Intracranial involvement in a patient with Hodgkin’s lymphoma

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ABSTRACT

Intracranial and intraspinal involvement is a rare complication of Hodgkin’s lymphoma. Intracranial involvement is observed in 0.2 to 0.5 percent of patients with Hodgkin’s lymphoma. No specific risk factors associated with intracranial involvement have been found. We report intracranial involvement of Hodgkin’s lymphoma in a patient who had previously undergone thyroidectomy due to thyroid papillary carcinoma.

Keywords: central nervous system, Hodgkin’s lymphoma, papillary carcinoma

INTRODUCTION

Hodgkin’s lymphoma (HL) is a disorder that originates in the lymphatic system and rarely involves the central nervous system (CNS). Approximately 25% of patients with systemic solid carcinoma suffer from metastasis in the CNS. However, intracranial and intraspinal involvement in HL is quite rare; even in HIV-positive populations, it has been observed in only 0.2%-0.5% of patients with systemic and usually recurrent diseases. For primary CNS-HL, immunosupression and Epstein-Barr virus (EBV) infection have been suggested, but there are no known risk factors for intracranial involvement in HL.

The common presenting features of intracranial HL include cranial nerve palsy, motor deficit, pain and sensory symptoms, altered mental status, seizures and other signs of increased intracranial pressure. The mechanism of brain metastasis is either through direct tumour extension or systemic haematogenous dissemination. Mixed cellular and nodular sclerosis histologies are the most frequent subtypes observed in intracranial involvement, but no association has been found between intracranial involvement and a specific HL histology. Two different studies have reported a median age of onset for intracranial HL involvement of 39.1 and 45 years, respectively. The median survival period following intracranial presentation ranges from eight months to two years.

We report intracranial involvement of HL in a patient who had previously undergone thyroidectomy due to thyroid papillary carcinoma.

Fig. 1 Photomicrographs of the macrofollicular variant of thyroid papillary carcinoma show (a) psammoma body formation in papillary carcinoma (Haematoxylin & eosin, x 200); (b) classical nuclear features of papillary carcinoma (Haematoxylin & eosin, x 400); (c) mixed cellularity Hodgkin’s lymphoma in the cervical lymph node (Haematoxylin & eosin, x 400); (d) immunoreactivity for CD30 in Reed-Sternberg cells (Immunohistochemical stain, x 400); and (e) immunoreactivity for CD15 in Reed-Sternberg cells (Immunohistochemical stain, x 400).
CASE REPORT

In September 2006, a 44-year-old Caucasian woman presented to the Department of General Surgery with swelling of the neck. Her thyroid gland was enlarged diffusely, and computed tomography (CT) of the neck showed multiple hyper- and hypoechogenic nodules with calcification. Total thyroidectomy was performed, and the pathological examination revealed thyroid papillary carcinoma (Figs. 1 a & b). One month after the thyroidectomy, the patient presented with multiple lymphadenopathies of both the cervical chains and supraclavicular areas. Fever, sweating and weight loss were present for two months. Excisional lymph node biopsy from the right anterior cervical chain was reported as mixed cellular HL (Figs. 1 c-e). CT of the neck showed that the thyroid gland had previously been operated on and also revealed conglomerate and lobulated lymphadenopathies in the bilateral cervical chains and submental and supraclavicular areas. No lymphadenopathies were observed on the CT images of the abdomen or thorax. Blood count revealed haemocrit 22.2%, erythrocyte sedimentation rate 59 mm/h and lactate hydrogenase 226 U/L. Serum antibodies for HIV and EBV were negative.

The patient was considered to be in the early unfavourable risk group and was treated with three courses of DBVD: doxorubicin (2.5 mg/m²), bleomycin (10 mg/m²), vincristine (1.4 mg/m²), and dactinomycin (375 mg/m²). On completion of the three courses, the patient was treated with irradiation, with a daily dose of 200 cGy right and left parallel lateral fields for the cervical chains and anterior fields for the supraclavicular-involved fields for 15 days with a linear accelerator. She received a total irradiation dose of 3,600 cGy. After irradiation, she underwent three courses of DBVD treatment again. In total, the patient completed six courses of DBVD. She was in complete remission and followed up for four months.

Subsequently, the patient presented with tonic-clonic convulsion and anaesthesia on the left arm. Contrast-enhanced cranial magnetic resonance (MR) imaging revealed a hypodense, solitary right parietal lobe mass measuring 1.0 cm × 1.5 cm (Fig. 2). The entire tumour, which was oedematous and free of dural infiltration, was surgically removed. The material was composed of irregular, white-red fragments macroscopically. Microscopic examination revealed diffuse eosinophils, lymphocytes, plasma cells and intermitten large uninnuclear or binuclear Reed-Sternberg cells (Figs. 3a & b). Immunohistochemical staining showed that the background was rich in CD45RO (+) T cells and contains CD20 (+) B cells. Reed-Sternberg cells were CD30- and CD15-positive (Figs. 3c & d), but CD20, CD45RO and epithelial membrane antigen were negative. Thyroglobulin staining of the biopsy material was performed in order to exclude papillary carcinoma, the result of which was negative. Therefore, the diagnosis of mixed cellular HL was made. Upon the diagnosis of intracranial involvement of HL, 300 cGy daily-dose irradiation of the whole brain was performed for ten days with a linear accelerator. The patient, who was in complete remission, was monitored for ten months and subsequently left follow-up.

DISCUSSION

Approximately 2.2% of systemic non-HLs show CNS involvement at presentation. In contrast, HL involves the CNS in only 0.2%–0.5% of the cases. The mechanism of brain metastasis is either direct tumour extension through the skull bone or systemic haematogenous dissemination. Haematogenous spread is the most common mechanism. CNS involvement is more common in patients with widespread relapsed diseases or as an initial diagnosis in immunocompromised patients. However, they can also be seen at the initial diagnosis in immunocompetent patients. Studies have reported a median age of 39.1 years and 45.0 years (range 11–69 years) and an equal male and female ratio. No specific risk factors associated with intracranial involvement have been found, but an association with EBV has been noted. CNS involvement in HL may be more frequent in familial HL, where immune deficiency is common.

Brain metastasis generally occurs many years after the evidence of systemic involvement. In our patient, it appeared ten months after the onset of nodal involvement.
Intraparenchymal, supratentorial lesions and mixed cellular history are more frequently observed, as in the case of our patient. Intramedullar involvement is uncommon and associated with poor prognosis, and no specific risk factors are associated with intracranial involvement. Although it is common to find lesions/masses in such patients, radiographic studies may be negative while cerebrospinal fluid cytology is positive, as illustrated by the case of Perez-Jaffe et al.\textsuperscript{12} and Orlowski et al.\textsuperscript{13} We detected intracranial HL in our patient with MR imaging based on the neurological symptoms. Cranial imaging is uncommon for staging of HL. Treatment strategies for brain metastasis include whole brain irradiation and systemic chemotherapy. Although age, histology, disease stage and initial treatment are important prognostic factors, the most crucial factors are the timing and dose of whole brain irradiation.\textsuperscript{17} Patients who experience a relapse in the CNS only or whose intracranial involvement is diagnosed at the initial stages of HL may have a better prognosis.\textsuperscript{18,19}

Positron emission tomography (PET) is an important imaging method for the diagnosis, staging and estimation of response to treatment and exposure of recurrence in lymphomas. The use of PET for evaluation of HL has increased during the last few years.\textsuperscript{16,19} PET is recommended for patients with curable lymphomas such as HL before treatment as it can determine the anatomical distribution of the disease. However, it is not always possible due to limitations of cost and availability.\textsuperscript{15} The advantage of PET over other imaging techniques such as CT or MR imaging is its capacity to differentiate between viable tumours, necrosis and fibrosis.\textsuperscript{13} In our patient, PET was not utilised, as there was no PET device in our hospital.

In conclusion, the diagnosis of HL brain metastasis in our case was based on the symptoms, radiological findings and histological report. Brain involvement was determined ten months after systemic diagnosis or four months after the completion of chemotherapy, which was considered early for the onset of HL. Cranial imaging at the initial diagnosis of systemic HL should be discussed in the absence of signs and symptoms of the CNS. PET may be useful for determining CNS involvement at the initial stages of HL.

REFERENCES