Mycosis fungoides during Imatinib Mesylate treatment – True lymphoma or cutaneous drug reaction?

Milena Jovanovic
Faculty of Medicine, University of Belgrade
11th September 2019, Nice
Case report

Female, 51-year-old

Initial diagnosis: **GIST**
- May 2017 – small intestine surgery due to GIST
- Jan 2018 – intraabdominal dissemination of GIST confirmed by NMR
- Imatinib Mesilate (Alvotinib®) in a dose of 400 mg once a day
- Aug 2018 – regression of intraabdominal metastases was confirmed by NMR
Case report

• Three months after the IM initiation non-pruritic erythematous scaly plaques appeared on the face, trunk and extremities.
  ➢ Dx: Hives.
  ➢ Tx: Methylprednisolone and antihistamines.

• Jun 2018 – spreading and progression of skin lesions on palms and feet.
  ➢ Acitretin (Keracutan ®) 30 mg daily, and
  ➢ Prednisone (Pronison ®) 20 mg every second day.
Laboratory findings

- TBC, ESR, CRP, routine biochemical analyses were in referent ranges.
- Tumor markers like AFP, Ca 15-3, Ca 19-9, and CEA were in referent ranges, except CA125 which was increased: 68 IU/mL (rr 0-35 IU/mL).
- Tests for syphilis (VDRL and TPHA tests) were negative.
- Microbiologic and parasitic tests of stool were negative.
Laboratory findings

- Antinuclear antibodies were increased:
  - ANA Hep2 (IgG): nucleoplasm +, a fine speckled pattern of immunofluorescence, 1:320;
  - ANA SS-A (IgG): 109,8 (referent ranges <20).

- Anti-dsDNA antibodies and complement components like C3 and C4 were in referent ranges.

- Direct immunofluorescence (DIF): negative.

- The lupus band tests (LBT) of photo-protected and photo-exposed skin samples: negative.
CD8, x100
CD7, x200
Diagnosis?

• Macroscopic findings: non-pruritic scaly plaques

• Microscopic findings:
  ✓ epidermotropic small to medium-sized atypical lymphocytes with a cerebriform nucleus
  ✓ dermal lichenoid infiltrate
  ✓ tumor cells are of T-cell phenotype with the following IHC profile: CD3 positivity, CD4 or CD8 positivity predomination and partial or diffuse loss of CD5 and/or CD7 positivity
FISH Analysis

Molecular characteristics of Mycosis fungoides:

- Deletion of CDKN2A and TP53,
- Translocation or amplification of c-MYC.

Our case:

deletion of CDKN2A, without concomitant c-MYC and TP53 rearrangement.
Gastrointestinal Stromal Tumor

- The most common mesenchymal tumor of the gastrointestinal system with high metastatic potential.

- 5-year survival rate for GIST is approximately 60%, while the survival rate for a disseminated disease is only 10-20 months.

- The most common site for metastases is liver.

- Tx of choice is surgical resection of the tumor.

- Tx of choice for disseminated disease is Imatinib Mesylate.
Imatinib Mesylate

- Imatinib mesylate (IM, Gleevec ®) is a selective inhibitor of several tyrosine kinases, the most common are ABL, ARG (ABL-related gene), C-KIT, and platelet-derived growth factor (PDGF) kinases.

- IM is the first-line treatment for chronic myeloid leukemia (CLM) or disseminated GIST.
Imatinib Mesylate - Side effects

• Most common: mild to moderate oedema, nausea, vomiting, diarrhoea, muscle cramps.

• In late chronic-phase patients who receiving 400 mg of IM daily the most common side effect is non-specific skin rash which clinically looks like MF.

• Secondary neoplasms:
  o Solid tumors (kidney, prostate, gastrointestinal),
  o Lymphomas and leukemias (clonal proliferation of lymphocytes).
Conclusions

- Partial loss of CD5/CD7 and FISH analyses can argue against pseudolymphoma
- True mycosis fungoides can not be excluded
- Close follow up of the patient
Thank you for your attention!

Contact details:
martinabb@gamil.com
milenaj300@gmail.com