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Case Report

Paclitaxel combined with trastuzumab chemotherapy-related posterior reversible encephalopathy syndrome: A case report and literature review ☆,☆☆,★,★★

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ABSTRACT

Posterior reversible encephalopathy syndrome (PRES) in breast carcinoma is a rare disease in clinical practice that is often misdiagnosed and ignored. This study reported a case of a patient admitted to our hospital and discussed the clinical, imaging, and pathogenesis properties of the disease. We retrospectively analyzed the clinical data of this patient and reviewed the relevant literature. Imaging was used to diagnose PRES based on clinical findings, and clinical symptoms improved after discontinuation of the relevant drugs.

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Introduction

Posterior reversible encephalopathy syndrome (PRES) was first reported in 1996 [1]. Clinical characteristics include acute onset, with the main manifestations including mental abnormalities, headache, epilepsy, and vision loss. Posterior white matter damage, which is reversible, can be observed on MRI and CT; hence, the PRES concept was proposed. PRES is mostly linked to hypertensive encephalopathy, and the use of cytotoxic and immunosuppressive agents is mostly caused by blood-brain barrier disruption and vascular endothelial cell injury, leading to vasogenic edema [2]. With improved survival of cancer patients in China, increased attention has been paid to drug-related complications, and PRES cases caused by cyclosporine have been reported [3]. Following chemotherapy, PRES has been reported in breast cancer patients. This article presents a case study focusing on chemotherapy-induced posterior reversible encephalopathy syndrome (PRES), offering an in-depth analysis of its pathogenesis, clinical manifestations, and imaging characteristics.

Case report

A 55-year-old woman was admitted to the authors' hospital. Five months after right breast cancer surgery, she was hospitalized for walking instability and lethargy for 6 days following 7 chemotherapy courses. On April 19, 2020, the patient underwent subcutaneous gland resection of the right breast with nipple and areola preservation, I-stage prosthetic breast reconstruction, sentinel lymph node biopsy, and right axillary lymph node dissection at our hospital. Postoperative pathology revealed a grade II invasive ductal carcinoma with high-grade ductal carcinoma in situ (approximately 10%) in the right breast. Immunochemical tip: CK5/6(-), EGFR (+), ER(SP1) (-), PR(1E2) (about 15% +, weak), HER-2(+++), and Ki67(35%+). Postoperative staging revealed that the patient was pT1N1M0IIa stage HER-2 positive. Therefore, an AC scheme (pyrrobicin + cyclophosphamide (2019.04.05, 2019.05.18, 2019.06.10, 2019.07.01) was provided Subsequently, the patient developed granulocytopenia. However, it did not affect the overall treatment regimen and was administered sequentially with paclitaxel + trastuzumab (TH (2019.07.25, 2019.08.21). Six days prior (September 9, 2020), the patient presented with walking instability, unstable holding, slurred speech, lethargy, and other symptoms without obvious inducement. She was referred to our hospital for further consultation.

The patients denied the following: hypertension, diabetes, hepatitis, tuberculosis, and other infectious diseases, in addition to surgical trauma, exposure to epidemic water, and any history of allergy to specific foods or drugs. There were no negative personal habits or customs, and no special. family history to The appearance, memory, and calculation were decreased, speech was less clear, drinking water choking cough, presence of gag reflex, suspicious defect in the right visual field, less stable finger-nose test, less stable heel-shin test, clumsy rapid rotation of both hands, Babinskin sign (+), Chaddock sign (+), and Hoffmann sign (+). Routine blood tests, liver and kidney function, electrolytes, blood coagulation, D-dimer, myocardial enzyme spectrum, rheumatic immune antibody, 3 items of cardiac function, urine, and defecation routine revealed no abnormalities, and the electrocardiogram (ECG) was normal. Ambulatory blood pressure monitoring showed that systolic blood pressure fluctuated between 100 and 160 mmHg, whereas diastolic blood pressure fluctuated between 70 and 100 mmHg, with a significant increase in blood pressure at night. Echocardiography revealed a small pericardial effusion. Lumbar puncture was performed, the cerebrospinal fluid pressure was 150 mmH2O, the cerebrospinal fluid routine and biochemistry results were normal, and the 7 autoimmune antibodies were negative. Paraneoplastic antibodies, including oligoclonal bands (OB) and aquaporin 4 (AQP4), were negative. Seven blood midbody immune antibodies and paraneoplastic antibodies were negative. Mini-Mental State Examination (MMSE) scores were 28 points, Montreal Cognitive Assessment (MoCA) scores were 26 points, and the patient had demonstrated high school culture. On September 9, 2020, head CT (Fig. 1) [1] revealed low-density lesions in the occipital lobe, suspicious low-density lesions in the brainstem, and excluded cerebral infarction, whereas MRI and other examinations were recommended. Brain MRI on September 15, 2020 (Fig. 1) [2–6]: abnormal signal in the posterior part of the lateral ventricle, PRES? Demyelination? Magnetic resonance arteriovenous imaging (MRI) of the head and neck revealed no significant abnormalities.

The administration of paclitaxel and trastuzumab was discontinued in response to the development of Posterior Reversible Encephalopathy Syndrome (PRES). Subsequently, edaravin was administered for cerebral protection therapy, while measures were taken to maintain blood pressure, stabilize electrolyte levels, and provide rehabilitation therapy. The patient was then advised to change the chemotherapy regimen, but the patient refused. The patient and his family refused tumor-related treatment but were willing to undergo neurological treatment, and MRI was reexamined more than 2 months later. On November 30, 2020, MRI (Fig. 2) [1–3]was performed and compared with the old film on September 15, revealing the disappearance of new white matter lesions in the posterior part of the brain and the appearance of new occupying lesions in the basal ganglia, demonstrating enhancement, and the possibility of metastases was not excluded. The appearance, memory, and calculation were normal, the speech was clear, cranial nerve examination showed no obvious abnormality, synkinesis was coordinated, and no pathological signs were elicited. Changes in chemotherapy and head radiotherapy were recommended because of tumor progression; however, the patient and his family refused.

Discussion

The mechanism of posterior reversible encephalopathy syndrome (PRES) remains unclear and is linked to hypertension, renal failure, cytotoxic substance use, autoimmune diseases, and eclampsia. It is generally accepted that brain edema is caused by blood-brain barrier disruption after endothelial

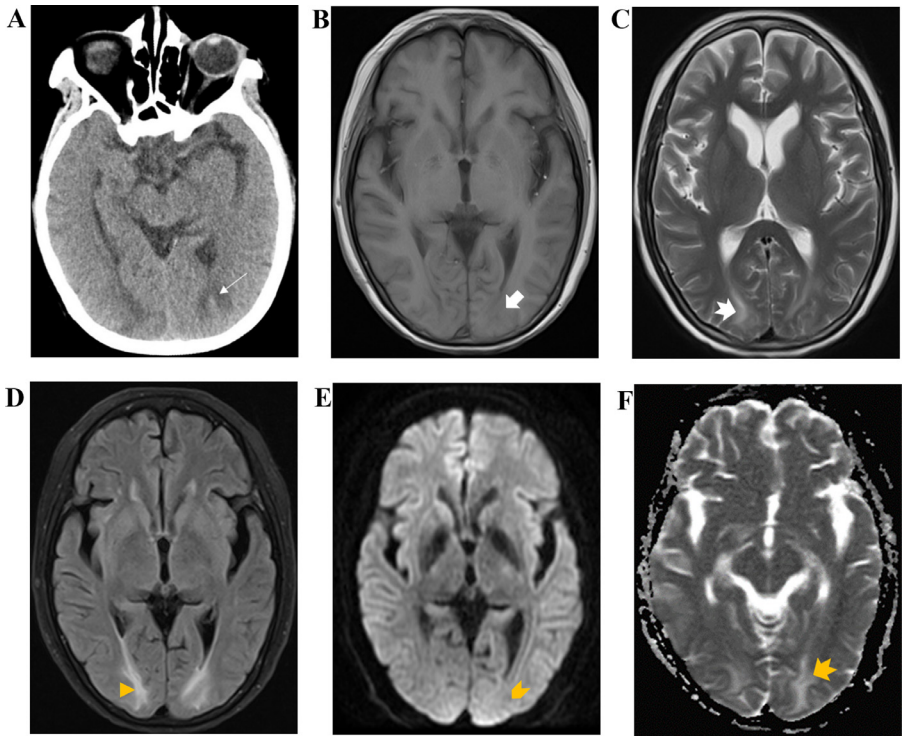

Fig. 1 – Image 1 shows low density in the posterior part of both lateral ventricles on CT (white thin arrow). Image2 demonstrates abnormalities behind both lateral ventricles on MRI (white thick arrow). Image 3 and 4 are T2flair; a high signal is seen at the occipital lobe (white dovetail arrow and yellow triangle). An isosignal can be shown in image5 (yellow pentagon). Image6 manifests a slightly higher signal (yellow dovetail arrow).

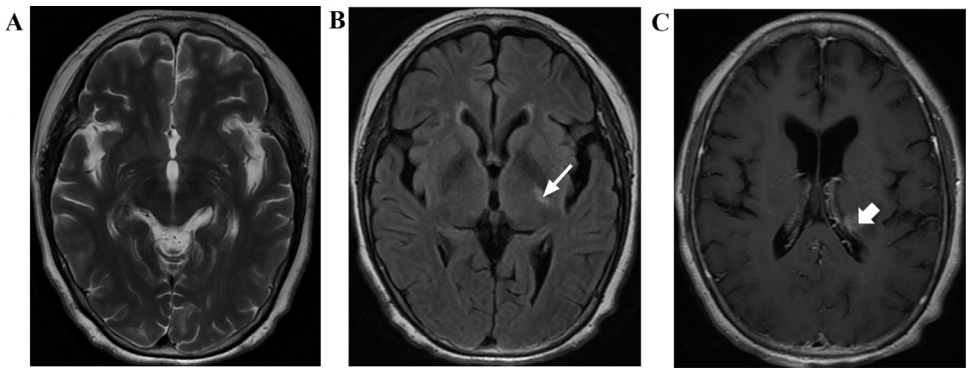

Fig. 2 – The lesions are disappeared from image 1 after treatment. Image 2 displays a high signal indicating metastasis (thin white arrow). Meanwhile, a suspicious metastatic lesion can be seen at the left basal ganglia of image 3 (white thick arrow).

injury of the vascular wall, and this process is reversible. On imaging, the lesions were widely distributed and multiple, often in the posterior part of the brain, such as parietal lobe, occipital lobe, temporal lobe cortex, and subcortical white matter, and most of them were bilateral symmetrical [4]. It is generally believed that hyperperfusion causes a sudden increase in arterial blood pressure that cannot be regulated by itself, causing cerebral hyperperfusion and blood-brain barrier disruption. In addition, circulatory factor overload is believed to cause abnormal endothelial cell function. Tumor necrosis factor-α (TNF-α), interferon-γ (INF-γ), interleukin 1 (IL-1), and other factors released by cytokines can increase blood vessel permeability, resulting in cerebral interstitial edema. Additionally, it has been demonstrated that immunosuppressive agents and cytotoxic drugs used after organ transplantation and chemotherapy are triggers [5–7]. This case was considered to be related to the use of chemotherapeutic drugs. Recent research indicates that the mechanism of paclitaxel-induced nerve injury is similar to that of platinum-based chemotherapeutic drugs: it destroys the mitochondrial function of sen-

sory neurons, thereby weakening mitochondrial respiratory function, reducing ATP yield, and causing nerve injury [8]. Carboplatin plus paclitaxel was reported to cause in one case of PRES [9]. Paclitaxel inhibits tumor vascular tissue growth and destroys intravascular growth factors, causing vascular damage [10]. Trastuzumab specifically binds to the extracellular membrane of the HER2 receptor and prevents the activation of intracellular tyrosine kinases. This mechanism is completed by suppressing the formation of HER2 receptors and inhibiting extracellular site shedding. Trastuzumab has also been shown to inhibit tumor angiogenesis by reducing VEGF production and activating anti-angiogenic factors. Trastuzumab may have an antiangiogenic effect and cause RPLS in patients treated with trastuzumab [11]. In 2006, an interesting study reported a relationship between PRES and bevacizumab [12]. Kaneda et al. reported a case after receiving trastuzumab treatment. Trastuzumab has been associated with hypertension in clinical trials. Although its incidence is low (approximately 10%), PRES is caused by blood pressure instability [13]. A systematic analysis of chemotherapy-induced PRES was conducted in 2016. Most of these cases occurred during the first week of chemotherapy. This study reported 30 PRES cases caused by platinum drugs (platinum, carboplatin, and oxaliplatin), but no cases were caused by trastuzumab [14]. In 2018, Abughanimeh et al. also reported a case of reversible posterior white matter lesions caused by trastuzumab, but the mechanism was unclear, and PRES caused by this drug is uncommon at present [15].

Conclusion

Combined with this case, PRES caused by the AC-TH chemotherapy regimen could be linked to blood pressure fluctuations or paclitaxel nervous system loss. Because of the scarcity of such reports, verification requires numerous case reports and animal experiments. The specific mechanism of PRES caused by these drugs remains unclear and requires further investigation. Simultaneously, in clinical practice, doctors should pay more attention to blood pressure variations and the timely administration of antihypertensive drugs.

Patient consent

The patient in this article was aware of the case in the case report and consented to the use of case data and imaging data.

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