Case report:

Primary Non-Hodgkin's lymphoma originating from the masseter muscle

Hyun Jin Min[1], Kyung Soo Kim[2]

Abstract

Recently, as we experienced a case of extranodal NHL originating from the masseter muscle completely cured by chemotherapy with radiotherapy, we present the clinical, US, CT, and MR imaging findings in additional one case of biopsy-proved extranodal NHL (NK/T cell lymphoma) involving predominantly the masseter muscle also review thoroughly our collected cases of primary non-Hodgkin's lymphoma involving the muscles of mastication and facial expression. On the basis of our comprehensive review, we suggest two conclusions. First, primary muscle lymphoma particularly originating from muscles of mastication and facial expression is extremely rare, but primary muscle lymphoma should be considered in the differential diagnosis of muscular masses. Second, primary muscle lymphoma particularly originating from muscles of mastication and facial expression has similar clinical and radiological characteristics to primary skeletal muscle lymphoma involving other sites. However, the prognosis is more favorable in primary muscle lymphoma originating from muscles of mastication and facial expression compared to primary skeletal muscle lymphoma involving other sites.

Keywords: Non-Hodgkin's lymphoma; NK-T cell lymphoma; Masseter muscle; Skeletal muscle; Prognosis

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Introduction

Lymphomatous involvement of skeletal muscle has been reported to occur in only 1.4% of cases, with 0.3% occurring in Hodgkin disease and 1.15% in Non-Hodgkin's lymphoma (NHL).[1] Lymphoma can involve any muscle and the sites reported most often, in order of prevalence, are the thigh, trunk, upper extremity, and leg.[2] However, involvement of the masticator muscles by lymphoma is extremely rare. To the best of our knowledge, only 8 cases of extranodal NHL that appeared to arise from the masticator muscles have been reported.[3-9] Recently, as we experienced a case of extranodal NHL originating from the masseter muscle completely cured by chemotherapy with radiotherapy, we present the clinical, US, CT, and MR imaging findings in additional one case of biopsy-proved extranodal NHL (NK/T cell lymphoma) involving predominantly the masseter muscle and also review thoroughly our collected cases of primary non-Hodgkin's lymphoma involving the muscles of mastication and facial expression with particular emphasis on the clinical, radiological findings, treatment modality and prognosis by comparing our data with skeletal muscle lymphoma involving other sites.

Case Report

A 78-year-old woman presented with a 2 months rapidly progressive facial swelling in the right cheek. She also complained of facial paresthesia. Initially, under the provisional diagnosis of facial cellulitis, she was treated by medical treatment including antibiotics, but the symptom was refractory to medical treatment. She didn't have a fever, weight loss, or experience night sweats. On physical examination, a hard, painless, 4x5 cm sized mass with uncircumscribed borders in the right masseteric region. There was no palpable lymphadenopathy, and the physical examination was otherwise normal. The laboratory values, including lactate dehydrogenase, alakaline phosphatase, beta 2-microglobulin and

1. Hyun Jin Min, M.D., Ph.D. Department of Otorhinolaryngology-Head and Neck Surgery, Chung-Ang University College of Medicine.
2. Kyung Soo Kim, Department of Otorhinolaryngology-Head and Neck Surgery, Chung-Ang University College of Medicine, 224-1, Heukseok-dong, Dongjak-gu, Seoul, Korea.

Correspondence to: Kyung Soo Kim, Department of Otorhinolaryngology-Head and Neck Surgery, Chung-Ang University College of Medicine, 224-1, Heukseok-dong, Dongjak-gu, Seoul, Korea. Postal Code: 156-755, Email: E-mail: entkks@cau.ac.kr

complete blood cell count with differential, were within normal ranges. US showed 2.3cm sized intramasseter mass lesion and a CT scan demonstrated a 3x4x4cm sized, well-marginated soft tissue density replacing right masseter muscle with uniform enhancement and surrounding soft tissue infiltration. MRI showed a well-defined soft tissue mass with homogeneous signal intensity in the right masseter muscle. The lesion was isointense to muscle on T1WI and hyperintense on T2WI. Immunohistochemical analysis showed that the tumor cells were positive for CD3, CD56, and Bcl-6 (weakly), whereas negative for CD20, CD10, and Bcl-2. Ki-67 staining was present in 70% of the neoplastic cells. The final diagnosis was extranodal NK/T cell lymphoma, nasal type. The bone marrow analysis did not reveal lymphomatous involvement, and cytogenetic analysis showed a normal karyotype. 18F-PET CT scan did not reveal other localizations. Therefore, the clinical stage was IEA (Ann Arbor). The patient underwent 5 cycles of CHOP (cyclophosphamide, doxorubicin, vincristine and prednisolone) therapy with radiation therapy (3600cGy). After 4 cycles of chemotherapy, the restaging procedures were performed and demonstrated no evidence of disease. No relapse has occurred in the patient during a follow-up 48 months.

Search Strategy of Literatures

In order to review all of the available English-language literature, we searched MEDLINE and PUBMED database using key words “Lymphoma” and “Masseter muscle”. Because the number of articles was small, we expanded our search by using key word “Mastication”, “Muscle” and “Masticatory space”. We found 7 articles relevant to our search. We thoroughly reviewed 7 articles[3-9] (8 patients including our case) except 1 recurrent case[9] and tried to elucidate the clinicopathological characteristics of lymphoma originating from the masticator muscles through the comparison with primary extranodal lymphoma arising from skeletal muscle of other sites.

Results

Patient Demographics

The mean age was 50.88 years, ranging from 6 years to 78 years with a female to male ratio of 1:1 (4:4). All eight patients had unilateral lesion with no side preponderance; the involved side was on the right side in 5 patients and on the left side in 3 patients.

Clinical symptoms

Of the presenting symptoms, the main symptom was facial swelling, which was seen in 6 patients and painless in 5 patients. Other symptoms were paresthesia, eye symptom and headache. The mean duration of symptoms was 8.7 months (2months ~ 2 years). Four patients did not have B symptoms (fever, weight loss, night sweats) and there was no information about B symptoms in remaining 4 patients. Most patients did not have any combined disease, but only one patient had AIDS. On physical examination, the mass was usually firm in consistency and fixed to the underlying soft tissue with irregular borders.

Image findings

The most common imaging technique used to evaluate the masses of masticatory muscles was CT, used in 7 patients. The CT findings described in enrolled reports were somewhat various including diffuse enlargement of involved muscle, well-defined mass with homogeneous soft tissue density, isodense to muscle, subcutaneous infiltration, loss of fat plane with preservation of tissue planes, and homogeneous enhancement after the intravenous contrast injection. In 5 patients, MRI was performed for further evaluation and the differential diagnosis. On the basis of our review of MRI findings, NHL was well-defined and altered signal intensity soft tissue mass which was isointense with normal muscles on T1-weighted images, hyperintense on T2-weighted image, and enhanced moderately in inhomogeneous manner on gadolinium enhanced MRI. In 3 patients, ultrasonography (US) was an initial procedure performed because it can differentiate intramuscular lesions from external ones. On US findings, NHL was hypoechoic intramuscular lesion with minimal vascularity. In only our case, 18FDG-PET/CT was performed for further evaluation. 18FDG-PET/CT images showed hypermetabolic cheek mass with the maximum standardized uptake value (SUV) of 11.9.

Histologic subtypes of NHL

All primary lymphomas of the masticatory muscles are of the NHL type. The histopathological subtypes of the 8 cases are shown in Table 1. Using the WHO classification, diffuse large B-cell lymphoma (DLBCL) and lymphoplasmacytoid B-cell lymphoma (LPC) were two cases each. One case was classified as acute lympoblastic phenotype NHL (LBL) and our case was in nasal type, extranodal NK/T cell lymphoma. In two cases, the histopathological subtypes were not described in detail.

Clinical staging (Ann Arbor)

The clinical stage of lymphoma was IEA in five cases, IIEA in one case and IVEA in one case. Stage II disease had lymph node involvement at peripancreatic, porta hepatis, celiac axis, retroperitoneal lymphadenopathy on a contrast enhanced CT scan of the abdomen: disseminated lymphoma. The majority of the cases were limited disease by the Ann Arbor staging system (Table 1).

Treatments

The treatment modality that 7 patients received is shown in Table 1. Five patients underwent initial therapy with systemic chemotherapy, of which 4 patients received chemotherapy alone and 1 patient was treated with the combination of chemotherapy and radiotherapy. Two patients were treated with only radiotherapy.

Discussion

Although nearly 25% of NHLs arise in extranodal locations, skeletal muscle involvement is rare.[3] Primary NHL of the muscle can be diagnosed on the basis of the following 3 criteria; 1) muscle NHL diagnosis from the histologic analysis, 2) absence of systemic nodal disease, 3) absence of bone marrow infiltration or marrow disease much less extensive that in the soft tissue.[10] All these criteria were satisfied in the present case. Malignant neoplasms, especially extranodal NHL, originating from the masticator space muscles are exceedingly rare which has been reported in only 7 cases so far.[3-9]

The most common histologic subtype of extranodal lymphoma involving skeletal muscle is DLBCL, followed by anaplastic large cell lymphoma (ALCL).[11] Although the number of cases in our study was small, DLBCL and LPC were common histologic subtype of NHL originating from the masticatory space muscle.

The diagnosis of extranodal NHL at atypical sites in the head and neck may be often delayed because of the nonspecific symptoms.[6,7] Clinical presentation of the skeletal muscle NHL varies from the indolent to the rapidly progressive including muscle pain, swelling, and a rapidly enlarging mass.[11,12] However, painless facial swelling was the most common symptom in our review. Therefore, physicians should be cautious and should always consider the possibility of lymphoma when patients present with cheek swelling. Also, in primary skeletal muscle NHL, systemic symptoms (B symptoms) occur in a minority[12], but there was no case with B symptoms in our study.

Although imaging studies play an important role in assessing primary skeletal muscle lymphoma[3], none of them is specific enough to make a definite diagnosis.[12] US is often an initial procedure performed because it can differentiate intramuscular lesions from external ones and its major role is as a guidance technique for biopsy.[12,13] US may show a solid, ill-defined hypoechoic lesion with thickened fibroadipose septa.[11,12] CT scans may reveal a hypodense to isodense with respect to muscle, ill-defined soft tissue mass with heterogeneous enhancement within the muscle[3], but are not sufficient for accurate evaluation. CT-derived information regarding deep-tissue tumor size and extent is critical to planning the radiotherapy ports.[6] Also, CT is best used for staging scans of the thorax and abdomen.[3,12] MRI provides the most detailed anatomical definition of skeletal muscle lymphoma and specific MRI findings of skeletal lymphoma would be of value in differential diagnosis.[12,13] MRI shows involvement of individual muscles, the extent of disease within a muscle and the infiltration of subcutaneous fat.[12] Based on MRI findings of our study, NHL originating from the masticatory space muscle has been described as isointense relative to normal muscle on the T1-weighted sequence and hyperintense on the T2-weighted sequence with moderate enhancement which is similar to the signal characteristics of primary NHL originating from other skeletal muscles.[3] Primary skeletal muscle NHLs show significant FDG uptake with a mildly increased activity on 18FDG-PET/CT.[3] Previous studies have shown that there is an excellent correlation between the area of abnormal uptake in 18FDG-PET/CT and the extent of signal abnormality in an MRI.[10] However, 18FDG-PET/CT may be falsely diagnosed as positive because of the nonspecificity of FDG uptake by skeletal muscle.[3]

The diagnosis of primary skeletal muscle NHL can be confirmed by the histopathological findings. So, having a larger core biopsy with more material may be necessary for the diagnosis.[11] Also, the appropriate handling of the tissue at biopsy including immunohistochemical analysis aids in the diagnosis and characterization of NHL, and thus ensuring appropriate treatment for these malignancies.[8]

Differentiation of primary skeletal muscle lymphoma from various neoplastic and inflammatory diseases often is difficult on the basis of clinical and imaging findings alone.[2,13] Also, primary skeletal

muscle NHL may mimic sarcoma, metastatic carcinoma, melanoma, rhabdomyoblastoma, rhabdomyosarcoma, and osteosarcoma causing diagnostic difficulties.[14] However, it is critical to differentiate lymphoma from sarcoma and other entities to avoid unnecessary excisions.[11]

The treatment of primary skeletal muscle lymphoma relies predominantly on the histology, the clinical stage and the patient's characteristics.[3] However, there is no specified treatment for primary skeletal muscle lymphoma so far. The more recent cases treated with immune (rituximab) and polychemotherapy showed much better outcomes.[3] Although the prognosis of primary skeletal muscle lymphoma is poor compared with that of lymph node lymphoma, especially at stages III-IV[15], previous cases of primary masticatory space muscle lymphoma have been reported to respond well to chemotherapy or local radiotherapy on the basis of our review.

Conclusions

On the basis of our, we suggest two conclusions. First, primary muscle lymphoma particularly originating from muscles of mastication and facial expression is extremely rare, but primary muscle lymphoma should be considered in the differential diagnosis of muscular masses. Second, primary muscle lymphoma particularly originating from muscles of mastication and facial expression has similar clinical and radiological characteristics to primary skeletal muscle lymphoma involving other sites except the more favorable prognosis.

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Author's contribution:

Data gathering and idea owner of this study: Hyun Jin Min, Kyung Soo Kim

Study design: Hyun Jin Min, Kyung Soo Kim

Data gathering: Hyun Jin Min, Kyung Soo Kim

Writing and submitting manuscript: Hyun Jin Min, Kyung Soo Kim

Editing and approval of final draft: Hyun Jin Min, Kyung Soo Kim

Table 1. The histopathological subtypes, clinical staging and treatment modality

Histotopathological subtypes	Number
Non-Hodgkin's lymphoma	8
Diffuse large B-cell lymphoma (DLBCL)	2
Lymphoplasmacytoid B-cell lymphoma (LPC)	2
Lymphoblastic lymphoma (LBL)	1
NK/T cell lymphoma	1(our case)
Not described in detail	2
Clincal staging (Ann Arbor)	
Stage IEA	5
Stage IIEA	1
Stage IVEA	1
Not described in detail	1
Treatment modality	
Chemotherapy	4
CHOP* only	1
CHOP + Rituximab	1
M-BACOD** + GM-CSF	1
Regiment not defined	1
Chemotherapy (CHOP) + Radiation therapy	1(our case)
Radiation therapy	2
Not described in detail	1

* : cyclosphsphamide, doxorubicin, vincristine, prednisolone

**: methotrexate, bleomycin, bleomycin, doxorubicin, clyclophosphamide, vincristine, dexamethasone

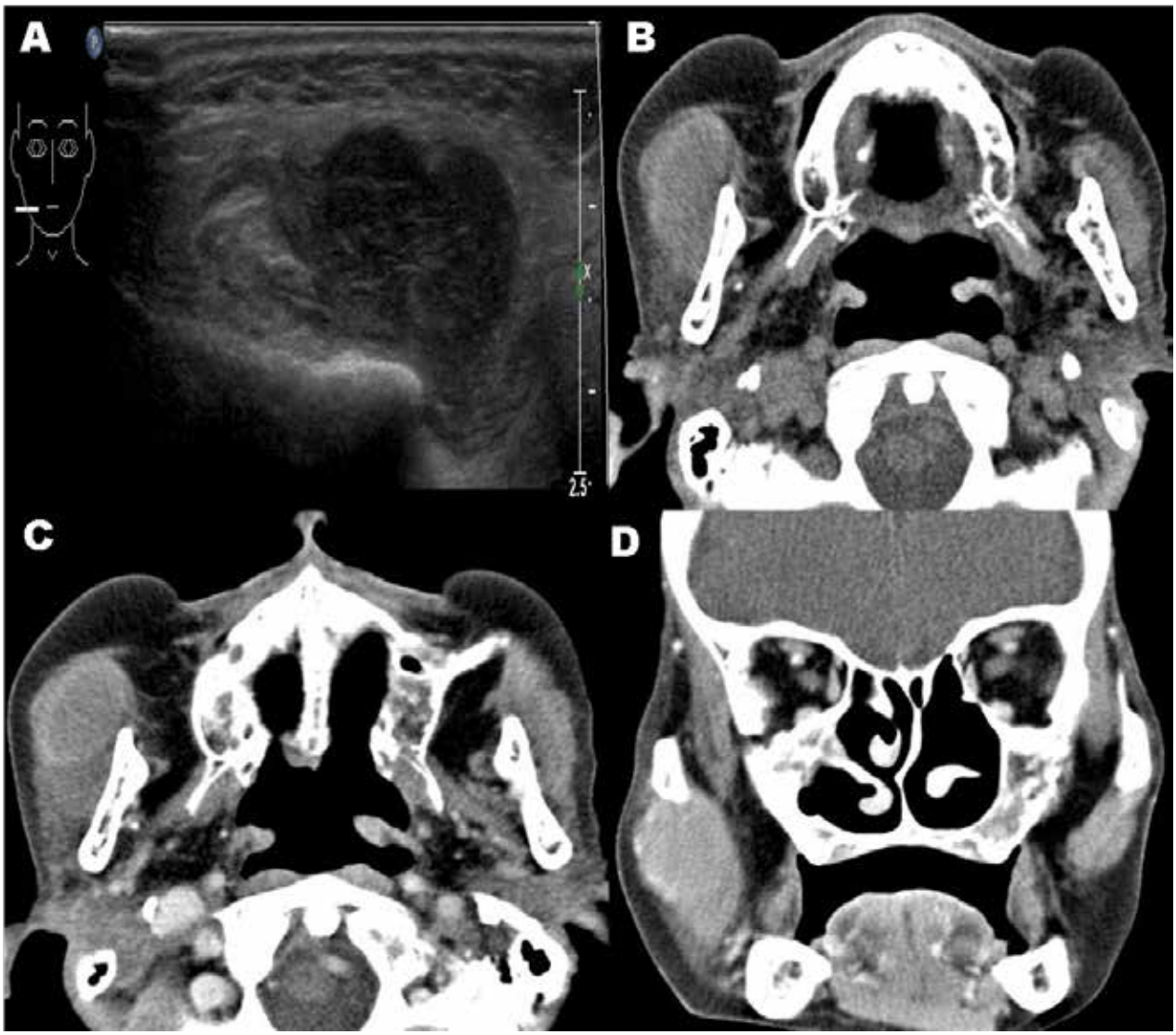

Figure 1. US (A) showed 2.3cm sized intramasseter mass lesion and CT scans (B: axial view without contrast enhancement, C & D: axial and coronal view with contrast enhancement) demonstrated a 3x4x4cm sized, well-marginated soft tissue density replacing right masseter muscle with uniform enhancement and surrounding soft tissue infiltration.

References:

1. Komatsuda M, Nagao T, Arimori S. An autopsy case of malignant lymphoma associated with remarkable infiltration in skeletal muscles. *Rinsho Ketsueki* 1981;**22**:891-895.
2. Hwang S. Imaging of lymphoma of the musculoskeletal system. *Radiol Clin North Am*. 2008;**46**:379-396.
3. Guastafierro S, Falcone U, Petriccione L, et al. An usual cause of facial swelling: Primary extranodal non-Hodgkin lymphoma of the masseter muscle. *Am J Med Sci*. 2011;**341:**160-162.
4. Chong J, Som PM, Silvers AR, Dalton JF. Extranodal non-Hodgkin lymphoma involving the muscles of mastication. *Am J Neuroradiol* 1998;**19:**1849-1851.
5. Set PAK, Somers JM, Britton PD, Freer CEL. Pictorial review: benign and malignant enlargement of pterygo-masseteric muscle complex. *Clin Radiol* 1993;**48**:57-60.
6. Harnsberger RH, Bragg DG, Osborn AG, et al. Non-Hodgkin's lymphoma of the head and neck: CT evaluation of nodal and extranodal sites. *Am J Roentgenol* 1987;**149:**785-791.
7. Cyesens C, Horvath M, Termote JL, Lemahieu SF. Extranodal non-Hogkin's lymphoma of the head and neck presenting as a mandibular swelling: report of two cases. *J Belge Radiol* 1992;**75:**37-39.
8. Muralee Mohan C, Thakral A, Bhat SK. Primary

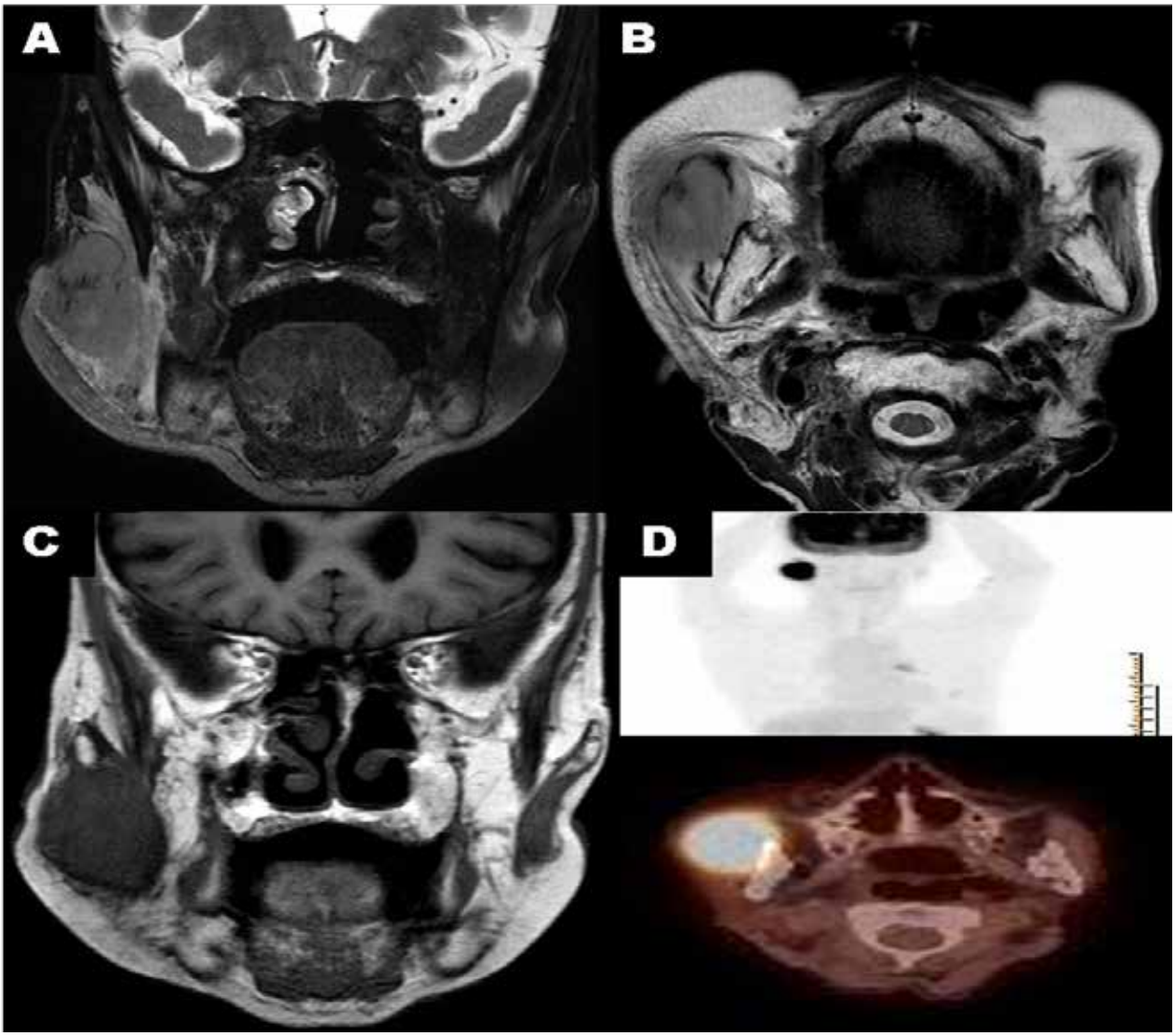

Figure 2. MRI showed a well-defined soft tissue mass with homogeneous signal intensity in the right masseter muscle. The lesion was isointense to muscle on T1WI (A) and hyperintense on T2WI (B & C). 18F-PET CT scans (D) showed hypermetabolic cheek mass with the maximum standardized uptake value (SUV) of 11.9, but did not reveal other localization

extranodal non-Hodgkin's lymphoma involving masseter and buccinators muscles. *Int J Oral Maxillofac Surg* 2012**;41:**1393-1396.

9. Connor SE, Chavda SV, West R. Recurrence of non-Hodgkin's lymphoma isolated to the right masticator and left psoas muscles. *Eur Radiol* 2000;**10:**841-843.
10. Lee VS, Martinez S, Coleman RE. Primary muscle lymphoma: clinical and imaging findings. *Radiology* 1997;**203:**237-244.
11. Hatem J, Bogusz AM. An unusual case of extranodal diffuse large B-cell lymphoma infiltrating skeletal muscle: a case report and review of the literature. *Case Rep Pathol* 2016;2016:9104839.
12. Beggs I. Primary muscle lymphoma. *Clin radiol* 1997;**52:**203-212.
13. Chun CW, Jee WH, Park HJ, et al. MRI features of skeletal muscle lymphoma. *AJR Am J Roentgenol* 2010;**195**:1355-1360.
14. Alamdari A, Naderi N, Peiman S, Shahi F. Non-Hodgkin lymphoma with primary involvement of skeletal muscle. *Int J Hematol Oncol Stem Cell Res* 2014;**8:**55-57.
15. Zhang L, Lin Q, Zhang L, Dong L, Li Y. Primary skeletal muscle diffuse large B cell lymphoma: A case report and review of the literatures. *Oncol Lett* 2015;**10**:2156-2160.