ANCO

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Case 1

- A 43 year old man with no past medical history, presents with nausea, vomiting, anorexia, foamy urine, fatigue, decreased exercise tolerance and leg edema.
- Labs: WBC 4.6 with a normal differential, hemoglobin 13.4, platelet 327, eGFR 90, creatinine 0.81, **24-urine total protein showed 5.1gm**
- GI biopsy and renal biopsy showed **AL amyloidosis, lambda-type** by IF.

Case 1 continued

- Placed on TPN. No significant social or past medical history. He is referred to you for further evaluation.
- Addtl labs: Calcium normal, liver function tests normal, PT/PTT/INR normal, LDH normal, **albumin 2.0**
- K-SFLC 12.2 mg/L , **l-SFLC 406.5 mg/L**, k/l ratio 0.11, **dFLC 393.8,** SPEP no M-protein with normal S-IFE, UPEP no M-protein with **U-IFE lambda light chains**, skeletal survey negative for lytic lesions.
- **NTproBNP 629 pg/ml**, troponin I <0.02 ug/L, EKG normal, TTE normal LVEF, **mild diastolic dysfunction**. **Cardiac MRI suspicious for cardiac amyloidosis.**
- Bone marrow biopsy shows **10% lambda-restricted plasma cells** on the core, **FISH + for t(11;14).**

Case 1 continued

- Assessment: 43 y/o M with a new diagnosis of systemic AL amyloidosis

Case 1 continued

- **First-line treatment for newly diagnosed AL amyloidosis?**
  - CyBorD, no autologous stem cell transplant
  - CyBorD while being considered for an autologous stem cell transplant
  - Straight to autologous stem cell transplant
  - Len-Dex, no transplant
  - Mel-Dex, no transplant

Case 1 continued

- He is started CyBorD while undergoing an autologous stem cell transplant (auto SCT) evaluation
- Completed 2 cycles of CyBorD. Achieved a partial remission, bone marrow PC 5%
- Underwent a MEL-200 ASCT w/o complications
- Attained a complete hematologic remission post-transplant with no evidence of clonal PCs on bone marrow

Case 1 continued

- **What is the next step in management of systemic AL amyloidosis in hematologic CR following an ASCT?**
  - Observation without further therapy
  - Start CyBorD for maintenance
  - Start bortezomib for maintenance
  - Start revlimid for maintenance

Case 1 continued

- Started on bortezomib every other week for around 1 year and stopped due to neuropathy
- Proteinuria improved to 2.4 gm and then stabilized. Leg swelling resolved though the patient continues to have mild DOE and mild fatigue. NT-proBNP normalized.
- 4 years post-transplant, the patient has a hematologic relapse with l-SFLC 60.3. He continues to have mild neuropathy (Gr 1).

Case 1 continued

- **What is the next line of therapy for relapsed systemic AL amyloidosis?**
  - Restart CyBorD
  - Start IMiD/dex
  - Start izaxomib/dex
  - Start daratumumab/dex
  - Start carfilzomib/dex

Case 1 continued

- Started on daratumumab. Achieves a CR on after 2 cycles. Completes 4 total cycles of DARA.
- He continues to have 2.4 gm proteinuria/day. Creatinine has risen to 1.37, eGFR 63.

Case 1 continued

- **What do you recommend for persistent proteinuria and worsening renal function?**
  - Continue DARA
  - Enroll in anti-amyloid fibril clinical trial
  - Switch to another chemotherapy

Case 2

- 44 y/o male with a h/o type II diabetes mellitus, hypertension, and depression p/w rectal bleeding
- Family History: Bladder ca (father)
- Social History: no smoker. ETOH use none.
- ROS: negative

Case 2 continued

- Physical exam was unremarkable
- Labs: WCC 4.5, Hb 14.2, Hct 44.5, Platelet 201k, Creatinine 0.75, LFTs normal
- Colonoscopy identified inflammation above the dentate line in the rectum
- Biopsy confirmed **lamda-restricted plasmacytoma**.

Case 2 continued

- Assessment: 44 y/o M with a diagnosis of rectal solitary extramedullary plasmacytoma (lambda-restricted)
- Bone marrow biopsy negative for clonal plasma cells
- The SFLCs, M-protein, CRAB criteria were all normal.
- PET/CT scan did not show evidence of disease anywhere else besides the rectum

Case 2 continued

- **What is the first-line therapy for solitary extramedullary plasmacytoma ?**
  - Surgical resection
  - Definitive radiotherapy
  - Chemotherapy then radiation
  - Chemotherapy followed by surgical resection

Case 2 continued

- Received definitive XRT 45gy/25fx
- Relapsed 11 months later based on PET/CT which showed avid uptake in rectum and repeat biopsy confirmed relapsed plasmacytoma.
- MRD+ bone marrow though no clonal PC.

Case 2 continued

- Clonoseq ID successful off the plasmacytoma. MRD by clonoseq off the bone marrow was 4000 cells/million.
- **What is the next line of therapy for relapsed extramedullary plasmacytoma?**
  - Chemotherapy
  - Surgery but patient will have a colostomy
  - Radiotherapy
  - Observation until symptomatic

Case 2 continued

- Started on chemotherapy with lenalidomide and dexamethasone (Rd)
- MRD +
- PET/CT negative (6 months later)

Case 2 continued

- MRD reduced to 353 cells/million
- **What is the next step based on persistent MRD positivity and PET/CT negativity?**
  - Stop chemotherapy
  - Continue chemotherapy at current regimen
  - Reduce chemotherapy to maintenance
  - Autologous stem cell transplant

Case 2 continued

- Switched to maintenance chemotherapy with lenalidomide 25 mg po every other day
- Dexamethasone discontinued due to hyperglycemia

Case 3

- 60 y/o F w/ a h/o low-grade B-cell lymphoma most consistent with marginal zone lymphoma of the right orbital & temporal LN diagnosed in 2008 (received RTX & fludarabine, achieved CR), relapsed low-grade B-cell lymphoma in 2010 (received bendamustine & rituximb, achieved CR), presented with **inguinal lymphadenopathy in 2014.**

Case 3 continued

- PMH: Extranodal MZL, follicular lymphoma
- FH: Gastric ca (father), lung ca (mother), NHL (twin sister)
- SH: non-smoker. No ETOH.
- ROS: + fevers + night sweats

Case 3 continued

- Physical Exam: **+ left inguinal adenopathy 3x3 cm**
- Labs: WBC 5.8, Hb 12.4, Hct 35.9, Platelet 199k, ANC 3630
- Imaging: PET/CT demonstrated disease progression with the development of **bulky right iliac and inguinal adenopathy along with persistent axillary adenopathy**
- Excisional left inguinal LN biopsy: large cell-rich germinal center-derived B-cell lymphoma, consistent with **diffuse large B-cell lymphoma** arising in a background of low-grade follicular lymphoma

Case 3 continued

- Assessment: 60 y/o F with DLBCL, transformed from marginal zone lymphoma/follicular lymphoma, stage III

Case 3 continued

- **What is the first line therapy for newly diagnosed DLBCL transformed from a low-grade B-cell lymphoma that has been previously treated?**
  - DA R-EPOCH
  - RDHAP
  - R-ICE
  - RCHOP
  - Transplant

Case 3 continued

- Received 6 cycles DA R-EPOCH.
- Achieved CR, duration 9 months. Relapsed DLBCL in 2015 (right temporal mass)

- **What is the recommended step for relapsed DLBCL transformed from a low-grade B-cell lymphoma?**
  - Clinical trial: LoCARB (bendamustine, carfilzomib and rituximab)
  - Lenalidomide
  - RDHAP
  - R-GemOx

Case 3 continued

- Enrolled in LoCARB trial (bendamustine, carfilzomib and rituximab)
- Progressed after 1 cycle (progressive cervical LAD)

- **What is the recommended step for relapsed progressive DLBCL transformed from a low-grade B-cell lymphoma?**
  - RICE
  - R-GemOx
  - Lenalidomide
  - RDHAP

Case 3 continued

- Received R-GemOx x 6 cycles
- Achieved partial metabolic response

- **What is recommended for relapsed DLBCL transformed from a low-grade B-cell lymphoma who has achieved a PR?**
  - CAR T-cell therapy
  - Allogeneic stem cell transplant
  - Autologous stem cell transplant
  - RDHAP

Case 3 continued

- Received CAR T-cell therapy CTL019 infusion (tisagenlecleucel/kymriah) and achieved CR after 1 month
- In CR 12 months out from receiving CAR T-cell therapy

Case 4

- 56 y/o M w/ no significant medical history p/w dyspnea on exertion, weakness, & bilateral lower extremity edema
- PMH: BPH
- PSH: none
- FH: thyroid ca (sister)
- SH: ex-smoker. No ETOH use
- ROS: bilateral lower extremity edema

Case 4 continued

- Physical Exam: Well appearing. + erythematous papules on back. No LAD. No hepatosplenomegaly
- Labs: **WCC 1.1, Hb 4.8, Hct 15.3, platelet 40k, ANC 100**, **6% blasts**, + nucleated RBCs
- BMBx: **acute myeloid leukemia**, 80% blasts. Normal cyto, **IDH2 mutated**. Also with BRAF, NRAS, KRAS, DNMT3A, BCOR mutations

Case 4 continued

- Assessment: 56 y/o M w/ intermediate risk IDH2 mutated AML, w/ additional mutations in BRAF, NRAS, KRAS, DNMT3A, BCOR

Case 4 continued

- **What is the first-line therapy for newly diagnosed IDH2 mutated AML?**
  - 7+3
  - Vyxeous (daunorubicin & cytarabine liposome)
  - 7+3 + Midostaurin
  - 7+3 + Mylotarg (gemtuzumab ozogamicin)

Case 4 continued

- Patient treated with 7+3.
- Refractory, persistent 70% blasts on bmbx
- **What is recommended for primary refractory AML?**
  - Hypomethylating agent (Azacitidine/ Decitabine)
  - MEC (mitoxantrone, etoposide, cytarabine)
  - Clofarabine/Cytarabine (Ara-C)
  - FLA-IDA (fludarabine, cytarabine, idarubicin)

Case 4 continued

- Received salvage chemo with Clo/Ara-C.
- Refractory, persistent 57% blasts on bmbx
- **What is next recommended for primary refractory AML?**
  - FLA-IDA (fludarabine, cytarabine, idarubicin)
  - Hypomethylating agent (Azacitidine/ Decitabine)
  - ICE (idarubicin, cytarabine, etoposide)
  - MEC (mitoxantrone, etoposide, cytarabine)

Case 4 continued

- Received azacitidine
- Refractory, persistent 68% blasts on bmbx
- **What is next recommended for primary refractory IDH2 mutated AML?**
  - Enasidenib
  - Gemtuzumab ozogamicin
  - MEC
  - FLAG-IDA

Case 4 continued

- Received enasidenib (stable disease for 8 months).
- Relapse, 30% blasts on bmbx

- **What is next recommended for primary refractory IDH2 mutated AML?**
  - Gemtuzumab ozogamicin
  - MEC
  - FLAG-IDA
  - Decitabine + Venetoclax

Case 4 continued

- Received decitabine + venetoclax.
- MRD negative by Seattle flow.

- **What is next recommended for MRD negative primary refractory AML?**
  - Maintenance hypomethylating agent
  - Consolidation with high-dose cytarabine
  - Allogeneic hematopoietic stem cell transplantation
  - Gemtuzumab ozogomicin

Case 4 continued

- Received an allogeneic HCT
- Currently ~ 95 days out from allo HCT, on post transplant azacitidine

Thank You