

A Case Report and Literature Review : Treatment of Nasopharyngeal Cancer(NPC) Patient with AOSD(Adult Onset Still's Disease)

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성인형 스틸씨 병에서 병발된 비인두암의 치료 및 문헌 고찰

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= 국문 초록 =

비인두암에서 시행되는 방사선 치료 이후에 구강건조증과 피부 변화는 흔하게 볼 수 있는 합병증 중 하나이다. 비인두암의 좋은 예후를 고려할 때, 그러한 치료와 관련된 독성들은 상대적으로 오랫동안 문제를 야기하며 삶의 질 저하를 불러온다. 특히 류마티스 관절염, 루푸스와 같은 결합조직 질환을 가진 환자들에게서 방사선 치료를 시행하였을 때, 빈번하게 심각한 독성이 관찰된다. 본 증례는 성인형 스틸씨 병에서 병발된 비인두암의 치료로 항암방사선 동시 치료를 실시한 결과, 비교적 경미한 구강 건조, 점막염, 불면증 등의 합병증이 관찰되었으나, 완전 관해가 획득되었다. 이에 저자들은 과거에 보고된 적 없는 성인형 스틸씨 병에 병발한 비인두암의 치료 경험을 다른 결합조직질환들에서 방사선 치료의 문헌들과 함께 보고하는 바이다.

중심 단어 : 비인두암 · 성인형 스틸씨병 · 항암화학방사선 동시치료.

Introduction

Nasopharyngeal cancer(NPC) is different from other head and neck cancers; it has a well defined geographic distribution, a strong relationship with Epstein-Barr virus in endemic regions, and a remarkable chemo-radiosensitivity. Most of NPC occur only in endemic area(South Eastern China, Southern and Northern Africa, and Inuit area such as Alaska, Greenland, North Canada), so there has not been many various cas-

es of NPC.¹⁻⁴⁾

In locally advanced head and neck cancer, chemoradiation therapy(CCRT) is a standard treatment method. However in NPC, the sensitivity to chemotherapeutic agents is relatively higher than other head and neck cancer, therefore, the CCRT with consolidation chemotherapy developed since the 1990s became a main therapeutic strategy to reduce local recurrence and distant metastasis as well as to improve overall survival.⁵⁾

Typically, NPC is asymptomatic in early stage and thus it is mostly diagnosed in locally advanced stage. Moreover, local recurrence or distant metastasis occurs frequently, the majority of these cases are necessitated by aggressive treatment including radiation therapy.^{6,7)} Various connective tissue diseases(CTD) have been reported to be associated with a malignant tumors and an increased incidence of radiation

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sequelae.⁸⁾ Chen et al. reported a significantly greater incidence of toxicity was found between the CTD groups(17%) and control groups(3%)($p=0.0095$) in breast cancer.⁹⁾ Even NPC, several cases were reported more toxicities in NPC patients with other CTD. Representatively, Teo et al. reported excessive adverse reactions in patients with NPC complicated by CTD.¹⁰⁾

Known toxicities for the radiation in NPC are xerostomia, skin toxicity, mucositis and that severely impairs quality of life.¹⁾ So radiation to patient with CTD have been considered as a relative contraindication.¹¹⁾

The NPC was found of the patient cared for adult onset still's disease(AOSD). In terms of NPC, CCRT followed by consolidation chemotherapy will be given to the patient as usual. But our patient had severe unexpected complication and so stopped planned treatment schedule.

To the authors' knowledge, this is the first case report of the radiation therapy to NPC with Still's disease. The article below shows complete remission by the CCRT on the NPC with AOSD.

Case Report

In April, 2013, a 43-year-old women undergoing treatment with prednisolone for AOSD from 2008, presented with a 4-month history of progressive pain on left neck. She was diagnosed AOSD based on arthralgia with spiking fever and rash on both upper arm, thigh and face, with negative ANA and Rheumatic factor test at other tertiary hospital. She had been difficult at swallowing and 7 kg weight loss during 6 months, Upon physical examination, painless non-movable neck mass on left side was palpated. Her initial laboratory analyses showed hemoglobin of 12.8 g/dL, leucocytes 7.5 K/uL(75.9% neutrophils, 14% lymphocytes) and 286 K/uL platelets, LDH of 175 IU/L, HBV Ag, HIV Ag negative but HCV Ab Positive, She has been working as a high school teacher.

The work-up included neck computed tomography(CT), magnetic resonance imaging(MRI) and 18-FDG-positron emission tomography(PET) scan that showed a well enhanced mass in the left rosenmullar fossa across midline with enlarged regional lymph nodes. The main mass extended longus coils, pterygoid muscle and clivus. Lymph node invasion was demonstrated at both cervical level II, III and left supraclavicular area(cT2N3bM0, stage IVb). Distant metastasis was not observed(Fig. 1).

Sono-guided fine needle aspiration was performed. Path-

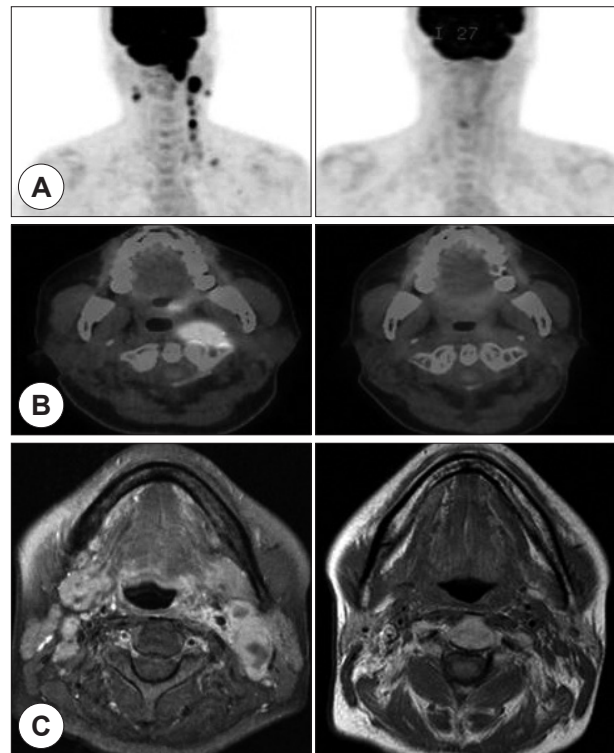


Fig. 1. Evaluation of 18-FDG-PET scan(A and B), MRI(C) according to 3 cycle of chemoradiation treatment : completely disappeared mass and enlarged malignant lymph nodes.

ological result was poorly differentiated carcinoma, R/O undifferentiated carcinoma.

She started on cisplatin 100 mg/m² every 21 days and concurrent radiation therapy with total of 67.2 Gy by T.C Chan's method since 29 April 2013.⁴⁾

She was treated with IMRT using ⁶⁰Co γ -ray to an area extending from the nasopharynx to the lower cervical area through opposing lateral parapharyngeal area at a rate of 2.24 Gy/day(67.2 Gy/30 Fx).

An analgesic agent was given to the patient to palliate the pain. Percutaneous feeding tube was not insert due to refusal.

One week after the start of radiation therapy, she complained of insomnia, emesis and dry mouth. At physical exam, there were pronounced acute mucosal reaction and mucosal ulceration of grade III according to the Common Terminology Criteria for Adverse Events(CTCAE).¹²⁾ However there was not observed any skin reaction(pigmentation, fibrosis) and bleeding. We added anti-anxiety agent(lorazepam), serotonin antagonist(ondansetron) and pilocarpine 5 mg, three times a day and salivary gland sparing radiation therapy was continuously given. The treatment was completed without omitting of radiation during the schedule and infusion of cisplatin was also administered as a triweekly schedule. At this time, most serious symptoms were insomnia, anorexia and dry mouth.

Dry mouth and oral pain were continually annoying her daily life after treatment. A few weeks later, improving mucositis, oral pain has subsided but dry mouth was sustained and kept her from eating. So we performed salivary scan, it reveals decreased excretion on parotid and submandibular glands(Fig. 2). Unlike xerostomia, response of CCRT was satisfactory. An 18-FDG-PET scan, neck CT scan and neck MRI after end of CCRT was demonstrated completely disappeared mass and enlarged malignant lymph nodes(Fig. 1). Two months later, her symptom was beginning to improve, at present, dry mouth has somewhat recovered up to grade I by the CT-CAE and she lives an ordinary life(Fig. 3).

Discussions

In our case, radiation toxicities such as skin reaction and xerostomia within this patient was lower than what was expected. However, due to the emotional change and drug dependency caused by benzodiazepine that was used for another symptom, a further consolidation chemotherapy was not executed. With the existence of CTD, possibility of arising xerostomia was concerned before the radiation treatment, so the amount of 15–20 Gy was limited in order not to destroy the

salivary gland. It is because that management of xerostomia is rarely effective, prevention is the best treatment.¹³⁾ Nevertheless, she suffered from several complications. Even if the salivary gland functionality was confirmed by salivary scan, the decreasing salivary flow and damage from the oral mucosal integrity were possible causes of the oral dryness. For this patient, additory hyperbaric oxygen therapy is doable.¹⁴⁾ If later on it were found out to be NPC combined with CTD, cytoprotective agent such as amifostine would be considered to be used. In order to relieve these oral discomforts, salivary stimulating drugs, such as pilocarpine and bromhexine, have been used for some years and their efficacy has been verified in some experimental studies. In some cases, careful use of narcotics such as benzodiazepine is rather to be recommended.¹⁵⁻¹⁷⁾ And other treatment for reduce xerostomia also used for submandibular gland transfer.¹⁸⁾ Despite of these toxicities, the patients treated in sympathy with protective and supportive treatment, the radiation therapy in this setting is enough to be recommended.

The prognosis of patients with NPC depends on the stage of the disease at diagnosis, unfortunately at diagnosis, 70% of patients have locally advanced, non-metastatic stage III or IV disease. CCRT is standard treatment for locally invasive

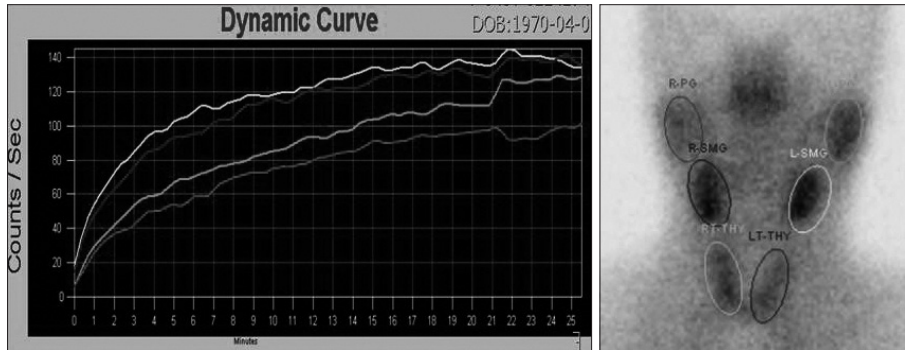


Fig. 2. Salivary scan after CCRT : distal curve(excretory phase) was fall at normal salivary function, in this case excretory phase does not exist.

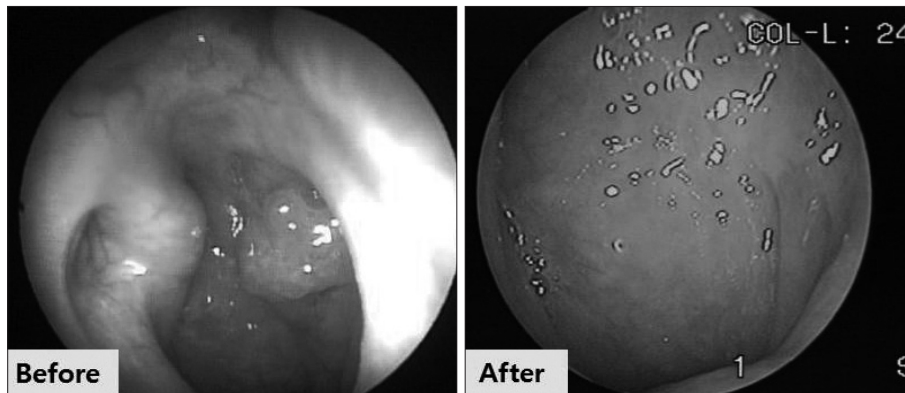


Fig. 3. Laryngoscopic image before and after CCRT.

NPC.^{1,7,19,20} Radiation therapy in patient with head and neck cancer including NPC have shown several toxicity. One of the most important toxicity is also xerostomia. Radiotherapy of head and neck may result in a decrease in salivary pH and its rate of secretion.²¹ Therefore, any discomfort of chewing, swallowing, speech and sleep may occur in the presence of xerostomia.²²

AOSD is a rare systemic inflammatory disorder of unknown etiology, characterized by spiking fevers with an evanescent rash, arthritis, and multiple organ involvement. It owes its name to George Still who published in 1897 his monograph. incidence over the age of 16 among men is 0.22/10,000 and among women 0.34/100.23 Although the diagnosis of AOSD necessitate to exclude malignancy, actually many AOSD was reported coincided with other malignancies such as leukemia, lymphoma, thyroid cancer and lung cancer.²⁴⁻³⁰ In that case, radiotherapy may need to treat of disease but there are few reports for treatment of head and neck cancer with AOSD.

We report a case about the treatment of NPC patient with AOSD. Although she suffered prolonged mucositis and dry mouth, she had a complete remission of NPC and immunosuppressive effect by CCRT resulted in remission of her arthritis. In conclusion, CCRT is highly effective and shows manageable toxicity so CCRT as a definitive treatment option is a consideration in NPC patients with AOSD.

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