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Primary Cerebellar Lymphoma in an Immunocompetent Host: A Case Report

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Abstract **Primary central nervous system lymphoma (PCNSL) has been rarely found, viz. it accounts for 2- 4 % of all primary brain tumors. Furthermore, PCNSL of the cerebellum is much more rarely reported than that of the cerebrum, particularly in immunocompetent patients. Herein we presented a case of Non-Hodgkin's lymphoma (NHL) confining within the cerebellum in an immunocompetent Thai man. He was a 62-year-old Thai patient who complained of gradually progressive headache and ataxia for two months without fever or weight loss. The physical examination found only ataxic gait, positive finger-to-nose test of the right side, no peripheral lymphadenopathy, and no hepatosplenomegaly. The computerized tomography (CT) and the brain's magnetic resonance imaging (MRI) showed a 2.5x3.0 cm. mass in the left cerebellum with obstructive hydrocephalus. The chest and abdomen CT showed only a few sub-centimeter lymph nodes in the chest and abdomen. The HIV antigen/antibody was tested negative. He was treated with the operation; the tumor mass was nearly entirely removed. The microscopic pathology of the mass resected was diffuse large cell lymphoma, but its specific immunophenotype could not be concluded because the study was not performed. Six courses of CHOP chemotherapy without high-dose methotrexate, and rituximab administration were the further treatment. He could tolerate chemotherapy well and survive without residual cerebellar mass. Finally, he was regularly treated with aspirin, simvastatin, and phenytoin and clinically followed for years till the date of this report writing.** ***(Thai Cancer J 2021;41:90-97)***

Keywords: Non-Hodgkin's lymphoma, Cerebellum

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มะเร็งน้ำเหลืองปฐมภูมิที่สมองน้อยในผู้ที่ภูมิคุ้มกันปกติ: รายงานผู้ป่วย 1 ราย

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บทคัดย่อ มะเร็งน้ำเหลืองปฐมภูมิที่ระบบประสาทส่วนกลาง หรือ primary central nervous system lymphoma เป็นโรคที่พบได้น้อยเพียง ร้อยละ 2-4 ของเนื้องอกปฐมภูมิของสมองทั้งหมดโดยเฉพาะมะเร็งน้ำเหลืองปฐมภูมิที่ส่วนสมองน้อย หาได้ยากมากเมื่อเทียบกับมะเร็งน้ำเหลืองปฐมภูมิที่พบที่สมองใหญ่ โดยเฉพาะในผู้ป่วยที่ภูมิคุ้มกันปกติ ในที่นี้จะนำเสนอผู้ป่วยชายไทยอายุ 62 ปี ภูมิคุ้มกันปกติ เป็นมะเร็งน้ำเหลืองที่สมองน้อย ชนิดที่ไม่ใช่ฮ็อดจกิ้น ผู้ป่วยมีอาการปวดศีรษะร่วมกับอาการเดินเซ มากขึ้นเรื่อย ๆ อย่างช้า ๆ ภายในเวลา 2 เดือน ไม่มีไข้ น้ำหนักไม่ลด ตรวจร่างกาย พบเพียงอาการเดินเซ ตรวจ finger-to-nose ให้ผลบวกทางซีกขวา ไม่พบต่อมน้ำเหลืองโตตับและม้ามไม่โต ตรวจสมองด้วยการเอกซเรย์คอมพิวเตอร์และคลื่นสนามแม่เหล็กไฟฟ้า (magnetic resonance imaging : MRI) พบเนื้องอกขนาด 2.5x3.0 ซม. ที่สมองน้อยซีกซ้าย ร่วมกับภาวะโพรงสมองคั่งน้ำแบบอุดกั้น ส่วนเอกซเรย์คอมพิวเตอร์ของทรวงอกและช่องท้อง พบต่อมน้ำเหลืองขนาดเล็ก ๆ อีกเล็กน้อย ตรวจเชื้อ HIV ไม่พบทั้ง แอนติเจนและแอนติบอดี ให้การรักษาก้อนเนื้องอกโดยการผ่าตัดได้เกือบทั้งหมด ซึ่งผลชิ้นเนื้อพบว่าเป็นมะเร็งน้ำเหลืองแบบ diffuse large cell แต่ไม่สามารถระบุรายละเอียดชนิดย่อยกว่านั้นได้เพราะไม่ได้ทำการตรวจย้อม ด้วยวิธี immunophenotyping ทำการรักษาต่อด้วยยาเคมีบำบัดชุด CHOP 6 ครั้ง ร่วมด้วยยา rituximab โดยไม่มี methotrexate ในขนาดสูง ผู้ป่วยสามารถทนยาเคมีบำบัดได้ดี รวมทั้งมีคุณภาพชีวิตที่ดีขึ้นโดยไม่เหลือร่องรอยของโรคในส่วนของสมองน้อยอีก สุดท้ายผู้ป่วยได้รับการรักษาต่อเนื่องด้วยยา aspirin, simvastatin และ phenytoin อีกทั้งยังมารับการตรวจรักษาอย่างสม่ำเสมอจนกระทั่งปัจจุบัน *(วารสารโรคมะเร็ง 2564;41:90-97)*

คำสำคัญ: มะเร็งน้ำเหลืองชนิดไม่ใช่ฮ็อดจกิ้น , สมองน้อย

Introduction

The central nervous system (CNS) may be involved by Non-Hodgkin's lymphoma (NHL), one of common neoplastic diseases of the lymphoid tissue. It can be one part of disseminated disease, secondary CNS lymphoma, or can be found as the only one site of the extra-nodal NHL, the so called primary central nervous system lymphoma (PCNSL) which is responsible for less than 3% of all extra-nodal NHL[1] meanwhile it accounts for 2-4% of all primary brain tumors[2,3]. Although PCNSL is generally considered the rare entity, its incidence is found gradually increased in the elderly, aged more than 65 years although it remains stable in other age groups and it can be found in either immunocompetent or immunocompromised hosts[4]. Its clinical and neurological presentations are non-specific, vary greatly depending on the location of primary lesion[5], around 50-70% may have personality change and cognitive impairment and less than half of cases may have symptoms and/or signs of increased intracranial pressure such as headache and vomiting[6]. PCNSL

generally has low tendency for systemic dissemination[7] but it rapidly progresses and has overall survival of 1.5 months if untreated compared with 2.2 months of the secondary CNS lymphoma after the diagnosis[8]. The most common location of PCNSL within the brain is the cerebrum especially the frontal region[9] and other less common sites include the basal ganglia, corpus callosum, and fornix[10]. In contrast, PCNSL confining within the cerebellum in immunocompetent patients has been occasionally reported worldwide[5,11-15] including in Thailand[16]. Herein we reported another case of PCNSL diagnosed in the cerebellum of a Thai patient who could survive more than five years after the diagnosis.

Case Report

A 62-year-old Thai man complained of gradually progressive headache, occasional vomiting and ataxia for two months. He had no fever, no weight loss, and no convulsion. The general physical examination revealed BP 180/95 mmHg, the temperature 37.1 degree Celsius, no palpable peripheral lymphadenopathy and no hepatosplenomegaly. The neurological examination showed ataxic gait and impaired finger-to-nose test of the right side but no nystagmus.

The blood investigations included: Hct 44.0 %, WBC 12,500/mm^3, N 82.9%, L 11.6%, M 5.2%, platelet 377,000/mm^3, FBS 98.0 mg%, BUN 15 mg%, creatinine 0.89 mg%, AST 36 U/L, ALT 44 U/L, alkaline phosphatase 64 U/L (normal 35-110), albumin 4.3 g%, globulin 3.1 g%, Ca 9.7mg%, P 4.3 mg%, LDH 397 U/L (normal 240-480), HIV antigen /antibody, anti-HCV and HBsAg-all negative, CA 19-9 8.4 U/mL (normal 0-37), CEA 0.63 ng/mL (normal 0-15), alpha fetoprotein 2.41 ng/mL (normal 0-12)

The computerized tomography (CT) of the brain revealed a 2.5x3.0 cm hypodense mass in the left cerebellar hemisphere with pressure effect and shift of the fourth ventricle to the right side and the obstructive hydrocephalus, low grade tumor is possible. And the magnetic resonance imaging (MRI) of the brain confirmed the ill-defined mass occupying at the left cerebellum which showed low signal intensity on T1W, isosignal intensity on T2W, restriction on density DW1 and homogeneous enhancement on post Gd, measured about 3.1x4.1x2.4 cm. The medial portion of this mass showed low signal intensity on T2W, DWI and susceptibility artifact on SWI, suspected of hemorrhage. Pressure effect of this mass to the 4^{th} ventricle and the brain stem was seen. Obstructive hydrocephalus was noted. Impression: Suspected of bleeding tumor, possibly primary brain tumor or single brain metastasis at the left cerebellum, causing pressure effect to the 4^{th} ventricle and brain stem.

The suboccipital craniectomy with ventriculostomy was performed and the nearly entire tumor mass could be removed. The microscopic pathology of the tumor was found to be non-Hodgkin's lymphoma (NHL), diffuse

large cell type. However the immunophenotyping study was not performed, hence specific subtype of NHL could not be stated.

The CT of the chest and the abdomen showed few small subcentimeter lymph nodes at the AP window, pre-carinal and peri-aortic regions, no hepato-splenomegaly. The diagnosis of primary cerebellar NHL was finally concluded. After the tumor mass was nearly totally removed, six courses of intravenous chemotherapy regimen containing cyclophosphamide, doxorubicin, vincristine and prednisolone (CHOP), without high-dose methotrexate and rituximab administration were sequentially added. He could tolerate the regimen well. After treatments, the patient could walk much better whereas the residual tumor mass completely disappeared on the new CT scan. He was followed with regular oral medications including aspirin, simvastatin, and phenytoin. He could walk without headache, ataxia or convulsion. No relapse of a tumor mass at the old location or new lesion on the successive CT brain scans was detected, peripheral lymph nodes or hepatosplenomegaly were not found on the physical examination and the serum LDH was within the reference level thorough the long course of follow-up. He was still alive up to five years after the diagnosis till the date of this report written.

Discussion

The cerebellar ataxia in our case was presumed to be directly associated with the tumor mass of lymphoma in the cerebellum itself, it is not just the paraneoplastic cerebellar degeneration due to various auto-antibodies against antigens on neurological cells that are also presented by tumor cells. It has been hardly found in a case of NHL of the stomach[17] and the neck lymph node[18]. And the patient clinically had good recovery after the tumor mass removal followed by systemic chemotherapy. And although the immunophenotyping study was not performed in our case, NHL was much more likely than Hodgkin's lymphoma because almost all cases of primary cerebellar lymphoma are NHL, opposed to Hodgkin's lymphoma that has been hardly found in the cerebellum[19,20].

For PCNSL, patients mostly were found to have hyper- or iso-attenuated lesions on the computerized tomography while our patient showed hypodense lesion. In contrast, on MRI, our case was found to have the lesion with low signal intensity on T1 weighted, and isosignal intensity on T2 weighted with homogeneous enhancement that was consistent with the findings of lymphoma mass[21]. And in immunocompetent patients, 70 % of cases with PCNSL have single lesion on imaging[22]. However, the definite diagnosis always needs tissue pathology of the lesion that is considered the standard for the diagnosis of PCNSL[23]. In most cases of PCNSL, the pathology is diffuse large B-cell lymphoma, opposed to T cell lymphoma that has been rarely found[24-28]. With

the chemotherapy, the median survival of the patients with PCNSL was found increased from 12.5 months in 1970 to 26 months in 2010 particularly in the group with less than 70 years of age[29]. Our patient could survive up to five years after the operation and chemotherapy although the regimen contained only CHOP, not including high-dose methotrexate[30] or rituximab[31].

In the study of 87 patients with PCNSL in Southern Thailand, only one had a lesion in the cerebellum. And their overall median survival was 7 months whereas their 1-, 2-, and 5-year survival rates were 29%, 21.5%, and 4.6%, respectively. In addition, the median survival in the palliative group was 1 month compared with 2, 7 and 15 months in the chemotherapy, brain radiotherapy and the combined treatment group, respectively[32]. In another study, the median survival was 17 months for a group of chemotherapy which consisted of high-dose methotrexate with/without cytarabine[33]. Our case seemed to survive quite long after treatment with CHOP regimen. However it needs further controlled studies before making any conclusion.

Conclusion

A case of diffuse large cell lymphoma exclusively confining in the cerebellum in an immunocompetent Thai man was reported. It is a very rare entity and found far less commonly than lymphoma in the cerebrum. The tumor mass was nearly entirely removed with surgery followed by six cycles of CHOP chemotherapy without high-dose methotrexate. He was able to walk with normal gait and survive up to five years until this report was written.

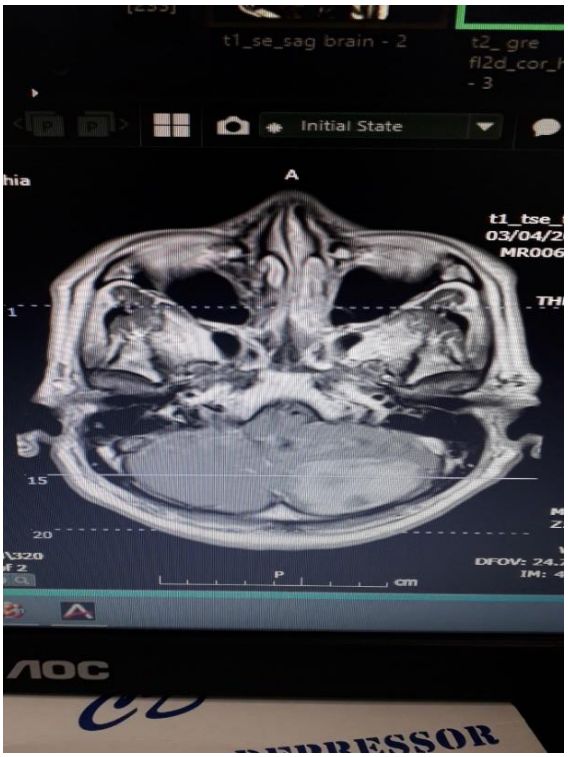

Figure 1 The imaging showed a solitary mass occupying a half of the left cerebellar hemisphere.

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