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ROHS
Российское профессиональное
общество онкогематологов



EHA-ROHS-NHS Tutorial on "Real world challenges and opportunities in diagnostics and management of onco- haematological patients today"

Self-assessment Case – Session 1

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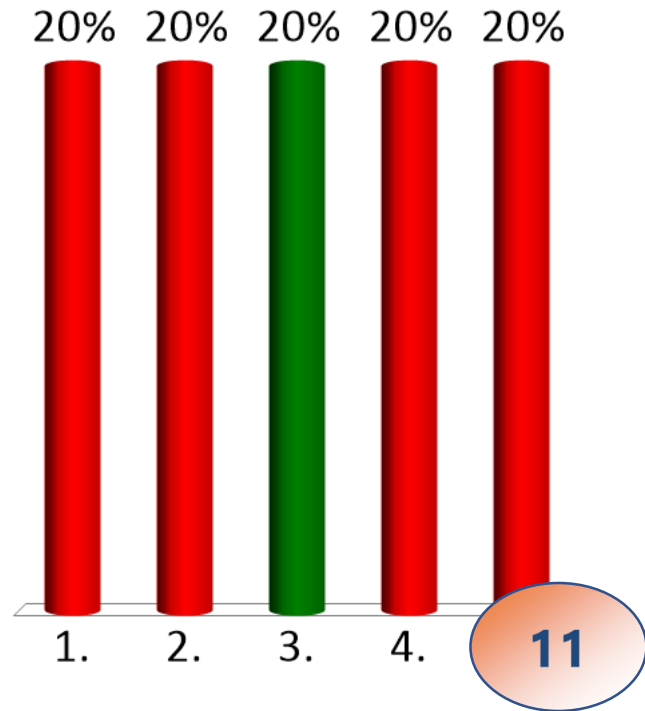
Introduction

- A 26 -year-old Caucasian girl presented with persistent cough
- Chest X Ray showed a mediastinal adenopathy
- CT scan: anterior mediastinal mass 4 × 5.5 × 6.5 cm with central necrosis
- PET/CT mediastinal uptake. Bone marrow diffuse uptake
- ESR 48mm/hr
- FBC: WBC $5.7 \times 10^9/l$, RBC $5.3 \times 10^{12}/l$, Hb 12.5 g/l, Hct 0.42, MCV 82 fl, platelet count $251 \times 10^9/l$
- **Mediastinal biopsy: Classic Hodgkin disease SN CD30+, EBV+ LMP1**



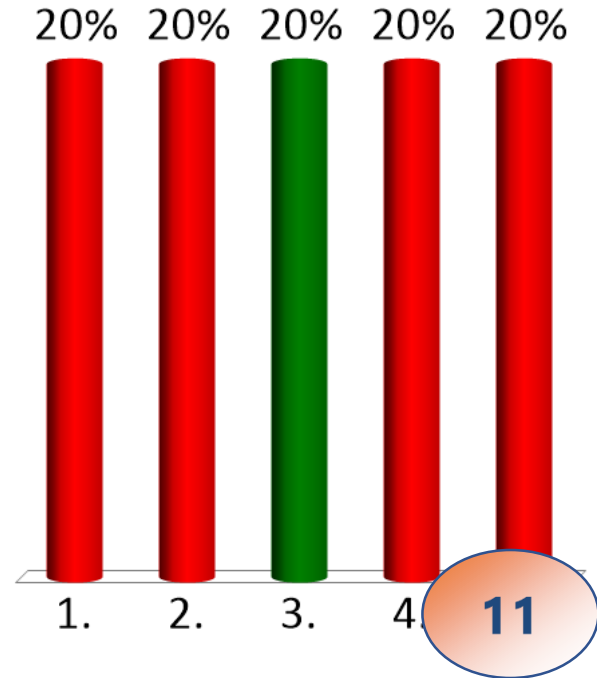
Q1) Based on the CT and PET/CT what stage of the Hodgkin lymphoma is most likely?

1. Stage IIA
2. Stage IIA bulky
3. Stage IA
4. Stage III
5. Stage IIB



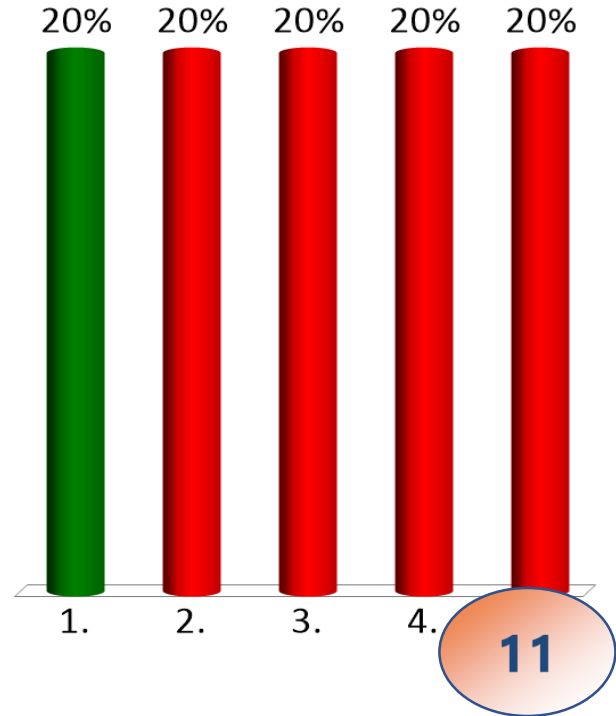
Q2) Based on the CT, PET/CT and biochemistry what early stage subgroup of the Hodgkin lymphoma is most likely?

1. Stage IIA unfavourable
2. Stage IIA favourable
3. Stage IA favourable
4. Stage IA unfavourable
5. Stage IB favourable



Q3) Based on stage what is the preferred frontline treatment?

1. 2 ABVD + RT 20 Gy
2. 2 ABVD + RT 30 Gy
3. 4 ABVD + RT 30 Gy
4. 6 ABVD
5. 2 eBEACOPP + 2 ABVD





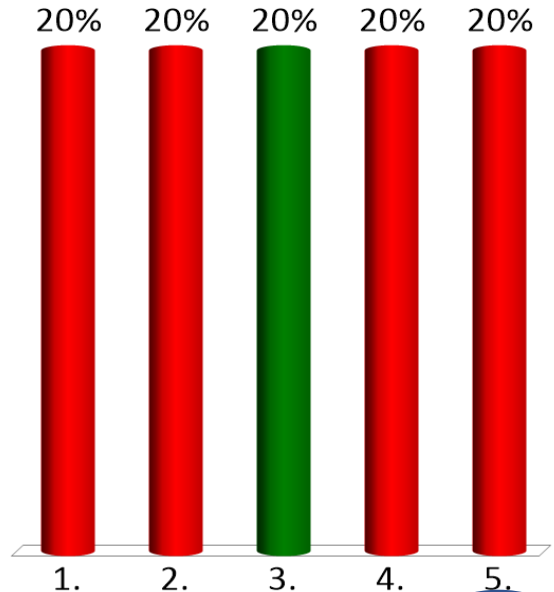
Frontline treatment

- 2 ABVD without significant toxicity
- 20 Gy RT to mediastinal site achieving CR PET negative
- CT and PET/CT three months after RT: diffuse re-uptake in mediastinal site
- No symptoms



Q4) Based on age and relapse what is the preferred salvage treatment?

1. Brentuximab Vedotin
2. HCT without ASCT
3. HCT and ASCT
4. Nivolumab
5. Allogeneic transplant





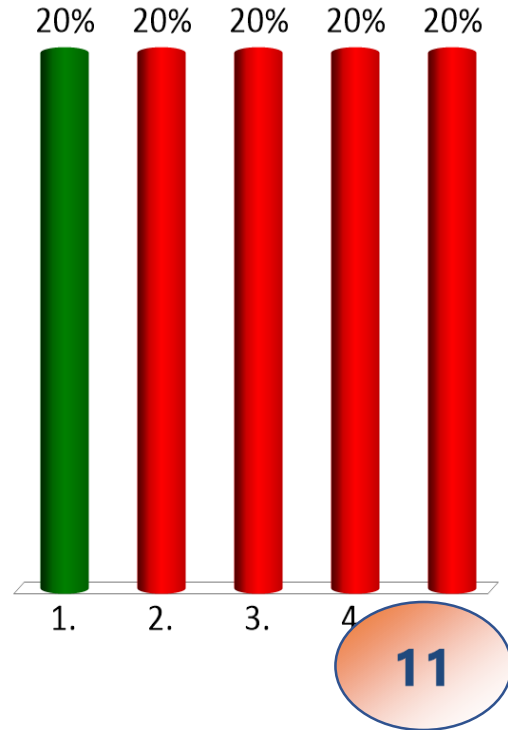
Salvage treatment and results

- 2 salvage cycles IGEV were given with mild skin toxicity and constipation
- Peripheral stem cells were collected after 1° IGEV
- PET/CT after two cycles was negative
- 2 further cycles IGEV were given
- CT and PET scan at the end: volume increase and recurrence of mediastinal uptake



Q5) Based on age, CT and PET scan and previous treatment what is the preferred 2nd salvage strategy?

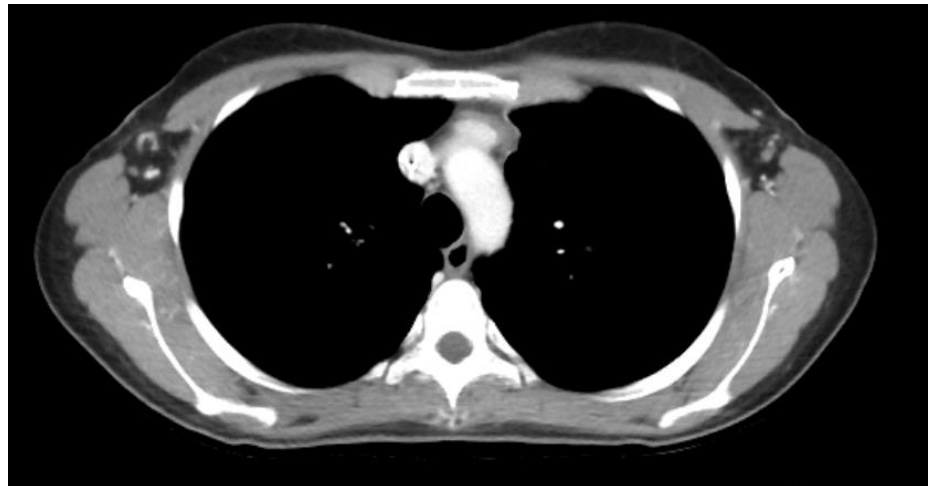
1. Brentuximab Vedotin followed by ASCT if CR or PR
2. ASCT
3. ASCT and brentuximab consolidation
4. Nivolumab
5. Allogeneic trasplant





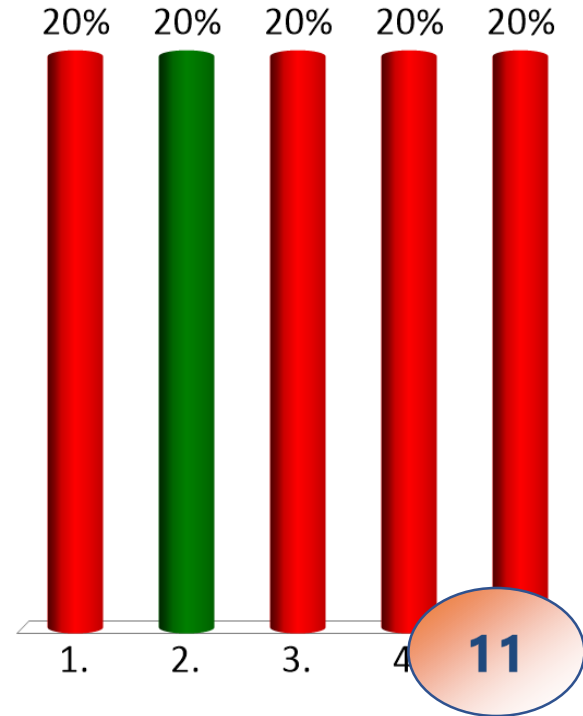
2nd Salvage treatment and results

- 4 standard doses of Brentuximab 1.8 mg/kg every three weeks were given
- No haematological or neurological toxicity
- CT and PET scan after 4 doses: no uptake



Q6) Based on age, CT and PET scan and previous treatment what is the preferred strategy at this point?

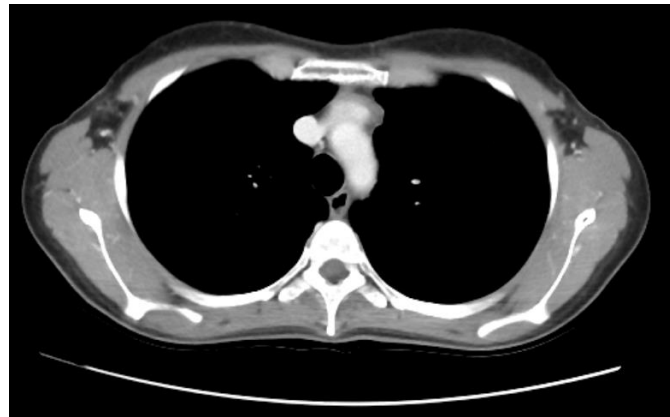
1. Complete 16 doses Brentuximab Vedotin without ASCT
2. ASCT
3. ASCT and brentuximab consolidation
4. Nivolumab
5. Allogeneic transplant





Follow up

- ASCT was performed with FEAM conditioning regimen
- Haematologic recovery was fast: 11 days for neutrophils $> 0.5 \times 10^9/l$ and day 13 platelets $> 50 \times 10^9/l$
- Grade 2 mucositis and grade 1 constipation as extrahematologic toxicity
- CT and CT/PET scan after ASCT: no uptake
- Continuing CR at 30 months





Feedback

- Q1 Patient had only 1 nodal site without bulky disease and B symptoms: stage IA
- Q2 ESR was under 50, without bulky disease: favourable risk
- Q3 Standard treatment in early I stage favourable is 2 ABVD + 20 Gy RT
- Q4 HDC followed by ASCT is the correct strategy for relapse/refractory HD
- Q5 Brentuximab vedotin in case of no or minor response to salvage chemotherapy before ASCT
- Q6 ASCT consolidation if CR or good PR



Discussion

- 2 ABVD followed by 20 Gy RT is considered standard treatment in early favourable stage HD.
- High dose chemotherapy (HDC) followed by autologous stem cell transplant (ASCT) is the best treatment in young patients with relapsed/refractory HD
- Different means of salvage such as gemcitabine, platinum or bendamustine containing regimens can be used



Discussion

- CR status at ASCT is predictive of outcome (5-yr EFS: 75% vs 31%). Extranodal disease and primary refractory or relapsed disease < 1 yr are also risk factors
- Brentuximab vedotin can be used after 1st salvage to obtain the best possible response before ASCT
- Brentuximab vedotin as consolidation treatment after ASCT is effective in patients with more than 2 risk factors: relapsed <12 months or refractory to frontline, best response of PR/SD to most recent salvage, extranodal disease at pre-ASCT relapse, B-symptoms at pre-ASCT relapse, and >2 prior salvage therapies.



References

1. Engert A, Plutschow A, Eich HT, et al. Reduced treatment intensity in patients with early-stage Hodgkin's lymphoma. *N Engl J Med.* 2010; 363(7):640-652.
2. Schmitz N, Pfistner B, Sextro M, et al; Lymphoma Working Party of the European Group for Blood and Marrow Transplantation. Aggressive conventional chemotherapy compared with high-dose chemotherapy with autologous haemopoietic stem-cell transplantation for relapsed chemosensitive Hodgkin's disease: a randomised trial. *Lancet.* 2002;359(9323):2065-2071
3. Moskowitz AJ, Yahalom J, Kewalramani T, et al. Pretransplantation functional imaging predicts outcome following autologous stem cell transplantation for relapsed and refractory Hodgkin lymphoma. *Blood.* 2010;116(23): 4934-4937



References

4. Santoro A, Mazza R, Pulsoni A. Bendamustine in Combination With Gemcitabine and Vinorelbine Is an Effective Regimen As Induction Chemotherapy Before Autologous Stem-Cell Transplantation for Relapsed or Refractory Hodgkin Lymphoma: Final Results of a Multicenter Phase II Study. *J Clin Oncol* 2016 Sep 20;34(27):3293-9
5. Younes A, Gopal AK, Smith SE, et al. Results of a pivotal phase II study of brentuximab vedotin for patients with relapsed or refractory Hodgkin's lymphoma. *J Clin Oncol*. 2012; 30(18):2183-2189.
6. Moskowitz CH, Nademanee A, Masszi T, et al; AETHERA Study Group. Brentuximab vedotin as consolidation therapy after autologous stem-cell transplantation in patients with Hodgkin's lymphoma at risk of relapse or progression (AETHERA): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2015;385(9980):1853-1862