Case Report
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Bell's palsy after concomitant chemoradiotherapy: a case report and literature review

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Concomitant chemoradiotherapy (CCRT) treated patients experience various complications. We present a rare case of post-CCRT Bell's palsy and describe its various possible causes, so as to increase awareness among clinicians about Bell's palsy being a CCRT-associated adverse effect.

The patient was a 48-year-old man diagnosed with squamous cell carcinoma who presented with post-CCRT Bell's palsy. After radiotherapy for 6 weeks (overall 67.5 Gy) and four rounds of cisplatin chemotherapy, he complained of paralysis of the entire left face. A test was performed 33 days after the last CCRT session to differentiate Bell's palsy from other causative factors. Based on magnetic resonance imaging findings, facial nerve invasion due to tumor size increase was determined to not cause Bell's palsy. Inflammation of the left Eustachian tube was observed. Hence, steroids and famciclovir were administered, which markedly improved the facial paralysis symptoms within 56 days after facial paralysis development.

In conclusion, patients can develop Bell's palsy owing to complex effects of various CCRT mechanisms. Although the exact cause of Bell's palsy has not been identified and the effectiveness of drug treatment was questionable in this case, unlikely causative factors should be excluded through various tests and appropriate and timely measures must be adopted.

Keywords: Bell Palsy; Concomitant Chemoradiotherapy; Complications; Facial Palsy; Oral Cancer; Squamous Cell Carcinoma.

INTRODUCTION

Bell's palsy is an unexplained episode of the facial nerve (the 7th cranial nerve) paralysis that results in acute, unilateral, partial, or complete facial muscle weakness [1,2]. Bell's palsy is more common in patients with diabetes and can affect individuals of any age, although the incidence peaks in the 40s. Its exact cause is unknown; however, experts hypothesize a reaction after a viral infection such as Lyme disease, Ramsay Hunt syndrome (facial palsy with herpes zoster oticus caused by varicella-zoster virus), sarcoidosis, parotid-nerve tumors, or amyloidosis as a cause. Bell's palsy usually progresses from symptom onset to maximal weakness within 3 days and almost always within 1 week [2]. Most people with paresis spontaneously recover within 3 weeks. Approximately 30% of patients, typically those with paralysis, have a delayed or incomplete recovery [1].

Bell's palsy is easily misdiagnosed as other conditions such as a stroke because specific evaluation tests are lacking; thus, differentiation is necessary. Once facial paralysis symptoms develop, many can mistake it as a stroke symptom; however, a few subtle differences exist.

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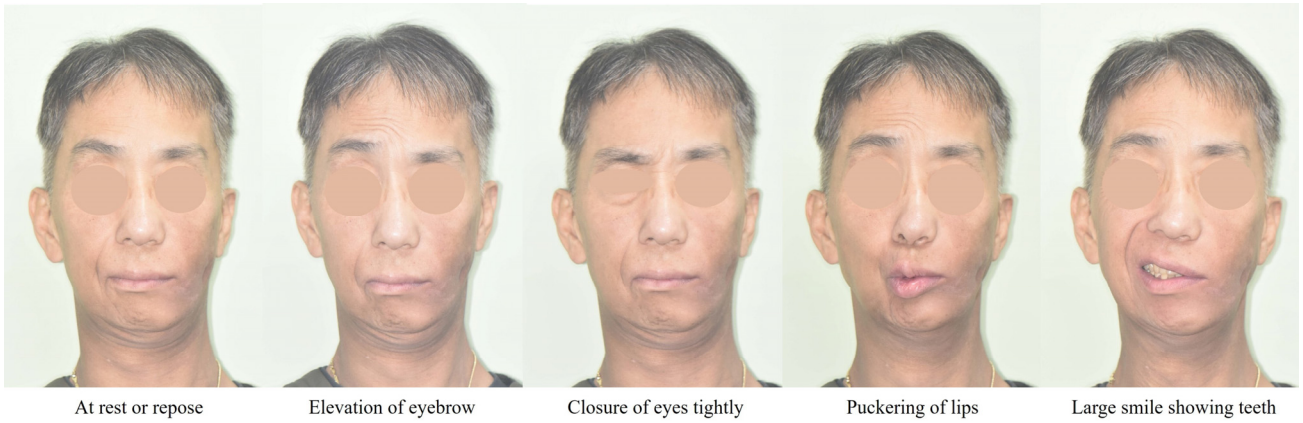

Fig. 1. Static views of facial palsy (02/21/2023). Clinical photograph obtained on the 6th day after the onset of facial paralysis symptoms. Even in the resting state, slight asymmetry can be observed, and paralysis of the frontal branch of the facial nerve was diagnosed based on the elevated left eyebrow and inability to tightly close the left eye. Abnormalities of the left orbicularis oris and buccinator muscles were observed through lip puckering, indicating buccal nerve paralysis. Symptoms of left facial paralysis were observed when smiling wide. Collectively, these findings led to a diagnosis of paralysis of the zygomatic, buccal, and marginal mandibular nerves [14].

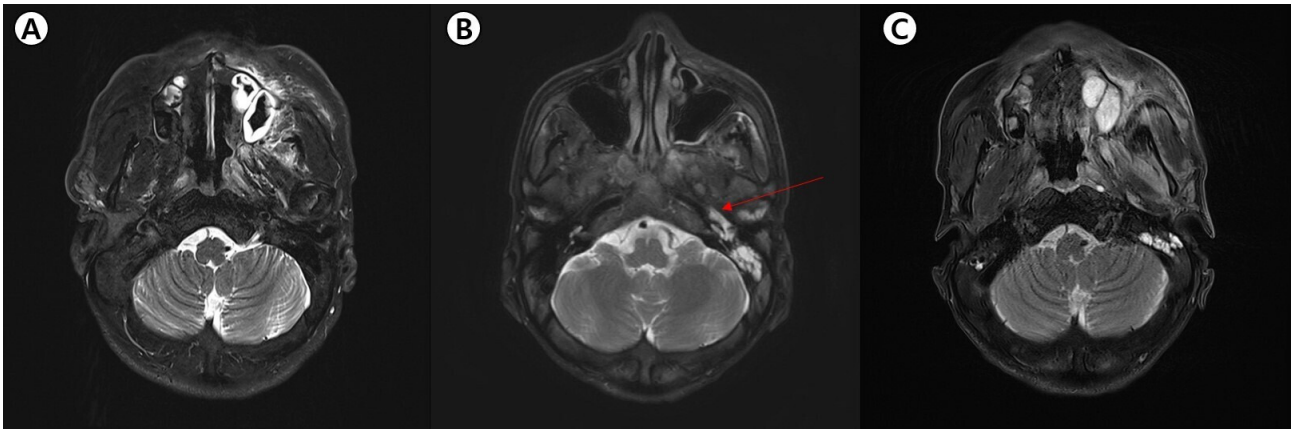

Fig. 2. Magnetic resonance imaging results. (A) (11/01/2022) Axial magnetic resonance imaging (MRI) performed before starting concurrent chemoradiation therapy (CCRT) (B) (02/21/2023) Axial MRI of the bony Eustachian tube performed 39 days after the final chemotherapy session and 6 days after symptom onset; swelling of the left nasopharyngeal wall (arrow) at the orifice of the Eustachian tube is visible. (C) (05/10/2023) MRI performed approximately 3 months after symptom onset showing persistent otitis.

A stroke will usually cause a few additional symptoms not associated with Bell's palsy, such as consciousness changes, seizure activity and motor and/or sensory deficits in one or more extremities. Furthermore, unlike patients with Bell's palsy, those with strokes can usually control the upper part of their face [3].

Numerous case reports of complications caused by concomitant chemoradiation therapy (CCRT) exist; however, cases of post-CCRT Bell's palsy are rare. In addition to reporting the present case, we reviewed references on the induction mechanism of post-CCRT Bell's palsy. Here, we summarize various possible causes of Bell's palsy, so that clinicians are aware of Bell's palsy as a CCRT-associated adverse effect.

CASE REPORT

A 48-year-old man with squamous cell carcinoma in the maxilla and no underlying diabetes who had received 6 weeks of radiotherapy (total of 67.5 Gy) with four rounds of weekly cisplatin chemotherapy at Seoul National University Hospital (SNUH) presented to the same hospital complaining of paralysis in the left face

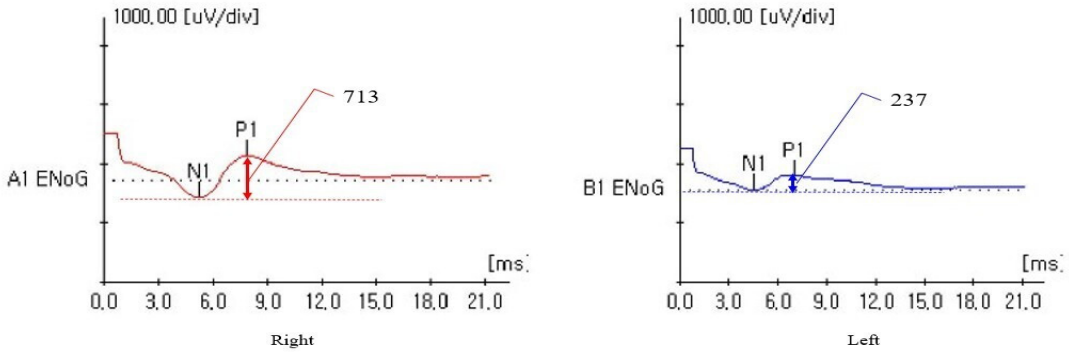

Fig. 3. Electroneuronography test (03/02/2023). Electroneuronography (ENoG) showing degradation of 33% on the left side. Facial nerve degeneration was calculated by comparing ENoG amplitudes for the involved and uninvolved (normal) sides. In the present case, the ENoG amplitude on the involved side (left side) was 237 microvolts compared with 713 microvolts on the uninvolved side (right side). The result indicates approximately 33% degeneration on the left side of the face [15].

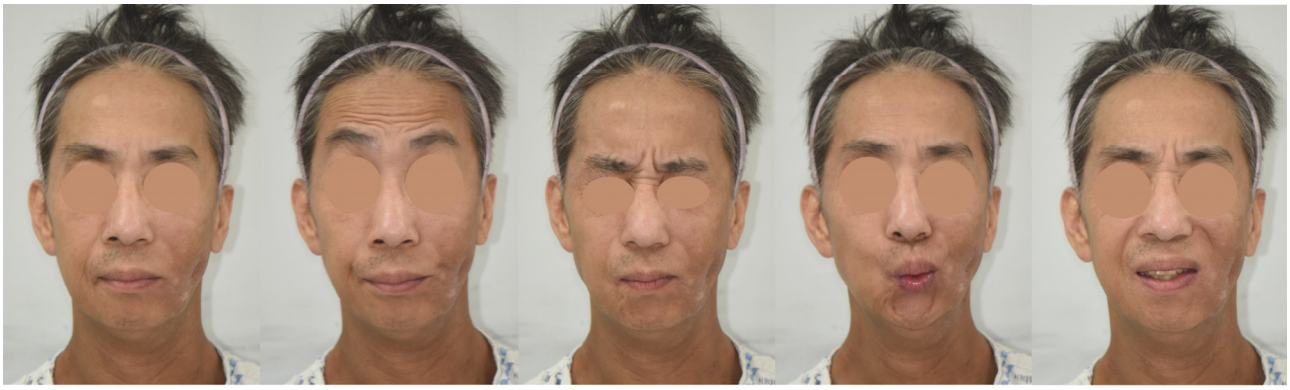

Fig. 4. Static views of facial palsy (04/06/2023). Clinical photograph obtained 56 days after the onset of facial paralysis symptoms, confirming the general resolution of facial paralysis.

(Fig. 1). Approximately 33 days after the final CCRT, left facial paralysis symptoms suddenly developed, and asymmetric facial muscle tone, inability to close eyes, and asymmetrical smile were noted during an examination. Laboratory blood tests were performed 2 days after the onset of left facial paralysis to determine the presence or absence of a viral infection due to reduced immunity, the results of which were as follows: white blood cell count, 4.43 × 10^3 mm^3/μL; red blood cell count, 4.2–6.3 × 10^6/μL; glucose level, 89 mg/dL; and high sensitivity C-reactive protein (hs-CRP) level, 0.37 mg/dL. No signs suspicious of acute viral infection were observed, and diabetes was ruled out because the glucose level was normal.

Magnetic resonance imaging (MRI) was performed 6 days after symptom onset to differentially identify tumor progression, stroke, or other factors. MRI (Fig. 2) revealed the carcinoma size was markedly reduced after CCRT but swelling of the location of the orifice of the pharyngotympanic tube (Eustachian tube), was increased, resulting in severe mastoiditis and otitis media. Because of the above findings, the patient visited the Department of Otorhinolaryngology, SNUH, approximately 15 days after symptom onset. Electroneuronography (ENoG) showed degradation of 33% on the left side (Fig. 3) and House-Brackmann grade (H-B grade) V facial paralysis. This result indicates greater degeneration in the left facial nerve than in the normal right facial nerve, and H-B grade V is associated with severe dysfunction and asymmetry that remains at rest (forehead: not movable, eye: incomplete closure, mouth: slight movement). After an otolaryngologist prescribed corticosteroid with

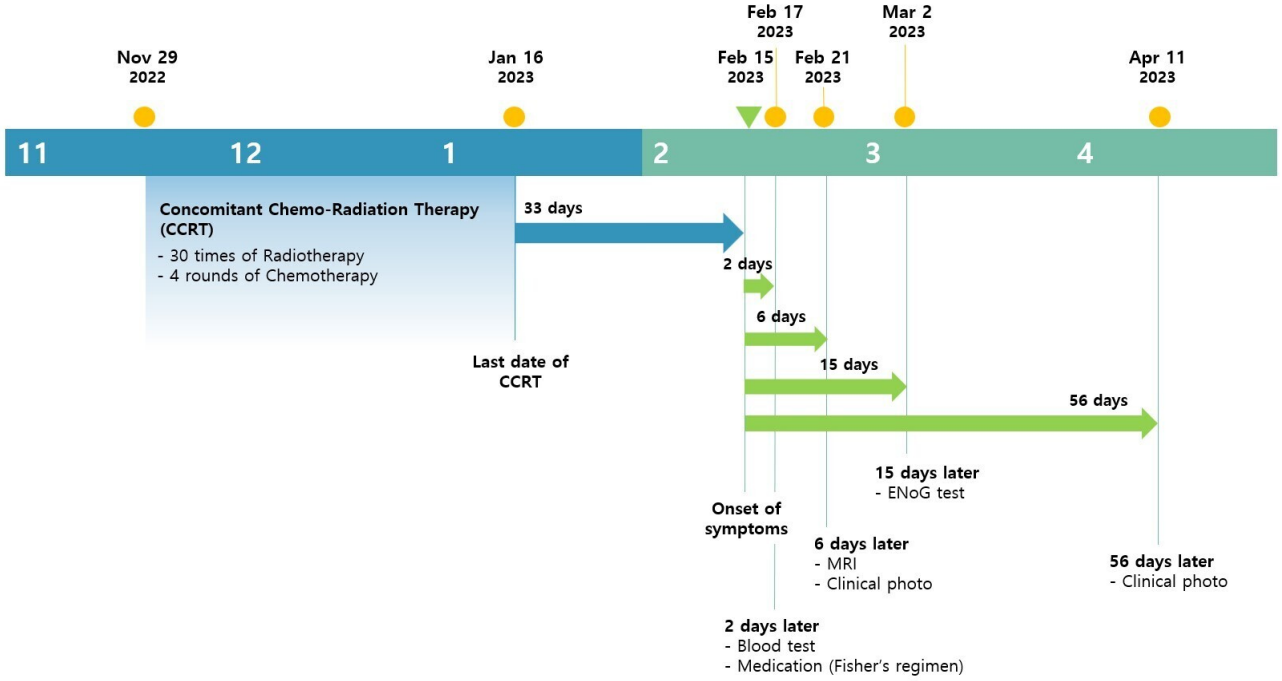

Fig. 5. Case timeline. CCRT, Concomitant chemoradiotherapy; ENoG, electroneuronography; MRI, magnetic resonance imaging.

famciclovir 2 days after symptom onset, overall sensory deterioration persisted in the left facial area, which the patient had been complaining about continuously owing to the carcinoma before CCRT. However, Bell's palsy symptoms were significantly alleviated based on the image obtained at 56 days after symptom onset (Fig. 4, 5).

DISCUSSION

Various complications caused by CCRT have been reported; selected studies about neuropathy after radiotherapy or chemotherapy have been listed in Table 1 [4-7]. However, cases of post-CCRT Bell's palsy are rare. The cause of acute Bell's palsy in our patient appears to have been a combination of factors: patients' compromised immune system, types of chemotherapy medications, radiation-induced neuropathy, and acute suppurative otitis. After reviewing the literature, the causes of facial paralysis seem to be divided into effects of chemotherapy or radiotherapy.

Chemotherapy-induced peripheral neuropathy (CIPN) is distinct from cancer pain, in which the tumor directly invades nerve tissue and compresses the nerves or spreads to the bone. Approximately 40% of the leading cancer drugs can cause peripheral neuropathy in patients receiving combination chemotherapy including platinum, vinca alkaloids, bortezomib, and taxanes [8,9]. CIPN develops when nerve cells are damaged in a mechanism similar to that of anticancer drugs on cancer cells. For example, cisplatin creates compounds within the DNA strands of nerve cells, causes cross-linking between strands, and modifies the tertiary structure of DNA, promoting nerve cell apoptosis [9].

However, in previous studies investigating peripheral neuropathy induced by cisplatin anticancer drugs, symptoms manifested bilaterally, starting from the distal part of the hands and feet and progressing to mainly cause sensory nerve abnormalities rather than affecting motor nerves [9]. In the present case, paralysis of the facial nerves, which are motor nerves, occurred approximately 1 month after the final chemotherapy session. Although cisplatin is not expected to have a marked effect, the present case shows that such an effect is possible. Therefore, cisplatin's effect cannot be completely excluded, and continuous monitoring is needed because there is currently no effective

Table 1. Selected studies on neuropathy after radiotherapy or chemotherapy

Author/date/country	Study design	Sex/age	Location of tumor	Treatment	Symptoms	Onset of symptom	Treatment for neuropathy
Azzam, et al. /2020/United kingdom	Review article			RT	Radiation-induced neuropathies		Not specified
Delanian, et al. /2012/Germany	Review article			RT	Radiation-induced neuropathies		A curative strategy has yet to be defined
Jassen, et al. /2015/United kingdom	Case report with cohort study	-/50Y	SCC of Right tonsil with unilateral lymph node metastasis	Adjuvant RT (36Gy-55Gy)	Bilateral XII nerve palsy	12 years later after RT	Not specified
		-/46Y	Left tongue carcinoma	IMRT (66Gy mean dose)	Left XII nerve RICNP	6 years later after RT	Not specified
Lee, et al. /1999/Netherlands	Case report	F/62Y	Left breast carcinoma and Bilateral lung metastasis	Chemotherapy with paclitaxel	Bilateral facial nerve palsy	Within the first week after high-dose paclitaxel administration.	Oral prednisone, 100 mg per day and amitriptyline was started (Total period not listed). Cyclophosphamide, Thiotepa, and Carboplatin (CTCb) was administered three months after high-dose paclitaxel.

F, female; Gy, gray; IMRT, Intensity-modulated radiation therapy; RICNP, Radiation-induced cranial nerve palsy; RT, Radiotherapy; SCC, Squamous cell carcinoma; Y, year.

preventive or established treatment for peripheral neuropathy caused by anticancer drugs [8].

Radiation-induced peripheral neuropathy (RIPN) is late-onset focal damage of mature neural tissue owing to initial microvascular damage, followed by radiation-induced fibrosis combined with specific neurological damage. Recently, knowledge regarding RIPN has improved based on the recognition of various clinical symptoms caused by various lesions of the nerve root, plexus, or trunk [9].

The immune system can also be affected by radiation therapy and cause secondary facial paralysis. The immune system compromised, it may play a role in acute and late radiation side effects, which can resemble acute and chronic inflammatory disease conditions. Radiation therapy may upset the balance of the immune system, causing inflammation [10]. Furthermore, infection, ischemic condition, and immunodeficiency can contribute to Bell's palsy. Based on preliminary studies in which radiation was shown to reactivate the herpes simplex virus, Khateri et al. hypothesized that radiation therapy could induce Bell's palsy [11].

In the present case, as in the previously reported case, Bell's palsy symptoms developed, and swelling of the left nasopharyngeal wall containing the orifice of the Eustachian tube was found to have increased on MRI (Fig. 2) owing to severe mastoiditis and otitis media.

Prasad et al. reported facial palsy as a rare complication of acute suppurative otitis media that requires early detection and appropriate treatment. Possible factors that can cause facial nerve palsy in acute suppurative otitis media are changes in the middle ear microenvironment, such as elevated pressure, otitis, or acute inflammation. These alterations can directly affect hearing through facial nerve physiology. The patient in this case also showed mild hearing loss with 38 dB HL in the left ear according to the results of pure tone audiometry performed 12 days after the onset of left facial paralysis. Surgery may not be required for facial nerve palsy secondary to acute otitis media if timely and appropriate antibiotic treatment is administered [12]. In this case, after the use of steroids and famciclovir for 2 weeks, which were prescribed 2 days after symptom onset, the patient's facial palsy symptoms improved. A facial photograph taken on April 12, 2023, 2 months after symptom onset, showed an improvement in overall facial palsy (Fig. 4). MRI performed approximately 3 months after the onset of Bell's palsy showed persistent otitis but improved inflammation

compared with T2-weighted MRI performed immediately after symptom onset (Fig. 2-B, C).

The present work has several limitations. According to studies on the prognosis of Bell's palsy based on ENoG, patients with facial palsy should undergo ENoG daily to determine paralysis progression. In the present case, ENoG could not be performed except at the first visit to the otolaryngology department. In actual clinical practice, repeated ENoG is not feasible for most patients. Furthermore, in ENoG, generally, only the buccal branch is evaluated, which limits the identification of paralysis severity in patients with severe facial paralysis of the temporal, zygomatic, mandibular, or cervical branches [13]. Further studies are needed to understand the clinical characteristics of and to elucidate the pathophysiology of post-CCRT Bell's palsy.

In conclusion, the patient in the present case developed Bell's palsy due to complex effects of various CCRT mechanisms, and the symptoms likely improved with the use of medication for otitis, along with spontaneous improvement. Although the exact cause of Bell's palsy has not been identified and the effectiveness of drug treatment is questionable, it is necessary to exclude unlikely causative factors through various tests and to perform appropriate and timely interventions.

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Mi Hyun Seo: Conceptualization, Writing - review & editing

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