Primary Cerebellar NonHodgkin's Lymphoma in Non-HIV Patient: The Rare Extranodal Lymphoma.

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Abstract:

Primary cerebellar nonHodgkin's lymphoma (NHL) in immuno-competent patient is very rare disease. Here we report one case of isolated NHL in the cerebellum. The patient was a Thai man, 56 years of age. He gradually developed progressive vertigo, headache and truncal ataxia for 2 weeks. He also had occasional vomiting, but no fever or weight loss. Physical examination confirmed that he had truncal ataxia and dysmetria, no other lymph node or hepatosplenomegaly. With the computerized tomography of the brain, a solitary cerebellar tumor was demonstrated and it was nearly all excised under general anesthesia. The pathology was diffuse large B cell lymphoma. Bone marrow study was normal. He was diagnosed as primary isolated cerebellar nonHodgkin's lymphoma. After operation, he was treated with irradiation, systemic chemotherapy plus intrathecal cytosine arabinoside. At 6-month follow-up, he could walk with limping gait and still survived 11 months when this reported was performed.

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บทคัดย่อ

Primary cerebellar nonHodgkin's lymphoma (NHL) ในคนที่ภูมิคุ้มกันปกติ เป็นโรคที่พบได้น้อยมาก ต่อไปนี้เป็นรายงานผู้ป่วย 1 ราย เป็นชายไทย อายุ 56 ปี มีอาการเวียนศีรษะ ปวดศีรษะ บ้านหมุน เดินเซ 2 สัปดาห์ อาการค่อยเป็นค่อยไป ร่วมกับอาการอาเจียนเป็นครั้งคราว อาการเป็นมากขึ้นตามลำดับ ผู้ป่วยไม่มีไข้ น้ำหนักไม่ลด ตรวจร่างกายพบว่า มี truncal ataxia และ dysmetria ไม่พบต่อมน้ำเหลืองหรือตับม้ามโต เอกซเรย์คอมพิวเตอร์สมองพบ ก้อนเนื้อ 1 ก้อนที่ cerebellum เมื่อตัดก้อนออกมาตรวจก็พบว่าเป็น diffuse large B cell lymphoma ตรวจไขกระดูกพบว่าปกติให้การวินิจฉัยว่าเป็น primary isolated cerebellar non-Hodgkin's lymphoma หลังผ่าตัด รักษาด้วยการฉายแสงที่ตำแหน่งเนื้องอก และให้ยาเคมีบำบัดทางหลอดเลือด และ cytosine arabinoside เข้าไขสันหลัง ภายใน 6 เดือนต่อมา ผู้ป่วยพอเดินได้หลังได้รับการฟื้นฟู และอยู่รอดนานถึง 11 เดือนนับถึงวันที่รายงานนี้

Introduction

NonHodgkin's lymphoma (NHL) is a malignant neoplasm of lymphoid tissue that does not contain Reed-Sternberg's cell. It usually originates from lymphatic organs. However around 25-40% can occur in other tissues, normally lacking lymphoid cells, so called extranodal lymphoma[1]. The most common extranodal site is the gastrointestinal tract whereas the other areas such as skin, orbit, uterus, testis[2] including central nervous system are unusual sites. Focus on primary CNS lymphoma, it is much more common in the immunocompromized than in the immunocompetent hosts and in most cases, it always originates from supratentorial part of the brain and it has tendency to be solitary more than multiple lesions. The common pathology is diffuse large B cell. Among various sites of CNS, it is extremely rare to find primary isolated NHL originating from the cerebellum. After the first case of Hodgkin's disease of the cerebellum had been reported in 1968[3], then non-Hodgkin's lymphoma of the cerebellum was occasionally reported[4-7]. So far, it has still been rare disease. Here is one case.

Case Report

A 56-year old man presented with gradual onset of progressive vertigo and truncal ataxia for 2 weeks. During this period, he had also headache, vertigo, vomiting and limping gait. However he had no constitutional symptoms such as fever or weight loss. His vision and hearing were not disturbed. The family members had never experienced any cerebellar disease. On physical examination, blood pressure 110/70 mmHg, pulse rate 67/min., he had normal level of consciousness but could not walk. Difficulty of speaking, truncal ataxia and dysmetria of the left limbs were revealed. The finger-to-nose test was impaired on the left side. The fundoscopic examination appeared normal. He had no fever, no nystagmus, no generalized lymphadenopathy and no hepatosplenomegaly. His basic laboratory tests consisting of CBC, urinalysis, BUN, creatinine, uric acid, serum calcium, magnesium, phosphorus, FBS and liver function test, were within normal ranges, except LDH 682 (240-480 U/L), total serum cholesterol 286 mg/dL. The chest film, the ultrasonography and the computerized tomography of the whole abdomen were

unremarkable.

HIV antibody, HIV antigen and HBsAg were repeatedly negative as well as anti-HCV antibody.

The computerized tomography of the brain showed a mixed low and isodense mass at right cerebellum and, with the contrast medium, the study showed inhomogeneous enhancement of the mass, size about 4.5x4.6x3.0 cm^3, fluid or fat collection at subgaleal region and mild degree of obstructive hydrocephalus. The preoperative diagnosis of brain tumor with mild hydrocephalus was proposed.

Under the general anesthesia, the right suboccipital craniectomy was performed and the mass at the right cerebellum was accessed and nearly all excised.

The pathological diagnosis was diffuse large B cell lymphoma (LCA+, CD20 +, CD3-).

His bone marrow aspiration and biopsy were normal, no involvement of NHL with decreased iron storage.

He was definitely diagnosed as the primary isolated cerebellar non-Hodgkin's lymphoma, stage IE.

After he recovered from the operation, he was treated with brain irradiation and followed by many courses of systemic chemotherapy which consisted of intravenous dexamethasone for 4 days, vincristine and high dose methotrexate 2 gram plus leucovorin rescue and finally intrathecal cytosine arabinoside 15 mg injection.

Six months after the operation, he regularly followed the training program for ambulation. With some supports, he could walk with limping gait. He could survive up to 11months when this reported was performed.

Discussion

The patient was approved to be diffuse large B cell non-Hodgkin's lymphoma stage IE, definitely diagnosed by the pathology and the immunohistochemistry. Among various pathology of the brain tumors, non-Hodgkin's lymphoma accounts for 2%[8]-6.6%[9] while the pathology of nearly all brain tumors are glioma. Most tumors always happen in the supratentorial part of the brain.

Actually, lymphoma of the central nervous system has 2 forms. For the first form, it originates and confines solely in the central nervous system, so called the primary central nervous system lymphoma (PCNSL) while in the second form, the central nervous system is just a part of systemic involvement of lymphoma. In our case, because the lesion outside the cerebellum cannot be demonstrated, it is assumed that the lymphoma primarily originates from the cerebellum itself, not a part of generalized spreading of lymphoma[10].

The primary central nervous system lymphoma (PCNSL) mainly occurs in the immunocompromised host, particularly in the HIV-infected persons. However, in our case, HIV antigen and antibody were shown to be negative after repeated examinations, and also he was demonstrated to be free from other conditions that had been well known to contribute to the immunocompromized status, such as EBV infection, steroid therapy, diabetes mellitus, leukemia or chronic kidney disease.

The computerized tomography of the brain in our case showed inhomogeneous enhancement which was not consistent with the typical finding of the CNS lymphoma in the immunocompetent host which would homo-

geneously uptake the contrast medium[11].

Concerning the pathology of the PCNSL, the aggressive form such as, diffuse large B cell, is much more common, around 77%[9]. The pathology in our case was consistent with that of the majority of cases.

In general, the prognosis of NHL generally depends on its grading of the histology and the extent of the disease. But in case of PCNSL, there are special considerations, firstly the central nervous system is not easily accessed by any chemotherapy although the tumor is sensitive to it. Standard systemic chemotherapy regimen for NHL, diffuse large B cell, such as CHOP (ie, cyclophosphamide, doxorubicin, vincristine prednisone)[12] are ineffective, presumably reflecting the difficulty of penetration of blood-brain barrier by these chemotherapeutic drugs[13]. Secondly, the operation of the central nervous system is limited by the site of tumor itself. To access it is to pass through the normal neural tissue which can be damaged permanently by such an access, moreover it does not improve prognosis[14]. Fortunately, in our case, the tumor can be easily accessed and nearly all tumor tissue can be removed without serious damage to normal brain tissue.

By these special limitations, the prognosis of PCNSL is always poorer than those of lymphoma of other sites.

The median age of the immunocompetent patients with PCNSL is 55 years whereas that of our patient is 56 years which is higher than that of the HIV-infected patients with CNS lymphoma which is 35 years[9].

For survival, it is much better if the patients are not immunocompromised. With radiotherapy alone, the median survival of the patients without AIDS was 18 months, compared with 4 months of those with AIDS. With Methotrexate-based chemotherapy, the median survival duration was approaching 48 months[13].

Because methotrexate (MTX) plus cranial radiotherapy (RT) and high-dose cytosine arabinoside can maintain the disease-free period longer than that of historical controls, our patient was treated with radiation after the removal of nearly all tumor mass, followed by chemotherapeutic regimen containing dexamethasone, vincristine, high dose methotrexate with leucovorin and intrathecal injection of cytosine arabinoside. He could still survive at least for 11 months after the definite diagnosis when this paper was written.

References

1. Krol ADG, le Cessie S, Snijder S, Kluin-Nelemans JC, Kluin PM, Noordijk EM. Primary extranodal non-Hodgkin's lymphoma (NHL): the impact of alternative definitions tested in the Comprehensive Cancer Centre West population-based NHL registry. Ann Oncol 2003; 14: 131-9.
2. Freeman C, Berg JW, Cutler SJ. Occurrence and prognosis of extranodal lymphomas. Cancer 1972; 29: 252-60.
3. White BE, Rothfleisch S. Primary cerebellar lymphoma. A case report. Neurology 1968; 18: 582-6.
4. Cha MH, Hwang SN, Kim BJ, Chi JG. A case of malignant lymphoma of the cerebellum. J Korean Neurosurg Soc 1981; 10: 619-24.
5. Sasahara A, Kawamata T, Kubo O, Okami N, Kawamura H, Hori T. Primary CNS malignant lymphoma originating from the cerebellum and extending along the lower cranial nerves. No Shinkei Geka 2000; 28: 879-83.
6. Taya K, Terao T, Tanaka T, Sawauchi S, Numoto RT, Murakami S, et al. Spontaneous regression of primary central nervous system lymphoma: a case report. No Shinkei Geka 2004; 32: 637-42.

7. Pirumyan G, Bakshi N, Fung KM. A 67-year-old woman with a cerebellar and a parietal enhancing lesions. Available at: http://moon.ouhsc.edu/kfung/JTY1/Com07/Com706-1-Diss.htm
8. Ramachandran TS. Primary CNS Lymphoma. Available at: http://www.emedicine.com/neuro/TOPIC519.HTM
9. Miller DC, Hochberg FH, Harris NL, Gruber ML, Louis DN, Cohen H. Pathology with clinical correlations of primary central nervous system non-Hodgkin's lymphoma. The Massachusetts General Hospital experience 1958-1989. Cancer 1994; 74: 1383-97.
10. Fertikh D, Artman CE, Brooks ML. Brain lymphoma. Available at: http://emedicine.medscape.com/article/338139-overview.
11. Garcia ME, Garcia AM, Catalan MJ. Primary cerebral lymphoma in an immunocompetent patient. Neurologia 2008; 23: 122-5.
12. Fisher RI, Gaynor ER, Dahlberg S, Oken MM, Grogan TM, Mize EM, et al. Comparison of a standard regimen (CHOP) with three intensive chemotherapy regimens for advanced Non-Hodgkin's lymphoma. N Engl J Med 1993; 328: 1002-6.
13. Lachance DH, Gockerman J, Halperin E. Cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP) for primary central nervous system lymphoma (PCNSL): short-duration response, multi-focal intracerebral recurrence preceding radiotherapy. Neurology 1992; 42(Suppl 3): 343.
14. Hochberg FH, Batchelor TB, Loeffler JS. Clinical and pathologic features of primary central nervous system lymphoma. In: UpToDate, Basow, DS(Ed), UpToDate, Waltham, MA, 2008.