Early Hodgkin Lymphoma

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Hodgkin Lymphoma

- Is the first curable malignant disease
- It is a model
- The majority of patients are cured
- Patients are young
- There are important long-term side effects
- Risk groups should be established to adjust the treatment
  - Maintain high cure rates and reduce secondary effects
Definition

- Early stage HL is defined as stage I or II disease
  - Stage I: involvement of a single lymph node region (I) or of a single extralymphatic organ or site (IE)
  - Stage II: involvement of two or more lymph node regions on the same side of the diaphragm (II) or with involvement of limited, contiguous extralymphatic organ or tissue (IIE)
Staging of lymphoma
Cotswolds Staging classification

Stage I  Stage II  Stage III  Stage IV
Subsequent stratification: favorable and unfavorable

- Presence or absence of certain clinical features such as:
  - age
  - B symptoms
  - erythrocyte sedimentation rate (ESR)
  - number of nodal regions involved
  - large mediastinal mass
<table>
<thead>
<tr>
<th>EORTC–GELA</th>
<th>LYSA</th>
<th>GHSG</th>
<th>NCI-C/ECOG</th>
</tr>
</thead>
<tbody>
<tr>
<td>No large mediastinal mass</td>
<td>No large mediastinal mass</td>
<td>No large mediastinal mass</td>
<td></td>
</tr>
<tr>
<td>Age &lt;50 years</td>
<td>No extranodal disease</td>
<td>Age &lt;40 years</td>
<td></td>
</tr>
<tr>
<td>No elevated ESR&lt;sup&gt;a&lt;/sup&gt;</td>
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<td>ESR &lt;50 mm/h</td>
<td></td>
</tr>
<tr>
<td>1–3 involved nodal regions</td>
<td>1–2 involved nodal regions</td>
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<td>LPHL or NS histology</td>
</tr>
</tbody>
</table>

<sup>a</sup>ESR <50 mm/h without B symptoms or ESR <30 mm/h with B symptoms

EORTC European Organization for Research and Treatment of Cancer, GELA Groupe d’Etude des Lymphomes de l’Adulte, GHSG German Hodgkin Study Group, NCI-C National Cancer Institute of Canada, ECOG Eastern Cooperative Oncology Group, CS clinical stage, ESR erythrocyte sedimentation rate, LPHL nodular lymphocyte-predominant Hodgkin lymphoma, NS nodular sclerosis
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<td></td>
<td>LPHL or NS histology</td>
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*ESR <50 mm/h without B symptoms or ESR <30 mm/h with B symptoms*
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<td>No large mediastinal mass</td>
<td></td>
</tr>
<tr>
<td>Age &lt;50 years</td>
<td>No extranodal disease</td>
<td>Age &lt;40 years</td>
<td></td>
</tr>
<tr>
<td>No elevated ESR(^a)</td>
<td>No elevated ESR(^a)</td>
<td>ESR &lt;50 mm/h</td>
<td>LPHL or NS histology</td>
</tr>
</tbody>
</table>

\(^a\)ESR <50 mm/h without B symptoms or ESR <30 mm/h with B symptoms

Favorable prognosis: Choice of Initial therapy

- Requires a **careful balance** between providing **sufficient therapy** to eradicate the tumor and **avoiding** unnecessary treatment that could result in **excessive long-term treatment-related side effects**
Despite the increasing availability of guidelines for the treatment of HL, there must remain room for the individualization of treatment:

- Patient preference
  - Higher risk of recurrence or less toxic regimen
- Special scenarios
  - Young females (irradiation of breast tissue)
  - Older individuals
Caution:

Trials in HL have required long follow-ups to demonstrate differences in overall survival between different treatment regimens.

Example:

The large EORTC H8F trial only demonstrated a survival benefit with combined modality therapy compared to radiation alone after a 10-year follow-up.
EORTC-GELA H8F:

3 MOPP/ABVD + IFRT vs STNI

- Survival benefit only after 10-year FU

Fermé C et al. NEJM 2007, 357: 1916
Favorable prognosis: Choice of Initial therapy

- Combination chemotherapy plus radiation therapy (IFRT) results in higher-disease free survival compared with chemotherapy alone

- Overall survival is similar with both approaches
Combined modality therapy

- Combination chemotherapy plus involved-site or node radiation therapy (ISRT)
  - While RT acts to control known tumor sites
  - Chemotherapy is aimed at occult disease outside the field of radiation
The 1960s / Radiotherapy alone

- First therapeutic option

- Total / subtotal (STNI) / mantle / and inverted lymphatic irradiation

- EFRT *(extended-field)*: not only the clinically involved nodes, but also adjacent, clinically uninvolved (mantle or inverted Y)

- IFRT *(involved field)*: RT is limited to the clinically involved regions (mediastinal)

- ISRT *(involved site)*: RT field only tumor volume + margin

- INRT *(involved node)*: RT field volume Tumor + limited margin of healthy tissue (0.5-1 cm)
Early stage favorable HL: randomized studies of radiotherapy alone

<table>
<thead>
<tr>
<th>Trial</th>
<th>Year</th>
<th>Study arms</th>
</tr>
</thead>
<tbody>
<tr>
<td>EORTC H1</td>
<td>1964–1971</td>
<td>A. Mantle field or inverted-Y RT</td>
</tr>
<tr>
<td>EORTC H2</td>
<td>1972–1976</td>
<td>node RT</td>
</tr>
</tbody>
</table>
| EORTC H5F     | 1977–1982  | Laparotomy negative patients  
|               |            | A. Mantle field RT                                                         |
| EORTC H6F     | 1982–1987  | B. STNI                                                                     |
|               |            | A. Laparotomy, if negative: mantle field RT for LP or NSc histology  
|               |            | STNI for MC or LD histology                                                |
|               |            | B. STNI                                                                     |
| EORTC H7VF-H8VF | 1988–1993 | Mantle field RT                                                 |
| GHSG HD4      | 1988–1994  | A. STNI 40 Gy                                                               |
|               |            | B. STNI 30 Gy + IFRT 10 Gy                                                 |
To summarize, in the 1990s, STNI was considered standard treatment for early, favorable HL. However, 25-30% of patients eventually relapsed with subsequent 10-year survival rates of only 60%.
Optimal radiation field size

- Over the years there has been a movement to decrease the field of radiation in order to limit acute and long-term toxicities and maintain survival rates.
Cumulative incidence of breast cancer after HL treatment

De Bruin ML et al. JCO 2009:; 4229-4231
Analysis of Competing Risks of Causes of Death and their Variation Over Different Time Periods in Hodgkin’s Disease

Mariano Provencio,1 Isabel Millán,2 Pilar España,1 Antonio C. Sánchez,1 José J. Sánchez,2 Blanca Cantos,1

Table 2. Cumulative incidence with 95% confidence intervals of Causes of death

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of patients at risk</th>
<th>Death from disease</th>
<th>Death from second tumor</th>
<th>Death from infection</th>
<th>Death from toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>464</td>
<td>3.8 (2.5-5.9)</td>
<td>0.4 (0.1-1.5)</td>
<td>2.7 (1.6-4.5)</td>
<td>2.3 (1.3-4)</td>
</tr>
<tr>
<td>5</td>
<td>371</td>
<td>8.3 (6.2-11.1)</td>
<td>2.1 (1.1-3.8)</td>
<td>4.3 (2.9-6.5)</td>
<td>3.7 (2.5-5.7)</td>
</tr>
<tr>
<td>10</td>
<td>230</td>
<td>10.4 (8-13.6)</td>
<td>6.3 (4.3-9.1)</td>
<td>5.6 (3.8-8.2)</td>
<td>4.4 (2.9-6.6)</td>
</tr>
<tr>
<td>15</td>
<td>130</td>
<td>11.7 (9-15.3)</td>
<td>8.1 (5.6-11.6)</td>
<td>5.6 (3.8-8.2)</td>
<td>4.7 (3.2-7.1)</td>
</tr>
</tbody>
</table>
Patients Receiving XRT + Chemotherapy for Early-Stage Disease

The International Lymphoma Radiation Oncology Group has published field guidelines for modern radiation in HL (Specht L IJROBP 2014, 89:854)

- ISRT (involved-site): includes pre- and post-chemotherapy volumes plus a margin of healthy tissue
- INRT: is considered a form of ISRT with more stringent requirements, including nodal volumes plus very limited margin of healthy tissue (0.5-1 cm) PET/CT
  - however it is technically challenging
Comparison between radiation field sizes

Girinsky T et al. Radiat Oncol IFRT INRT

IFRT

INRT

Girinsky T et al. Radiat Oncol
Due to the high rate of relapses and long-term secondary effects:

- STNI and EFRT were abandoned
- and the role of QT was studied

Induction with MOPP:

- reduces relapses without improving OS
- high rate of hematological toxicity and secondary neoplasias
Early stage and good prognosis: therapy

- Chemotherapy regimen in combination with RT
  - doses
  - number of cycles
- Radiation
  - field size
  - dose
- Chemotherapy alone
Early stage and good prognosis: therapy

- Chemotherapy regimen in combination type
  - ABVD is the preferred combination chemotherapy
  - Stanford V remains an acceptable alternative

- Few randomized trials have compared different regimens in combination with RT
  - most used regimens that contained an alkylating agent (MOPP)
Chemotherapy regimen

- Preference ABVD rather than alkylating-agent:
  - extrapolation of trials in patients with more advanced HL
    - ABVD superior efficacy and less toxicity
      - ABVD plus IFRT has not been directly compared with Stanford V plus RT in the treatment of early favorable prognosis
  - Omission of dacarbazine and/or bleomycin from ABVD decreases its efficacy
    - German Hodgkin Study Group (GHSG) HD 13
GHSG HD 13 (1500 patients) with favorable I-II

Treatment: 2 cycles: (ABVD, AVD, ABV, AV) + 30 Gy IFRT

AV, ABV arms **were closed** early due to high rates of progression during initial therapy

- 3% - 5% versus <1% with ABVD
- Overall five-year survival was not significantly different
  - 98, 98, 94 and 98 percent

Neither bleomycin nor dacarbazine should be omitted from ABVD

Behringer K et al. Lancet 2015, 385:1418
Early stage and good prognosis: therapy

- Chemotherapy regimen in combination
  - type
    - ABVD
  - number of cycles
- Radiation field size
- Radiation dose
- Chemotherapy alone
Early stage and good prognosis: therapy

- Chemotherapy regimen in combination
  - type
    - ABVD
  - number of cycles
    - Most trials have evaluated **four or more** cycles of ABVD
  - *German trial...*
    - GHSG

At a median follow-up of 7.5 years: there was no significant difference between four and two cycles in overall survival (97.1% vs 96.6%) and progression-free survival (93.5% vs 91.2%)

More toxicity (WHO grade III/IV events): 52% vs 33%

Engert A et al. NEJM 2010; 363: 640

The results of this trial suggest that 2 cycles ABVD + 20 Gy, may be sufficient treatment for patients with favorable presentation, as defined by GHSG

No more than 2 sites, no extranodal extension, no mediastinal mass > 1/3 and ESR < 50

Engert A et al NEJM 2010; 363: 640
Chemotherapy alone

- A number of clinical trials have compared chemotherapy alone vs combined therapy, but with problems:
  - suboptimal chemotherapy
  - different regimens
  - large field
  - higher doses of radiotherapy
  - variations in type of chemotherapy
  - …
4-6 cycles of ABVD vs STNI 35 Gy. (450 patients, FU 11 years)

- QT less local control 87% vs 92%
- QT better OS, at 11 years
  - 94% vs 87%
  - 80% can be cured with QT alone

The treatment phase of the HD.6 trial preceded the use of positron-emission tomography (PET), and no patients underwent this type of scanning.
Treatment adaption based on PET Scan response

- Most studies with early interim PET were performed in patients with advanced stages.
- There are two randomized trials evaluating whether radiation therapy could be avoided.
Treatment adaption based on PET Scan response

**H10F:**
- 2 cycles ABVD → FDG PET → Any outcome → 1 cycle ABVD + IN-RT 30 Gy
- Negative: → 2 cycles ABVD
- Positive: → 2 cycles BEACOPP esc + IN-RT 30 Gy

**RAPID:**
- 3 cycles ABVD → FDG PET → Negative → IF-RT 30 Gy
- Positive → 1 cycle ABVD + IR-FT 30 Gy

**PFS:**
- 87.1% if no RT
- 99% if RT

**OS:**
- 99.6% if no Rt
- 100% if RT

**European H10-F trial**
- Trial closed early due to futility
  - 444 patients
  - Median follow-up 13 months
  - Futility analysis based on 33 events
  - Non-inferiority margins 10%
  - PET2-negative patients:
    - 1-year PFS 94.9 % if no RT
    - 1-year OS 100 % if INRT

**UK RAPID trial**
- Trial considered positive
  - 600 patients
  - Median follow-up 48.6 months
  - Final analysis based on 36 events
  - Non-inferiority margins 7%
  - PET2-negative patients:
    - 3-year PFS 90.8 % if no RT
    - 3-year OS 99.5 % if IFRT

Raemaekers JM, et al. HD10 trial. JCO 2014; 32.1188
Cologne 2016
The question of whether RT can be omitted in patients with complete metabolic response at interim PET is currently a matter of debate and cannot be fully answered to date.

Interim PET-guided treatment in limited stage HL is not recommended outside clinical studies (ESMO Guidelines).

*Risk factors include large mediastinal mass, extranodal disease, high ESR and/or ≥3 involved areas.
Conclusions

- 2 ABVD + 20–30 Gy IFRT is the standard
- At 8 years: DFS: 86% and OS: 95%
- More patients die as a result of secondary effects due to the treatment than from the disease itself
- With QT alone (ABVD), disease local control is lost in 7-10%, but not in OS
Reflections

- RT after PET (-) improves PFS, but at the cost of irradiating more patients, the majority (approx 90%) of whom are already cured.

- The loss of disease control may be compensated by less long-term secondary effects.
  - 3 cycles of QT and PET(-): gives a good option for cure but is not yet considered a standard.
  - Longer follow-ups are required (10-20 years).
### Early Unfavorable Hodgkin Lymphoma

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>EORTC</th>
<th>GHSG</th>
<th>NCIC/ECOG</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(a) Large mediastinal mass</td>
<td>(a) Large mediastinal mass</td>
<td>(a) Histology other than LP/NS</td>
</tr>
<tr>
<td></td>
<td>(b) Age ≥50 years</td>
<td>(b) Extranodal disease</td>
<td>(b) Age ≥40 years</td>
</tr>
<tr>
<td></td>
<td>(c) ESR ≥50 without B symptoms or ≥30 with B symptoms</td>
<td>(c) ESR ≥50 without B symptoms or ≥30 with B symptoms</td>
<td>(c) ESR ≥50</td>
</tr>
<tr>
<td></td>
<td>(d) ≥4 nodal areas</td>
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<td>(d) ≥4 nodal areas</td>
</tr>
<tr>
<td>Favorable</td>
<td>CS I–II (supradiaphragmatic) without risk factors</td>
<td>CS I–II without risk factors</td>
<td>CS I–II without risk factors</td>
</tr>
</tbody>
</table>

_EORTC_ European Organisation for Research and Treatment of Cancer, _GHSG_ German Hodgkin Study Group, _NCIC_ National Cancer Institute of Canada, _ECOG_ Eastern Cooperative Oncology group, _ESR_ erythrocyte sedimentation rate, _LP_ lymphocyte predominance, _NS_ nodular sclerosis, _CS_ clinical stage
## Randomized clinical trials in unfavorable CS I/II

<table>
<thead>
<tr>
<th>Trial (ref)</th>
<th>Treatment</th>
<th>Number of patients included</th>
<th>PFS (years)</th>
<th>OS (years)</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>EORTC/GELA</td>
<td>ABVDx6 + IF-RT 30–36 Gy</td>
<td>276</td>
<td>91 % (4)</td>
<td>95 % (4)</td>
<td>Not final analysis</td>
</tr>
<tr>
<td>H9U [14]</td>
<td>ABVDx4 + IF-RT 30–36 Gy</td>
<td>277</td>
<td>87 % (4)</td>
<td>94 % (4)</td>
<td>EFS instead of PFS</td>
</tr>
<tr>
<td></td>
<td>BEACOPPx4 + IF-RT 30–36 Gy</td>
<td>255</td>
<td>90 % (4)</td>
<td>93 % (4)</td>
<td>n.s.</td>
</tr>
<tr>
<td>GHSG HD11 [15]</td>
<td>ABVDx4 + IF-RT 30 Gy</td>
<td>356</td>
<td>87 % (5)</td>
<td>94 % (5)</td>
<td>Final analysis</td>
</tr>
<tr>
<td></td>
<td>ABVDx4 + IF-RT 20 Gy</td>
<td>347</td>
<td>82 % (5)</td>
<td>94 % (5)</td>
<td>n.s.</td>
</tr>
<tr>
<td></td>
<td>BEACOPPx4 + IF-RT 30 Gy</td>
<td>341</td>
<td>88 % (5)</td>
<td>95 % (5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>BEACOPPx4 + IF-RT 20 Gy</td>
<td>351</td>
<td>87 % (5)</td>
<td>95 % (5)</td>
<td></td>
</tr>
<tr>
<td>GHSG HD14 [16, 17]</td>
<td>ABVDx4 + IF-RT 30 Gy</td>
<td>757</td>
<td>89 % (5)</td>
<td>97 % (5)</td>
<td>(p&lt;0.001) (PFS)</td>
</tr>
<tr>
<td></td>
<td>BEACOPPesc.x2 + ABVDx2 + IF-RT 30 Gy</td>
<td>744</td>
<td>95 % (5)</td>
<td>96 % (5)</td>
<td>(p=0.7) (OS)</td>
</tr>
<tr>
<td>Intergroup USA [18]</td>
<td>ABVDx6 + IF-RT 36 Gy</td>
<td>395</td>
<td>74 % (5)</td>
<td>88 % (5)</td>
<td>n.s.</td>
</tr>
<tr>
<td></td>
<td>Stanford V + IF-RT 36 Gy</td>
<td>399</td>
<td>71 % (5)</td>
<td>88 % (5)</td>
<td>70 % CSIII/IV</td>
</tr>
</tbody>
</table>

Engert-Younes 2015; Book Hodgkin Lymphoma
GHSG HD11

- 1300 patients
- 4 cycles of ABVD + 30 Gy IFRT standard

Number of Cycles of Chemotherapy

- Only a few randomized trials have addressed the issue of the number of cycles required.

**EORTC/GELA randomized H8 trial**
comparing different numbers of cycles with different radiation fields

**EORTC/GELA H9U:** 4 vs 6 ABVD + IFRT 30 Gy, EFS at 4 years: 87% vs 91%
Dose-Intensification in Early Unfavorable Hodgkin’s Lymphoma: Final Analysis of the German Hodgkin Study Group HD14 Trial

Bastian von Tresckow, Annette Plütschow, Michael Fuchs, Beate Klimm, Jana Markova, Andreas Lohri, Zdenek Kral, Richard Grün, Max S. Topp, Juliu Meissner, Josée M. Zijlstra, Martin Soekler, Harald Stein, Hans T. Eich, Rolf P. Mueller, Volker Diehl, Peter Borchmann, and Andreas Engert

1,655 patients

<table>
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<td>GHSG HD14 [16, 17]</td>
<td>ABVDx4 + IF-RT 30 Gy</td>
</tr>
<tr>
<td></td>
<td>BEACOPPesc x2 + ABVD x2 + IF-RT 30 Gy</td>
</tr>
</tbody>
</table>

Table 2. Failure Events and Late Effects*

<table>
<thead>
<tr>
<th>Event/Effect</th>
<th>Treatment Arm†</th>
<th>A (n = 765)</th>
<th>B (n = 763)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No. of Patients</td>
<td>%</td>
</tr>
<tr>
<td>Death resulting from:†</td>
<td></td>
<td>17</td>
<td>2.2</td>
</tr>
<tr>
<td>HL</td>
<td></td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Toxicity of study chemotherapy</td>
<td></td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Toxicity of salvage therapy</td>
<td></td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Secondary neoplasia</td>
<td></td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Suicide</td>
<td></td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Respiratory</td>
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<td>0</td>
<td>2</td>
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<tr>
<td>Brain</td>
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<td>0</td>
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<td>Other disease</td>
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<td>1</td>
<td>3</td>
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<tr>
<td>Unclear</td>
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<td>1</td>
<td>1</td>
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<tr>
<td>Progression or first relapse‡</td>
<td></td>
<td>64</td>
<td>8.4</td>
</tr>
<tr>
<td>Progression</td>
<td></td>
<td>23</td>
<td>3.0</td>
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<tr>
<td>Early relapse</td>
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<td>23</td>
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<tr>
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<td>18</td>
<td>2.4</td>
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<tr>
<td>Second relapse¶</td>
<td></td>
<td>11</td>
<td>3</td>
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<tr>
<td>Secondary malignancy¶</td>
<td></td>
<td>17</td>
<td>2.2</td>
</tr>
<tr>
<td>AML/MDS</td>
<td></td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>NHL</td>
<td></td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>Solid tumor</td>
<td></td>
<td>8</td>
<td>8</td>
</tr>
</tbody>
</table>
Control of disease and long-term effects: Dilemma

- EORTC/LYSA/FIL H10 trial (U)
- Hypothesis: patients who attain a negative PET after 2 cycles would not need additional RT

Non-inferiority trial: a maximum 10% decrease in 3-year EFS was accepted as the non-inferiority margin, to compensate for presumed long-term effect of omitting RT.

- PFS: 89.6% if no RT
- PFS: 92% if RT
- OS: 98% if no RT
- OS: 96% if RT

Cologne 2016

Median follow-up: 1.1 years
7 events out of 251 patients in standard arm
16 out of 268 in non-RT arm (p:0.026)
Randomization was stopped

Raemaekers JM, et al. HD10 trial. JCO 2014; 32.1188
Interim PET-guided treatment in limited stage HL is not recommended outside clinical studies (ESMO Guidelines)
acute appendicitis

HL 12 yo

Mariano Provencio
Germinal center transformation

16 y-o HL, III

Biopsy of the mass by bronchoscopy  
Fine-needle aspiration puncture of the gluteus nodule
A GANGLIO LINFÁTICO (NEOM) PAAF, valoración in situ e inmediata del material aspirado

DESCRIPCIÓN MICROSCÓPICA
Extendidos citológicos compuestos por un fondo serohemático sobre el que se dispone celularidad linfóide polimórfica propia de procedencia de ganglio linfático en moderada cuantía, con representación de linfocitos pequeños maduros, formas intermedias y algunos elementos precursoros, que aparecen tanto sueltos como en fragmentos de tejido de ganglio linfático. Se acompañan de macrófagos con pigmento antracórico, células columnares ciliadas y caliciformes bronquiales y células escamosas superficiales sin atipia, tanto sueltas como en grupos cohesivos tipo placa, y de un discreto número de células inflamatorias de tipo mixto. En este contexto se observan en algunos extendidos, sobre un fondo necrótico, numerosos agregados granulomatosos de histiocitos epitelioïdes, algunos de los cuales muestran patrón periférico "en empalizada", que se acompañan de linfocitos pequeños maduros y otras células inflamatorias parcialmente degradadas. No se identifican microorganismos patógenos específicos. No se observa cellularidad epitelial o linfóide atípica.

DIAGNÓSTICO ANATOMOPATÓGICO
"Adenopatía subcarinal": Punción aspiración de ganglio linfático con LINFADENITIS GRANULOMATOSA NECROTIZANTE (ver descripción microscópica y nota).
Stage 1b cervical cancer. Obstet Gynecol 2015
Fig. 3. Lymph node with dark granular carbon pigment in the cortex and medulla. Hematoxylin and eosin stain, original magnification ×100 (A) and original magnification ×400 (B).
Conclusions

- 4 ABVD + 30 Gy IFRT is the standard

- or 2 cycles of BEACOP esc + 2 cycles of ABVD (<60y) + 30 Gy IFRT or ISRT

- At 5 years, DFS: 85% and OS: 94%

- Identify those patients who:
  - can be treated with ABVD alone
  - require combined treatment
  - require intensified treatment
Thank you !!

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