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Successful Treatment of Concurrent Chemoradiotherapy for Stage I Nasal NK/T Cell Lymphoma: A Report of Two Cases

YUZURU NIIBE[1], KAZUSHIGE HAYAKAWA[1], MASASHI KITANO[1], HIROMICHI ISHIYAMA[1], MEIJIN NAKAYAMA[2], KAZUO YAO[2] and MAKITO OKAMOTO[2]

Departments of [1]Radiology and [2]Otorhinolaryngology, Kitasato University School of Medicine, Kanagawa 228-8555, Japan

Abstract. *Nasal natural killer/T cell (NK/T cell) lymphoma is a rare subtype of lymphomas, being a subtype of non-Hodgkin's lymphoma with a much worse prognosis than other subtypes. One reason for this worse prognosis is that nasal NK/T cell lymphoma is resistant to standard sequential chemoradiotherapy. Thus, we adopted concurrent chemoradiotherapy using a CHOP-like regimen for treating stage I nasal NK/T cell lymphoma. Case 1 was treated with concurrent chemoradiotherapy using 41-Gy irradiation with 12 cycles of the CHOP-like regimen (THP-CVP). Case 2 was treated with concurrent chemoradiotherapy using 50-Gy irradiation with 10 cycles of THP-CVP. In both Case 1 and Case 2, the tumors disappeared after chemoradiotherapy. The Case 1 patient is still alive with 45 months free of relapse. The Case 2 patient is also still alive with 39 months free of relapse. These results suggest that concurrent chemoradiotherapy using a CHOP-like regimen for stage I nasal NK/T cell lymphoma provided sufficient dose intensity and may be a useful treatment option.*

Nasal natural killer/T cell (NK/T cell) lymphoma is a rare subtype of lymphomas. However, in Asia and native populations of Mexico and Central and South America this subtype of lymphomas is more common than in the United States and Europe (1). In Japan, NK/T cell lymphoma comprised 1.85% of all non-Hodgkin's lymphomas (2), while in the United States or Europe, it was less than 1% of all non-Hodgkin's lymphomas (3). This subtype of non-Hodgkin's lymphoma has a much worse prognosis than other subtypes such as diffuse large B cell lymphoma. The 5-year overall survival rate of localized nasal NK/T cell lymphoma was reported to be 14-87% (4-8) and that of localized intermediate- or high-grade lymphoma was 70-82% (9, 10). One reason for the worse prognosis is that nasal NK/T cell lymphoma is resistant to the standard treatment of sequential chemoradiotherapy, such as 3-8 cycles of CHOP followed by involved radiation therapy of 30–55 Gy. Recently, concurrent chemoradiotherapy was reported to achieve a better initial response for localized nasal NK/T cell lymphoma (11). This treatment method employed an increased dose intensity.

We adopted concurrent chemoradiotherapy to treat stage I nasal NK/T cell lymphoma in November 2000. In this report, we present two consecutively diagnosed cases of stage I nasal NK/T cell lymphoma treated with concurrent chemoradiotherapy using a CHOP-like regimen. As a result of this treatment, the patients have achieved more than 3 years relapse-free survival.

Correspondence to: Yuzuru Niibe, MD, Ph.D., Department of Radiology, Kitasato University School of Medicine, 1-15-1, Kitasato, Sagamihara, Kanagawa 228-8555, Japan. Tel: 042-778-8111, Fax: 042-778-9436, e-mail: joe-n@hkg.odn.ne.jp

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Case Reports

Case 1. A 28-year old woman had sudden severe pain in her right nasal ala region on July 28, 2001. She was treated with antibiotics at a regional hospital, where she was diagnosed as having acute inflammation. Her symptom, however, did not improve and her cheek began to swell. When she was referred to Kitasato University Hospital, Japan, in early August, her right nasal cavity was filled with a tumorous mass. Subsequently, biopsy was performed. The lesion was diagnosed as NK/T cell lymphoma. The patient underwent a detailed systemic evaluation, with tests including physical examination, computed tomography, Ga-scintigraphy and bone marrow aspiration. No tumor was identified anywhere except in her right nasal and paranasal cavities (Figure 1). The disease was, therefore, classified as stage I by the Ann-Arbor classification. At this point, the patient's lactose dehydrogenase (LDH) level was 419 mg/dl. From August 16 to October 4, the patient received 31-Gy irradiation to the entire nasal, paranasal and neck regions and an

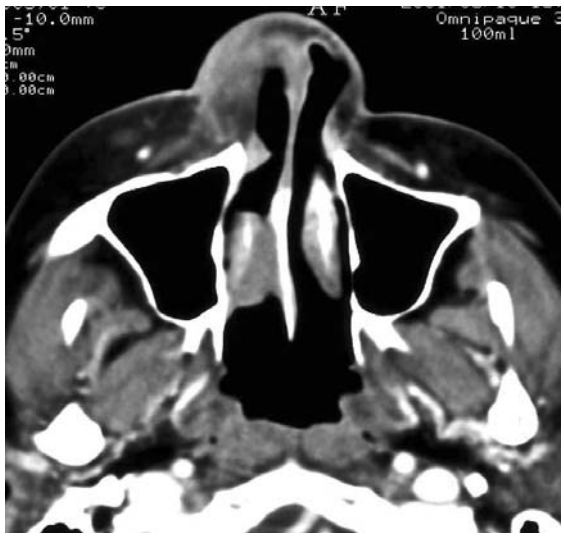

Figure 1. *Computed tomography taken before treatment of Case 1. The tumor can be detected in the patient's nasal cavities.*

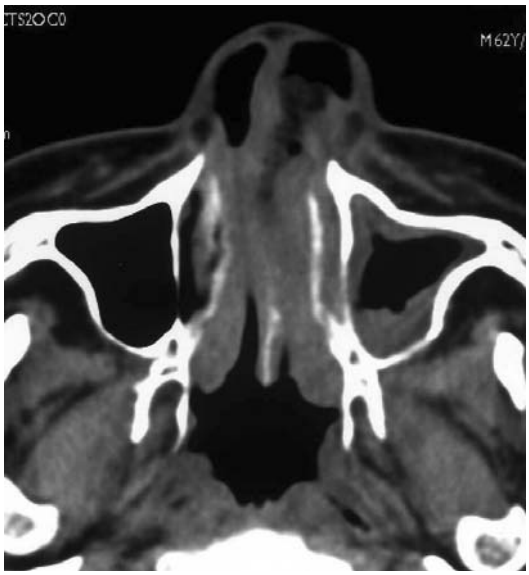

Figure 3. *Computed tomography taken before treatment of Case 2. The tumor can be detected in the patient's nasal and paranasal cavities.*

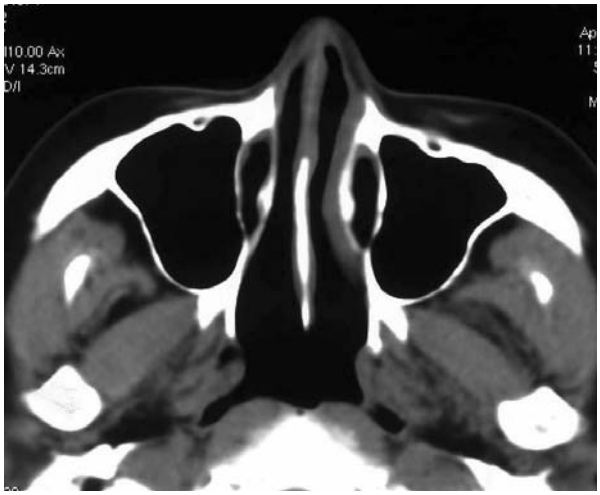

Figure 2. *Computed tomography taken after treatment (chemo-radiotherapy) of Case 1. The tumor disappeared from the patient's nasal and paranasal cavities.*

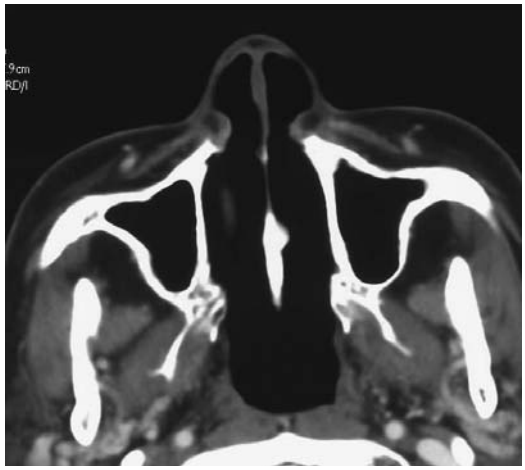

Figure 4. *Computed tomography taken after treatment (chemo-radiotherapy) of Case 2. The tumor disappeared from the patient's nasal and paranasal cavities.*

additional 10-Gy irradiation to the right nasal and paranasal regions. Concomitantly, beginning on August 17, the patient received the first course of CHOP-like chemotherapy (THP-CVP: therarubicin, 40 mg/body, Day 1; endoxan, 1000 mg/body, Day 1; firudecin, 3 mg/body, Day 1; predonine, 100 mg/body, Days 1-5). The tumor disappeared after 4 courses of chemotherapy. The LDH level at this time was 375 mg/dl. The patient received a total of 12 courses of chemotherapy. No severe morbidity was recognized during and after the treatment course. She is well and has achieved 45 months of relapse-free survival to date (Figure 2), and her LDH level has decreased to181 mg/dl.

Case 2. A 62-year-old man had been suffering from nasal obstruction for a few months. In July 2001, the nasal obstruction became exacerbated and the patient was admitted to a regional hospital. A deviated nasal septum was found

and, on November 6, the patient was referred to Kitasato University Hospital, where he underwent surgery of reptoplasty. At this point, only inflammation was noted in the pathological specimen of the inferior chonca. In January 2002, the patient's nasal obstruction rapidly worsened and the man was readmitted to our hospital. On admission, a tumorous swelling of the inferior chonca in his left nasal cavity was detected and biopsy was performed. The lesion was diagnosed as NK/T cell lymphoma. The patient underwent a detailed systemic evaluation. No tumor was found anywhere except in his nasal and paranasal cavities (Figure 3). The disease was classified as stage I. The patient's LDH level at the time of diagnosis was high, at 355 mg/dl. From February 13 to May 29, 2002, the patient received 30-Gy irradiation to the entire nasal, paranasal and neck regions and an additional 20-Gy irradiation to the left nasal cavity. Concomitantly, he received the first and second courses of THP-CVP chemotherapy (therarubicin, 40 mg/body, Day 1; endoxan, 1000 mg/body, Day 1; firudecin, 3 mg /body, Day 1; predonine, 100 mg/body, Days 1-5). The patient received a total of 10 cycles of chemotherapy. The tumor disappeared completely at the end of radiation therapy and 2 courses of chemotherapy. The patient's LDH level had decreased to 299 mg/dl at that time. No severe morbidity was recognized during or after the treatment course. The patient is well and has achieved 39 months of relapse-free survival to date (Figure 4), and his LDH level has decreased to 185 mg/dl.

Discussion

Treatment of NK/T cell lymphoma with standard therapy consisting of sequential chemoradiotherapy with a total radiation dose of 30-55 Gy has not been satisfactory. Ye *et al.* reported that the 5-year survival rate of stage I-II nasal NK/T cell lymphoma treated with chemotherapy followed by radiation therapy was 14% (4). Kwong *et al.* also reported that the 5-year survival rate of stage I CD56+ nasal lymphoma treated with chemotherapy followed by radiation therapy was 28% (5). On the other hand, Miller *et al.* reported that the 5-year survival rate of localized intermediate- or high-grade lymphoma, mainly consisting of diffuse large B cell lymphoma, treated by 3 cycles of CHOP followed by 40-55 Gy of radiation therapy was 82% (9). These results suggest that there is a need for a more intense treatment to improve the results in NK/T cell lymphoma. Thus, we began treating nasal NK/T cell lymphoma with concurrent chemoradiotherapy using THP-CVP. However, advanced stages of NK/T cell lymphoma are not considered to be curable by this regimen, because the radiation field can not cover all viable tumors, thus reducing the intensity. Therefore, our target was designed mainly to treat stage I-II nasal NK/T cell lymphomas. In the absence of a stage II case in which treatment had been completed, this report contains only cases of stage I nasal NK/T cell lymphoma.

Treatment based on this regimen was completed for both Case 1 and 2. Case 1 received 41-Gy irradiation with 12 cycles of THP-CVP as a concurrent (1st course) and adjuvant chemotherapy and achieved 45 months of relapse-free survival. On the other hand, Case 2 received 50-Gy irradiation with 10 cycles of THP-CVP as a concurrent (1st and 2nd course) and adjuvant chemotherapy and achieved 39 months of relapse-free survival. Yamaguchi *et al.* reported that concurrent chemoradiotherapy including DeVIC, which was usually used as salvage treatment, resulted in long-term relapse-free survival in 2 cases of localized nasal NK/T cell lymphoma (11). However, no studies have reported that concurrent chemoradiotherapy using a standard CHOP-like regimen including THP-CVP was effective and safe for treating localized nasal NK/T cell lymphoma. The reason why we adopted THP-CVP rather than standard CHOP is that the latter, including adriamycin and oncovin, could easily cause heart disorders and bone marrow suppression, respectively, and could exacerbate radiation toxicity in a concurrent regimen.

The 2 cases reported here achieved more than 3 years of relapse-free survival with acceptable toxicity. These results suggest that concurrent chemoradiotherapy using THP-CVP for treating stage I nasal NK/T cell lymphoma achieves a sufficient dose intensity and may be a useful treatment option.

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