Large B-cell lymphoma with IRF4 rearrangement in a 63 year old male (SH2017-0341).

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Clinical History

• 63-year-old man with dysphagia, odynophagia and 10-20 lb weight loss X 3-4 months. History of cigarette smoking and heavy alcohol use.

• CT Scan- large spherical pedunculated mass arising from the base of tongue filling the oropharynx and obscuring the vallecula, larynx, and left pyriform sinus and occupying approximately 80% of the oropharynx was seen.

• No other adenopathy or organomegaly was noted.
Oropharyngectomy specimen

4.0 x 3.5 x 3.0 cm tan-white, firm, fleshy, homogenous, pedunculated mass with ill-defined borders
Flow cytometry

B-cells: CD20+, CD19 variable+

CD5-, CD10+

Kappa light chain restricted
Karyotype

45, X, dic(Y;17)(p11.2; p11.2), i(1)(q10), del(4)(q12q35), t(4;15)(p16;q22), +7, -15
FISH for *IRF4/DUSP22* breakapart DNA probe

Positive for disruption at or near the IRF4/DUSP22 region
apparently normal chromosome 6 with a stable signal for IRF4/DUSP22

5' IRF4/DUSP22 signal

abnormal chromosome 6 with a 3' IRF4/DUSP22 signal
Proposed diagnosis and Panel diagnosis

• LARGE B-CELL LYMPHOMA WITH IRF4 REARRANGEMENT.
Salient features of this case

• Follicular and diffuse areas composed of mostly large cells and a high Ki67 index.
• IHC- Germinal center phenotype (CD10+, BCL6+) but with a significant expression of IRF4/MUM1.
• Cytogenetic abnormalities

• Follow up- 3 cycles of R-CHOP chemotherapy and shows no evidence of disease on most recent PET CT Scan 9 months after the initial diagnosis.
Diagnostic clues

- Site- Head and neck region including Waldeyer’s ring
- Limited disease stage
- Age- Mostly childhood and young adulthood (mean about 30 years) but older individuals have been reported.
- Morphology- Diffuse large B-cell lymphoma (DLBCL) or follicular lymphoma (FL) grade 3 or a combination
- IHC- strong expression of IRF4/MUM1 and BCL6 and lack both PRDM1/BLIMP1 expression and t(14;18)/BCL2 breaks
- CD5 (~30%, cases are usually CD10-), BCL2 (~60%), CD10 (~60%) can be expressed. By Hans algorithm- can be classified as GCB or Non-GCB
- On cytogenetics- 95% demonstrate chromosomal alterations with an average of 6/ case
- FISH- for IRF4/ MUM1 breakapart- as rearrangement is cryptic
- BCL6 and MYC breaks have been described.
E: IRF4 expression

F: BCL6 expression

(Blood. 2011;118(1):139-147)
Prognosis- favorable prognosis

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Copy number analysis of IRF4 translocated DLBCL and FL

Figure 2. Copy number profiles of 23 IRF4 translocation-positive lymphomas. On the x-axis, the chromosomes are represented horizontally from 1 to x, on the y-axis, the percentage of cases showing copy number alterations. Gains are represented on the positive y-axis and colored in green, whereas losses are represented on the negative y-axis in red. The most frequent alterations were gains of Xq28, 11q22.3-qter, and 7q32.1-qter, and losses of 6q13-16.1, 15q14-22.31, and 17p. Candidate genes in regions of gain are displayed in green and in regions of loss in red.

Cytogenetics from our case –
45,X,dic(Y;17)(p11.2;p11.2),i(1)(q10),del(4)(q12q35),t(4;15)(p16;q22),+7,-15
DLBCL of Waldeyer’s ring

• Most patients (92%) had stage I–II disease.
• GCB immunophenotype 61% and BCL2 expression in 55%.
• *BCL2*, *BCL6*, *IRF4* and *MYC* breakpoints in 7%, 25%, 8% and 10% respectively.
• Variable follicular pattern in 44%.
Differential diagnosis

- CD10-/MUM1+ FL –
  - Elderly
  - poor prognosis
- CD10+/MUM1+ DLBCL, NOS –
- Pediatric type FL
Final Panel diagnosis

• LARGE B-CELL LYMPHOMA WITH IRF4 REARRANGEMENT.
Thank you