Case Report

Transient Cortical Blindness during Chemotherapy (PVB) for Ovarian Germ Cell Tumor

Tarinee Manchana MD*, Nakarin Sirisabya MD*,
Ruangsak Lertkhachonsuk MD*, Damrong Tresukosol MD*

** Gynecologic Oncology Unit, Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University*

A 17 year-old female with stage IIIc endodermal sinus tumor of the ovary developed transient cortical blindness and severe hypertension after 5 cycles of PVB regimen consisting of cisplatin, vinblastine and bleomycin. Clinical and radiological findings were compatible with Posterior LeukoEncephalopathy (PLE). Her visual acuity and blood pressure completely recovered within a few days after supportive treatment with antihypertensive drug. This condition is unpredictable but it can be reversible without long term sequelae. Most reports suggested that this rare toxicity was from cisplatin therapy. However, the exact pathophysiogenesis of this condition was not known precisely. Prompt reduction in blood pressure and withdrawal of immunosuppressive agents might lead to rapid reversal of this syndrome and prevent permanent brain damage.

Keywords: *Cortical blindness, Posterior leukoencephalopathy, Chemotherapy, Germ cell tumor*

J Med Assoc Thai 2006; 89 (8): 1265-8
Full text. e-Journal: *http://www.medassocthai.org/journal*

Combination of chemotherapy consisted of cisplatin, vinblastine and bleomycin (PVB regimen) for treatment of advanced malignant germ cell tumor of the ovary was a clinically important treatment modality[1]. However, the combination of cisplatin, vinblastine and bleomycin may result in serious toxic complications, including cortical blindness and seizure[2]. The term "cortical blindness" means total loss of vision with a normal fundoscopic examination and normal papillary response due to a lesion involving the bilateral occipital lobes[3]. Cortical blindness following chemotherapy (with PVB regimen) was first reported in a patient with embryonal cell carcinoma[4]. The patient in the present article was the second reported case having cortical blindness and hypertension in an ovarian germ cell tumor with PVB regimen. Long term follow-up for this toxicity was also reported.

Case Report

A 17-year old woman presented at a private hospital in April 2002 with pelvic pain and a palpable abdominal mass for one week. She underwent an exploratory laparotomy with left salpingooohorectomy and tumor debulking. A large cystic ovarian mass (diameter 18 centimeters), intact capsule that was densely adhered to the cul-de-sac, urinary bladder, omentum and a 3 centimeters nodular mass on liver serosa were found. Pathological diagnosis was endodermal sinus tumor (Stage IIIc). She was referred to King Chulalongkorn Memorial Hospital for adjuvant chemotherapeutic treatment. Chemotherapy regimen consisting of cisplatin, bleomycin and vinblastine were planned for 6 cycles. Serum alpha fetoprotein before starting chemotherapy was 15,981 IU/ml (normal range 0-10 IU/ml).

The first cycle was started from May 18 to 22, 2002; intravenous cisplatin 20 mg on day 1-5, intravenous vinblastine 9 mg (6 mg/m^2) on day 1 and intravenous bleomycin 15 units (10 units/m^2) on day 1 and day 5. The following cycle was given in the next three weeks. Declining of serum alpha fetoprotein was found (6 Jun, 2002 = 2,448.9 IU /ml; 18 Jul, 2002 = 18.1 IU/ml; 3 Sep, 2002 = 3 IU/ml).

Four days after completion of the fifth cycle, she presented with sudden loss of vision, nausea, vomiting and severe headache. Initial physical examination revealed good consciousness, blood pressure

Correspondence to : Manchana T, Gynecologic Oncology Unit, Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand. Phone: 0-2256-4241, Fax: 0-2254-9292, E-mail: T_manchana@hotmail.com

was 160/110 mmHg and normal light perception without abnormal visual field defect. Decreased deep tendon reflex and absent plantar reflex were also detected. Complete blood count and serum biochemistry including calcium, magnesium, total protein, glucose and creatinine were within normal limits. However, serum sodium, potassium and chloride were 2.8, 128 and 87mEq/L, respectively.

An emergency Magnetic Resonance Imaging (MRI) of the brain showed increased signal intensity in the white matter of both occipitoparietal lobes (Fig. 1). Nevertheless, the magnetic resonance venography appeared normal. During hospitalization, her blood pressure was 150-160/100-120 mmHg then an antihypertensive drug was given. Her visual acuity improved gradually and completely recovered within the next three days. The antihypertensive drug and the sixth cycle of PVB were cancelled two weeks later. She was followed regularly every three months in the first two years and then every six months later. On September 2005, at the 41 months follow-up, there was no long term sequelae detected and there was no evidence of disease with normal serum alpha fetoprotein level.

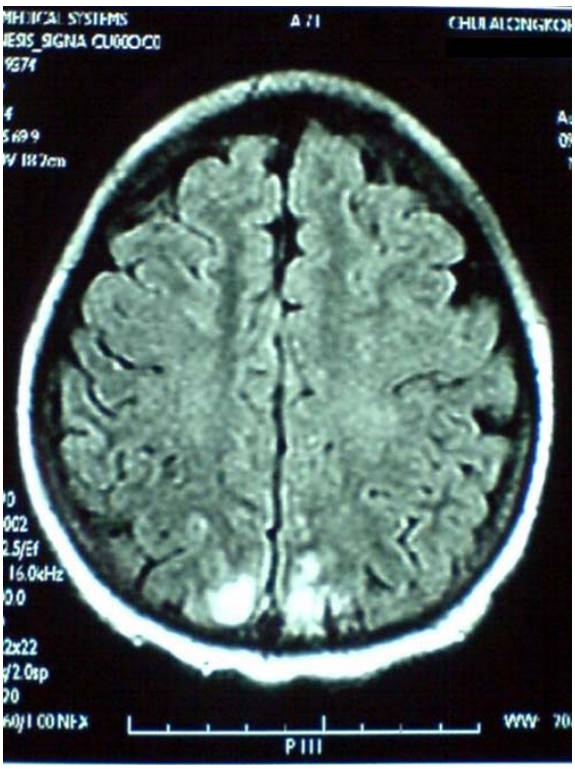

Fig. 1 Magnetic resonance imaging (MRI) of brain shows increasing signal intensity in white matter of both occipitoparietal lobes

Discussion

The reported patient presented with cortical blindness and hypertension. All laboratory tests were within normal limits except mild hyponatremia and hypokalemia. These might be from severe nausea and vomiting. Brain MRI showed increased density in the white matter of both occipitoparietal lobes. This finding was compatible with PLE and could present with various manifestations such as headache, altered sensorium, confusion, seizure and visual disturbance[5]. Known causes of the PLE were hypertensive encephalopathy, eclampsia, renal failure, immunosuppressive agents and cytotoxic drugs such as cisplatin, vincristine, cyclosporine A, and erythropoietin[5-8]. However, most studies suggested that hypertensive encephalopathy was the most common cause of PLE.

Review of the literature found only six cases of PLE that developed in germ cell tumor patients who received combination chemotherapy composed of cisplatin, vinblastine and bleomycin[2,4,9-12]. However, only three cases (including this patient) were demonstrated in patients with germ cell tumor of the ovary[2,12]. The first case presented with hypertension, cortical blindness and seizure. The second case presented with hypertension and seizures. Evidently, hypertension was the first presenting symptom and could be detected in all cases. Early detection of hypertension and prompt reduction might reduce this serious complication. Moreover, this was the first study that demonstrated the long term follow-up. It was confirmed that if the patient received adequate treatment, PLE might be reversible without long term sequelae.

Most reports suggested that chemotherapy induced PLE might be associated with cisplatin[13-15]. However, vinblastine overdose was reported to produce seizures in one study but there was no reported study about ophthalmologic toxicity from bleomycin and vinblastine[11,16]. Cisplatin has been known to have many adverse effects such as nausea and vomiting, renal dysfunction, myelosuppression and neurotoxicity. The incidence of neurotoxicity was 49-92% and included peripheral neuropathy, auditory impairment and visual disturbance[15]. Previous cisplatin kinetic study demonstrated that a platinum concentration in brain and cerebrospinal fluid was minimal. Alteration of blood brain barrier might enhance cisplatin accumulation in the central nervous system and produced neurotoxicity[11]. However, the exact pathophysiogenesis was not known precisely.

Current combined chemotherapy regimen has improved the overall survival of patients with germ cell

tumor but there were many toxic complications including this rare complication. Although it seemed to be unpredictable and serious, it could be reversible without any sequelae. Prompt reduction in blood pressure and withdrawal of immunosuppressive agents might lead to rapid reversal of this syndrome and prevent permanent brain damage.

References

1. Williams SD, Blessing JA, Moore DH, Homesley HD, Adcock L. Cisplatin, vinblastine, and bleomycin in advanced and recurrent ovarian germ-cell tumors. A trial of the Gynecologic Oncology Group. Ann Intern Med 1989; 111: 22-7.
2. Young DC, Mitchell A, Kessler J, Christman JE. Cortical blindness and seizures possibly related to cisplatin, vinblastine, and bleomycin treatment of ovarian dysgerminoma. J Am Osteopath Assoc 1993; 93: 502-4.
3. Merimsky O, Loewenstein A, Chaitchik S. Cortical blindness-a catastrophic side effect of vincristine. Anticancer Drugs 1992; 3: 371-3.
4. Berman IJ, Mann MP. Seizures and transient cortical blindness associated with cis-platinum (II) diamminedichloride (PDD) therapy in a thirty-year-old man. Cancer 1980; 45: 764-6.
5. Garg RK. Posterior leukoencephalopathy syndrome. Postgrad Med J 2001; 77: 24-8.
6. Byrd RL, Rohrbaugh TM, Raney RB Jr, Norris DG. Transient cortical blindness secondary to vincristine therapy in childhood malignancies. Cancer 1981; 47: 37-40.
7. Jarosz JM, Howlett DC, Cox TC, Bingham JB. Cyclosporine-related reversible posterior leukoencephalopathy: MRI. Neuroradiology 1997; 39: 711-5.
8. Delanty N, Vaughan C, Frucht S, Stubgen P. Erythropoietin-associated hypertensive posterior leukoencephalopathy. Neurology 1997; 49: 686-9.
9. Cohen RJ, Cuneo RA, Cruciger MP, Jackman AE. Transient left homonymous hemianopsia and encephalopathy following treatment of testicular carcinoma with cisplatinum, vinblastine, and bleomycin. J Clin Oncol. 1983; 1: 392-3.
10. Crispino S, Pizzocaro G, Solero CL, Rodari A, Monfardini S. Transient left homonymous hemianopsia during treatment of testicular carcinoma with cisplatinum, vinblastine, and bleomycin. Chemioterapia 1984; 3: 337-9.
11. Hitchins RN, Thomson DB. Encephalopathy following cisplatin, bleomycin and vinblastine therapy for non-seminomatous germ cell tumour of testis. Aust N Z J Med 1988; 18: 67-8.
12. Sueblinvong T,Noophun P, Pataradool K, Suwanwela N, Phanthumchinda K, Tresukosol D. Posterior leukoencephalopathy following cisplatin, bleomycin and vinblastine therapy for germ cell tumor of the ovary. J Obstet Gynaecol Res 2002; 28: 99-103.
13. Ito Y, Arahata Y, Goto Y, Hirayama M, Nagamutsu M, Yasuda T, et al. Cisplatin neurotoxicity presenting as reversible posterior leukoencephalopathy syndrome. Am J Neuroradiol 1998; 19: 415-7.
14. Pippitt CH Jr, Muss HB, Homesley HD, Jobson VW. Cisplatin-associated cortical blindness. Gynecol Oncol 1981; 12: 253-5.
15. Al-Tweigeri T, Magliocco AM, DeCoteau JF. Cortical blindness as a manifestation of hypomagnesemia secondary to cisplatin therapy: case report and review of literature. Gynecol Oncol 1999; 72: 120-2.
16. Conter V, Rabbone ML, Jankovic M, Fraschini D, Corbetta A, Pacheco C, et al. Overdose of vinblastine in a child with Langerhans'cell histiocytosis: Toxicity and salvage therapy. Pediatr Hematol Oncol 1991; 8: 165-9.

ภาวะตามองไม่เห็นระหว่างให้ยาเคมีบำบัดในผู้ป่วยมะเร็งรังไข่ชนิด Endodermal sinus tumor

ธาริณี แม่นชนะ, นครินทร์ ศิริทรัพย์, เรืองศักดิ์ เลิศขจรสุข, ดำรง ตรีสุโกศล

ผู้ป่วยอายุ 17 ปี วินิจฉัยว่าเป็นมะเร็งรังไข่ชนิด endodermal sinus tumor ระยะที่ 3 มีอาการตามองไม่เห็นอย่างเฉียบพลันและมีความดันโลหิตสูง ภายหลังได้รับยาเคมีบำบัดเสริมครั้งที่ 5 ซึ่งประกอบด้วย Cisplatin, vinblastine และ bleomycin อาการและภาพถ่ายด้วยคลื่นแม่เหล็กไฟฟ้า (MRI) เข้าได้กับภาวะ Posterior leuko-encephalopathy (PLE) ความสามารถของการมองเห็นของผู้ป่วยและความดันโลหิตเป็นปกติภายใน 2-3 วัน หลังจากให้การรักษาแบบประคับประคองโดยให้ยาลดความดันโลหิต รายงานส่วนใหญ่มีความเห็น ว่าภาวะนี้น่าจะเกิดจาก Cisplatin แต่อย่างไรก็ตามกลไกการเกิดโรคที่แท้จริงยังไม่ทราบแน่ชัด PLE เป็นภาวะที่เกิดขึ้นโดยไม่สามารถทราบล่วงหน้า แต่เป็นภาวะที่สามารถหายได้และไม่พบผลข้างเคียงระยะยาว การรักษาภาวะความดันโลหิตสูงอย่างทันท่วงทีและการหยุดให้ยาเคมีบำบัดอาจทำให้โรคนี้หายอย่างรวดเร็วและป้องกันการทำลายของเนื้อสมองอย่างถาวร