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IRF4-Rearranged Large B-cell lymphoma on Waldeyer's Ring; A Case Report

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To the editor,

Large-B cell lymphoma (LBCL) with IRF4 rearrangement is a newly recognized and rare entity. LBCL is characterized with co-expression of MUM1 and BCL6. It has been associated with young age and a favorable outcome. Most patients present with predominantly Waldeyer's ring or neck or head lymph node involvement (1,2,3). Here, we present a case with LBCL with IRF4 rearrangement in an old male.

A 67-year-old man admitted to hospital with sore throat, dysphagia and a lump in the right cervical region. Physical examination showed that the right palatin tonsil was enlarged and there was a 2 cm cervical lymphadenopathy unilaterally. After one week's antibiotic therapy, the lymphadenopathy still persisted. Patient underwent excisional lymph node biopsy which was consistent with large B-cell lymphoma of germinal center type, **mainly follicular and focally diffuse pattern.** Immunohistochemistry panel was positive for CD20 **(clone L26; Scytek)**, CD10 **(clone 56C6; Biocare)** , bcl-6 **(clone LN22; Biocare Medical)** and MUM1 **(clone BC5; Biocare Medical)** ; bcl-2 **(clone 12 4; Scytek)** and myc **(clone MYC; Biocare)** were negative (figure 1a). **Different from follicular lymphoma and diffuse large B cell lymphoma, neoplasm is mainly composed of centroblast like large cells with germinal center phenotype and strong co-expression of MUM1. Morphologic and immunohistochemical findings reminded us the possibility of IRF4-rearranged large B-cell lymphoma.** FISH analysis for IRF4 rearrangement **(IRF4, DUSP22 dual color break apart probe)** was performed and thus rearrangement was positive (figure 1b). Based on these findings, a large B-cell lymphoma with IRF4 rearrangement was diagnosed. PET-CT showed an increased FDG-uptake on the right tonsil with level IIA-III cervical stations (figure 1c). Clinical staging studies led us to stage I disease, IPI-score was calculated as 1. After four cycles of R-$CHOP_{21}$, PET-CT showed complete remission (figure 1c). No further therapy was indicated and 3 months after the chemotherapy, no evidence was observed for any recurrence. Salaverria et al. studied 720 lymphomas and screened a group of 427 cases for IRF4. They identified 20 lymphomas with proven IG/IRF4 fusion with a median age of 12 years. The IRF4 positive lymphomas were mostly presented as a limited disease in the head and neck region especially in Waldeyer's ring, and was associated with a better prognosis (1).

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Ramis-Zaldivar et al. studied 20 LBCL-IRF4 pediatric and young adult cases with a median age of 14 years. Eight patients had nodal involvement of head and neck region, 8 cases had tonsillary involvement. Fifteen patients had complete remission after therapy without evidence of relapse up to 99 months in follow-up, thus a very favorable outcome was showed among LBCL-IRF4 cases (4).

Older age is considered to be an adverse prognostic factor in patients with Waldeyer's ring NHL and as an independent risk factor for inferior survival among patients with DLBCL (3,5). FLYER study results show that four cycles of CHOP chemotherapy has the same effect among young patients with aggressive B-cell lymphoma who have favorable risk profile and stage I-II disease (6). Our patient had no other risk factors except his age, and had IRF4 gene arrangement, thus we ended the chemotherapy after fourth cycle of chemotherapy by negative PET-CT result.

In conclusion, IRF4 gen analysis should be considered by the patients in any age with Waldeyer's ring LBCL with germinal center origin, **follicular and/or diffuse pattern** and strong MUM1 expression on pathological examination. The presence of IRF4 rearrangement may affect prognosis of the disease and the duration of chemotherapy.

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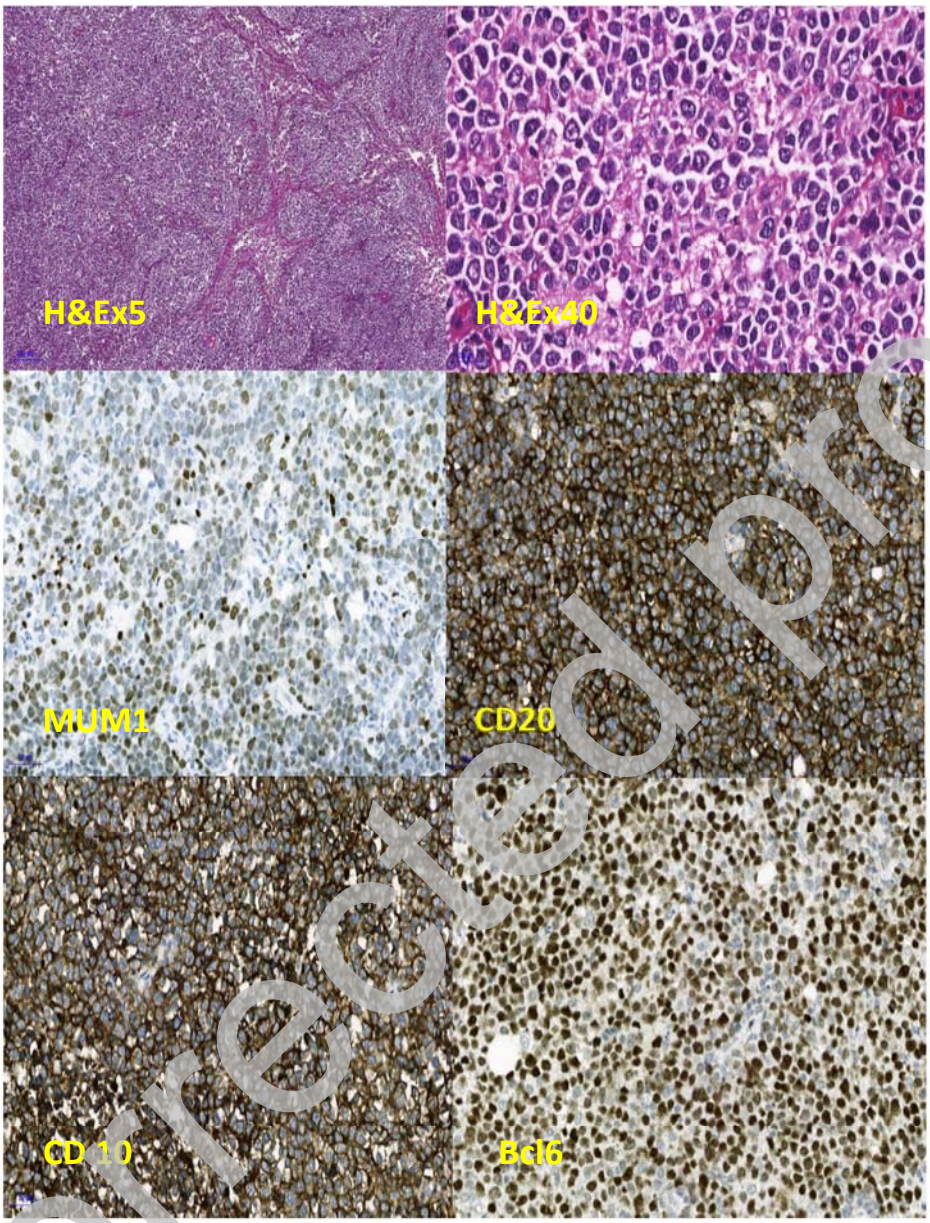
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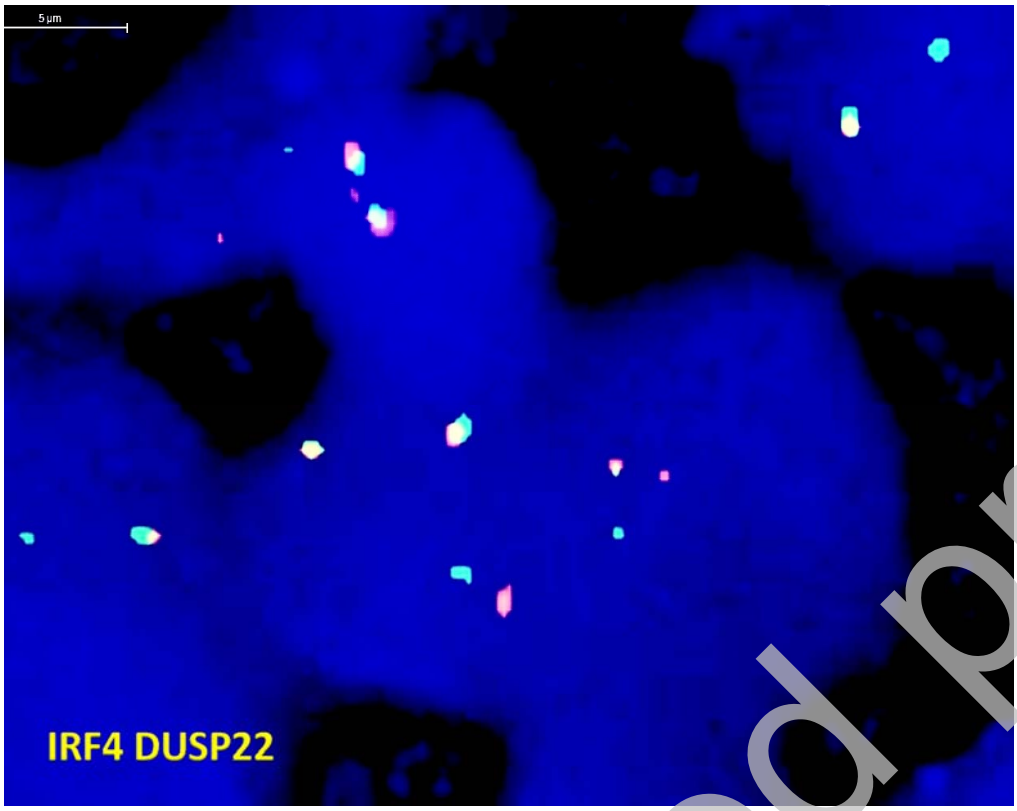
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B.

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C.

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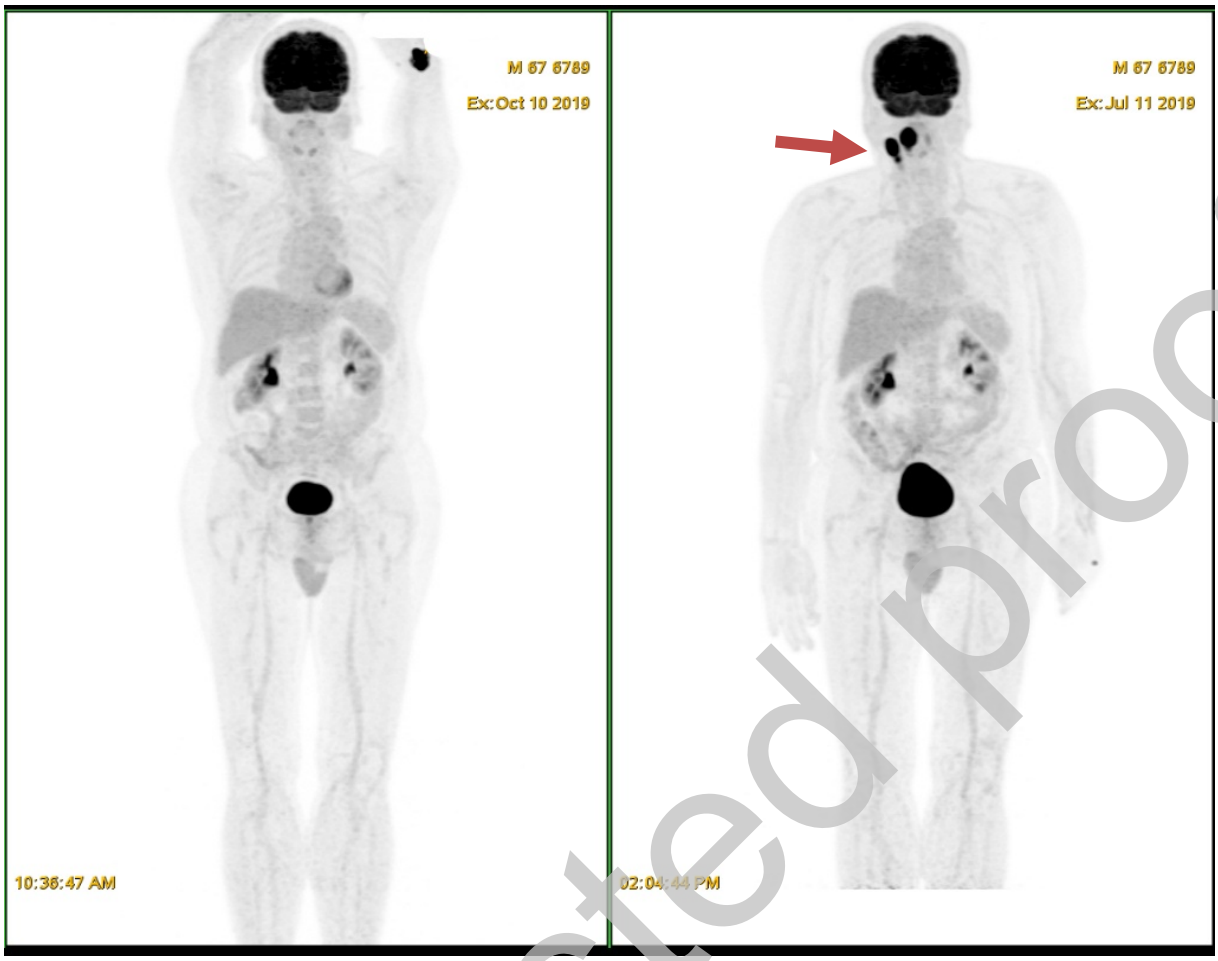


Figure 1. Large B-cell lymphoma with IFR4 rearrangement.
(A) Follicular and diffuse pattern, HE, original magnification x5
Medium to large- sized neoplastic cells with vesicular chromatine and 2-3 nucleoli, HE, original magnificationx40
The large cells with positive expression of MUM1, CD20, CD10 and bcl6, original magnification x20
(B) FISH analysis demonstrated a positive IRF4 translocation
(C) Comparative PET-CT images (before and after treatment)

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