ESMO Clinical Practice Guidelines

Diffuse Large B Cell Lymphoma
Clinical Case Presentation

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Disclosure slide

Roche           Gilead
Cellgene        Bayer
Mundipharma     Millenium
Janssen         Servier
Introduction

• Male, DOB 16.05.1975 (39 y.o.)

PAST MEDICAL HISTORY

• Nothing relevant

HISTORY OF PRESENT ILLNES

03-03/2014: progressive dyspnea; loss of appetite; drenching night sweats, fever
Introduction

• Investigated in private clinic for a suspicion of a lymphoproliferative disease.

• Urgent transfer to the ICU of public hospital for gradually increasing leg pain and rapidly developing paresis of the legs.
Introduction

LABORATORY (2.4.2014)

• Hb 134 g/l, Plt and wbc normal
• protein and albumin, liver tests, creatinine normal
• LDH 1248 U/l, β2-microglobuline 3.0 mg/l (normal 1.09-2.53)
• CRP 16 mg/l

INFECTIONS WORK-UP

• Serologies for HIV, HBV, HCV negatives
Introduction

BONE MARROW BIOPSY
• negative for lymphoma

NEUROLOGIC EVALUATION
• Lumbar puncture: No lymphoma cells, increased proteins, normal cell counts (albumino-cytologic dissociation)
• Brain CT scan: negative
• MRI of the spine: not performed (claustrophobic)
Splenomegaly (17 cm) with increased FDG uptake
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Q1: How would you proceed?

1. Splenectomy for diagnosis
2. Splenic biopsy for diagnosis
3. Start the patient on steroids
4. Try large spectrum antibiotics
5. Perform additional investigations
Neoplastic cells were:

**positive** for CD45, CD20, CD79a, BCL-2 (weak), BCL-6, MUM1 and CD5 (weak)

**negative** for CD3, CD38, CD23, CD30, CD10, cycline D1

Ki67 90%

**Final diagnosis:**

DLBCL
Course of disease complicated by:
• significant worsening of dyspneoa
• worsening of the lower limbs paresis

**DIAGNOSIS:**

**DLBCL** of the spleen, stage IBE (S)  
**Guillain-Barré syndrome** as paraneoplastic syndrome

Treatment starts with iv immunoglobulin's and steroids.
Q2: How would you treat the lymphoma?

1. R-CHOP
2. R-DA-EPOCH
3. R-Hyper-CVAD-HDArac-MTX
4. R-bendamustine
5. Other «ad-hoc» regimen
THERAPY:

• 6 cycles of R- CH(O)EP from 28.04-27.09.2014 with omission of vincristine

• 2 cycles of HD methotrexate as CNS prophylaxis (27.09 and 11.10.2014)
  • chemotherapy well tolerated, no major toxicity
  • progressive improvement of the neurologic deficits

PET/CT after cycle 2

• complete remission (morphologic and metabolic)
11/2014 (1 month later):
• he represented with episodes of night sweats
• muscular pain in the lower limbs

**LUMBAR PUNCTURE with flow cytometry (7/11/2014)**
• clonal B cell population in keeping with secondary lepto-meningeal involvement

**BRAIN AND SPINE MRI (7/11/2014)**
• multiple contrast-enhancing parenchymal brain lesions (basal ganglia, right temporal and frontal lobe)
• thickening and enhancement of the nerve roots
How would you treat the early CNS relapse?

1. HD-MTX + HD-AraC
2. HD-MTX + HD-AraC + i.t. chemo
3. Chemo + radiotherapy
4. Induction CT + autologous transplant
5. Induction CT + allogeneic transplant
THERAPY:

- 2 cycles of HD cytarabine and etoposide (CYVE) according to C. Soussain jco 2008
- 2 courses of IT sustained release liposomal Ara-C (DepoCyte®)
- stem cell mobilisation after 2\textsuperscript{nd} cycle
- High dose chemotherapy with carmustine (BCNU) and thiotepa followed by autologous stem cell transplant
- Radiotherapy of the residual disease post-treatment in spine
1 month after the end of the treatment the patient relapsed systemically (liver and CNS) and died.

Questions raised by this case:
1. When is a CNS prophylaxis indicated in DLBCL?
2. Which prophylaxis, if any, is the best?
3. How to treat DLBCL relapsing in the CNS?