinium-enhanced images, there was no invasion of the SSS. Initially, the patient underwent medical therapy based on acetazolamide, without clinical benefit. Then, the patient underwent a 72 h spinal CSF drainage connected to LiquoGuard® system that showed elevated intracranial pressure (ICP) values, ranging between 13 and 21 mmHg/24 h with a mean value of 17 mmHg. Subsequently, she reported a transitory relief of symptoms with a corresponding decrease in ICP equal to a mean value of 13 mmHg. The patient was then addressed to the ophthalmologist, who documented a bilateral papillary stasis. At the beginning, a diagnosis of pseudotumor cerebri was made but it was object of controversies during multidisciplinary oncologic discussions. We repeated brain MRI scan, fundus oculi examination, and we performed PET scan with gallium to confirm the meningiomatosis hypothesis, with the plan to perform Gamma Knife treatment to control at least some of the meningiomas.

Clinical considerations and management

In our opinion, the patient was not affected by pseudotumor cerebri due to the normal global brain anatomy with good representation of the cisterns and sulci and the very high ICP values. Our hypothesis was that the absence of hydrocephalus was related to previous RT and intrathecal chemotherapy in pediatric age and that the tentorial meningioma causes compression of the Sylvian aqueduct; we elaborated two options for a multimodal treatment strategy: (a) surgical resection of the tentorial meningioma and Gamma Knife treatment to control the other lesions, with ventriculoperitoneal shunt (VPS) to be considered in a second surgical time after clinical postoperative evaluation and (b) VPS to resolve intracranial hypertension and radiosurgery to control mainly the tentorial meningioma and avoid further growth with associated compression of the brainstem. In agreement with the patient, we decided to perform the latter option. First, she underwent Gamma Knife treatment of the tentorial meningioma because the presence of the ventricular catheter could cause artifacts and negatively affect the accuracy of radiosurgery planning. The following day, with the guidance of the neuronavigation, we introduced the ventricular catheter at the right Kocher’s point and connected the distal catheter with a single route, without the typical skin interruption at the cervical level, to the peritoneum in the epigastric-suprahepatic site. A programmable valve with virtual off option was implanted and set at the 5th setting (145 mmH2O).

Postoperative imaging and clinical follow-up

The postoperative period was uneventful, a postoperative brain computed tomography scan [Figure 3] showed correct catheter positioning and stability of the ventricular diameters. The patient had a fast recovery with resolution of headache,
visual disturbance, and tinnitus. A postoperative fundus oculi and optical coherence tomography scan documented an improvement of papillary stasis and a significant improvement in the thickness of the optic nerve fibers.

After a 6-month follow-up, she is doing well, without clinical disturbance. MMSE gave a score of 25. She will continue to be followed for the other meningiomas and the VPS function with brain MRI every year and further Gamma Knife treatment of the lesions.
DISCUSSION

It is known that RT in children affected by cancer can cause structural changes in the brain, linked to cognitive late effects. These effects can clinically manifest as cognitive, behavioral, social, or hormonal deficits, months, or years after RT. Radiation injury causes cellular changes, including alterations in neuronal cytoarchitecture and loss of oligodendrocyte and oligodendrocyte precursor cell populations and impaired neurogenesis. In mice, brain structure changes after RT are consistent with observations in human survivors. During the developmental period, the entity of radiation damage to one brain region is difficult to assess globally, as the brain is an exceedingly interconnected organ, with interdependence mediated not only by neuronal connections but also related to cellular migration, vascular supply, physical restrictions, and other factors. As a result, radiation damage to one brain area can cause a global perturbation of the brain development.

The aim of intrathecal chemotherapy is to increase central nervous system drug exposure through direct CSF introduction, while reducing systemic drug toxicity. Intrathecal chemotherapy can cause potentially tragic effects. Chemical arachnoiditis, mediated by headache, back pain, vomiting, fever, meningism, and CSF pleocytosis, is common and potentially serious consequences. Far worse symptoms also have been described, such as cauda equina syndrome, seizures, paraplegia, papilledema, encephalitis, cranial nerve palsies, and myelopathy.

Gállego Pérez-Larraya et al. reported that 28% of patients affected by non-Hodgkin lymphoma and treated with intrathecal liposomal cytarabine developed moderate or severe neurotoxicity. In our opinion, the patient was not affected by pseudotumor cerebri due to good representation of the cisterns and sulci despite the presence of multiple meningiomas. Our hypothesis was that the tentorial meningioma caused compression to the Sylvian aqueduct, but this hypothesis was debated, as there was no ventricular dilation. After multidisciplinary oncological discussion, we focused on the clinical history, characterized by WBRT and intrathecal chemotherapy in pediatric age. We hypothesized that the RT could have caused the development of meningiomatosis; WBRT in pediatric age could have altered the normal compliance of the brain parenchyma, justifying its resistance to intracranial hypertension, which prevented the development of the typical radiological finding of the hydrocephalus, but not the indirect signs of the duplication of optic nerve sheaths on the brain MRI and stasis papillae at the fundus oculi examination. RT and the combination of intrathecal chemotherapy resulted in reactive ependymitis, with increased ventricular stiffness as well as reduced compliance. Clearly, the meninges had also been affected with an increase of pial stiffness. Our theory was confirmed during surgery by the fact that after dural opening, on coagulation of the brain parenchyma, usually made to avoid bleeding during catheter introduction, presented the peculiar characteristic of a rubbery consistence, and it was not possible to proceed further with bipolar forceps, forcing the surgeon to use a #11 scalpel to incise the parenchyma which was then coagulated, although it was bleeding less. At the best of our knowledge, this is the first report of such a condition, which we can define as slit-like hydrocephalus causing intracranial hypertension as a rare multifactorial complication of RT and intrathecal chemotherapy in pediatric age. Sylvian aqueduct compression caused by meningioma in a patient affected by meningiomatosis, which is in itself a challenging condition to manage, due to the young age of the patient. The present report, although unique, presents two main limitations linked to the documentation of the cerebral stiffness. First, we thought to perform a brain biopsy during the shunt procedure to evaluate histopathological alterations, but the patient did not give her consent to such an invasive sampling. Second, we discussed about the possibility to perform magnetic resonance elastography (MRE), which is an emerging technique to evaluate brain stiffness in neurodegenerative pathologies, to study meningiomas consistency and patients affected by hydrocephalus. However, MRE is an experimental technology, and there are conflicting data about the brain areas to evaluate and obtain pathognomonic results of brain stiffness. Moreover, the patient was treated 29 years before our observation, and it was impossible to have MRE data to compare with the brain consistency before the radiochemotherapy treatments. Finally, we do not have the possibility to perform MRE in our region, but we are planning to provide it and to follow-up the patient with MRE to study eventual further brain stiffness modification.

CONCLUSION

With the present report, we suggest an in-depth and complex diagnosis to justify a very rare case characterized by concomitant pathologies, multifactorial direct and indirect effects of the disease, and late radio/chemotherapy side effects. At the best of our knowledge, this is the first report of obstructive hydrocephalus without ventricles dilation caused by brain stiffness related to oncologic treatments. To achieve these complex diagnostic conclusions, we conducted a multidisciplinary and multicentric debate. This report could be a guide for further complex patients diagnoses and for improving treatments efficacy. MRE could represent a useful tool, if available, but further implementation and validation of the technique are required.
Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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How to cite this article: Umana GE, Raudino G, Alberio N, Inserra F, Giovinazzo G, Fricia M, et al. Slit-like hypertensive hydrocephalus: Report of a late, complex, and multifactorial complication in an oncologic patient. Surg Neurol Int 2020;11:219.