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ESMO Clinical Practice Guidelines

Waldenström's Macroglobulinaemia Clinical Case Presentation

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Disclosures

No potential conflicts of interest declared

Introduction

2002: 51 years

- Arterial hypertension, BP=160/90 mmHg, systolic BP: sometimes 190 mmHg
- IgM kappa “MGUS” (no marrow assessment)
- Hb=12.7 g/dL, WBC=6.2 10^9/L, PMN=3.16 10^9/L, Platelet=289 10^9/L, IgM concentration: 9g/L

Introduction (continued)

May 2011:

- Epistaxis, No other symptoms
- No lymph nodes
- Hb=10.2 g/dL, WBC=3.7 10^9/L, PMN=2.07 10^9/L, Platelet=198 10^9/L
- SEP: β2-globulin: 11.3 g/L; IgM concentration: 60.9 g/L; β2-microglobulin: 2.4 mg/L
  FLC kappa: 300 mg/L, lambda: 6.59 mg/L
- Bone marrow biopsy:
  diffuse lymphoid infiltration (>80%)
  CD20 positive
  MYD88 (L265P) positive (posterior assessment)
  Trisomy 4, del(6q)

Introduction (continued)

May 2011 (continued)

- Cryoglobulin: positive, high titer, preventing the identification of the type
- Fundoscopic:
  - February 2011 (at this time done at home for arterial hypertension): central retinal hemorrhages, tortuous blood vessels
  - Adjust treatment of arterial hypertension → good control of BP
  - May 2011: small blot-like retinal hemorrhages, tortuous blood vessels with venous sausaging

June 2011:

- Hb=9.1 g/dL, Platelet=214 10^9/L, WBC=3.9 10^9/L, PMN=1.99 10^9/L

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Q 1: Please indicate indisputable criteria for initiating therapy in May 2011

1. Epistaxis
2. Fundoscopic abnormalities
3. Anemia
4. IgM concentration
5. none

Q 2: Please indicate the ISSWM subgroup

1. Low
2. Intermediate
3. High

Initial Therapy

DRC regimen (Dexamethasone, Rituximab, Cyclophosphamide) is initiated

	Date	Hb (g/dL)	IgM (g/L)
1st cycle DRC	25/06/2011	9.1	66.4
6th cycle DRC	05/12/2011	11.7	19.4
Best response	22/05/2013	13.6	6

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Q 3: Which response category was achieved?

1. Complete remission
2. Very good partial remission
3. Partial remission
4. Minor remission
5. Stable remission
6. Progression

First Progression

December 4, 2013:

- Weight loss (7 kg), asthenia (ECOG=3)
- Epistaxis, no lymph node
- Hb=7.8 g/dL, Platelet=134 10^9/mm3, WBC=3.6 10^9/mm3, PMN=2.23 10^9/mm3
- IgM concentration: 94.5 g/L, viscosity 7.11 Cst
- Fundoscopy:

⑩ -- multiple retinal hemorrhages, tortuous blood vessels

Q 4: Work-up should include: Free light chain?

1. Yes

2. No

December 4, 2013:

- Weight loss (7 kg), asthenia (ECOG=3)
- Epistaxis, no lymph node
- Hb=7.8 g/dL, Platelet=134 10^9/L, WBC=3.6 10^9/L, PMN=2.23 10^9/L
- IgM concentration: 94.5 g/L, viscosity 7.11 Cst
- Fundoscopy:

⑩ -- multiple retinal hemorrhages, tortuous blood vessels

Q 5: Work-up should include: β2-microglobulin?

1. Yes

2. No

December 4, 2013:

- Weight loss (7 kg), asthenia (ECOG=3)
- Epistaxis, no lymph node
- Hb=7.8 g/dL, Platelet=134 10^9/L, WBC=3.6 10^9/L, PMN=2.23 10^9/L
- IgM concentration: 94.5 g/L, viscosity 7.11 Cst
- Fundoscopy:

⑩ -- multiple retinal hemorrhages, tortuous blood vessels

Q 6: Work-up should include: Bone marrow examination?

1. Yes

2. No

December 4, 2013:

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- Epistaxis, no lymph node
- Hb=7.8 g/dL, Platelet=134 10^9/L, WBC=3.6 10^9/L, PMN=2.23 10^9/L
- IgM concentration: 94.5 g/L, viscosity 7.11 Cst
- Fundoscopy:

⑩ -- multiple retinal hemorrhages, tortuous blood vessels

Q 7: Work-up should include: Coagulation test?

1. Yes

2. No

December 4, 2013:

- Weight loss (7 kg), asthenia (ECOG=3)
- Epistaxis, no lymph node
- Hb=7.8 g/dL, Platelet=134 10^9/L, WBC=3.6 10^9/L, PMN=2.23 10^9/L
- IgM concentration: 94.5 g/L, viscosity 7.11 Cst
- Fundoscopy:

⑩ -- multiple retinal hemorrhages, tortuous blood vessels

Q 8: Work-up should include: Complication assessment (NT-proBNP, proteinuria)?

1. Yes

2. No

December 4, 2013:

- Weight loss (7 kg), asthenia (ECOG=3)
- Epistaxis, no lymph node
- Hb=7.8 g/dL, Platelet=134 10^9/L, WBC=3.6 10^9/L, PMN=2.23 10^9/L
- IgM concentration: 94.5 g/L, viscosity 7.11 Cst
- Fundoscopy:

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Work-up Recommendations

December 4, 2013:

- Weight loss (7 kg), asthenia (ECOG=3)
- Epistaxis, no lymph node
- Hb=7.8 g/dL, Platelet=134 10^9/L, WBC=3.6 10^9/L, PMN=2.23 10^9/L
- IgM concentration: 94.5 g/L, viscosity 7.11 Cst
- Fundoscopy:
  -- multiple retinal hemorrhages, tortuous blood vessels
- Coagulation test:
  -- prothrombin time test & partial thromboplastin time: normal
  -- VWF Ag: 42% VWF RCo: 37%
- Bone marrow examination:
  -- Diffuse infiltrate of B-cells (50%)
  -- Mastocytes
  -- Eosinophil deposit (light chain deposit?)
- Prognostic assessment
  -- β2-microglobulin: 3 mg/L
- Other complication assessment
  -- NT-proBNP: not available because of hyperviscosity, after plasmapheresis: 1600 pg/mL
  -- Proteinuria: negative

→ Emergency procedure: plasmapheresis

Q 9: What is the recommended treatment?

1. Dexamethasone/rituximab/cyclophosphamide
2. Bortezomib/dexamethasone/rituximab
3. Fludarabine/rituximab/cyclophosphamide
4. Bendamustine/rituximab
5. Alkylating agent (chlorambucil or cyclophosphamide) and rituximab
6. Other

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Outcome…

1. Plasmapheresis from December 5-11, 2013
2. December 16, 2013: fever, blood culture staphylococcus lugdunensis despite Augmentin® (amoxicillin/clavulanate potassium)
3. Endocarditis with abscess of aortic valve
4. Cardiac surgery
5. February 20, 2014: asthenia, no lymph node
   1. Hb=7.4 g/dL, platelet=130 $10^9/mm^3$, WBC=2.47 $10^9/mm^3$, PMN =1.16 $10^9/mm^3$
   2. BDR

Date	SEP: M-spike (g/L)	IgM conc (g/L)	Viscosity (cSt)	Protein (g/L)	comment
02/04/2014	13,5	84,6		104	
16/04/2014	16	90,1	4,14	102	
22/04/2014	13,8	56,13	2	79	
07/05/2014		52,26	2,03	95	
28/05/2014	12,2	49,24	1,88	83	No cryoglobulin
25/06/2014	4,8	43,54		88	