Restored Response to Infliximab after Treatment with Rituximab to Decrease Anti-drug Antibodies in Psoriasis

Wiggin Wu Lee, MD
Jae Jung, MD, PhD

City of Hope Comprehensive Cancer Center
University of California, San Diego
Case Presentation

59 year old male with a >20 year history of psoriasis and psoriatic arthritis presenting for evaluation and management of worsening disease

• Treatment history
  – Topical steroids under occlusion (clobetasol), PUVA, NBUVB, soriatane, MTX (many years), CSA (severe adverse reaction), etanercept, adalimumab, infliximab, ustekinumab

• Current therapy: none for last 6 months as he felt he had exhausted all treatment options

• Progressive cutaneous and joint disease
History and labs

• Past medical and surgical history
  – Testicular cancer
    • s/p orchiectomy, chemotherapy, and retroperitoneal lymph node dissection
  – Thyroid cancer
    • s/p thyroidectomy
  – Cholangiocarcinoma
    • s/p partial resection

• Family history
  – Extensive family history of psoriasis, including a severely affected brother

• Labs
  – Normal LFTs except for a slight increase AFP (followed due to history of cholangiocarcinoma)
Physical Exam
Next steps in management

• TNF inhibitor plus MTX was favored, but patient was not an ideal candidate.
  – History of cholangiocarcinoma and partial resection
  – Slightly elevated AFP 9.1 (normal 1.3-8 ng/mL)
  – Unknown total dosage of MTX

• Repeat trial of etanercept
  – No improvement after 2 months

• Repeat trial of adalimumab
  – No improvement after 2 months

• Apremilast
  – No improvement after 12 weeks
  – Worsening PSA, increasingly disabled, bilateral knee effusions, required narcotic pain medication
Anti-drug antibodies

• Postulated that TNF-inhibitor failures were secondary to neutralizing anti-drug antibodies (ADAs)

• Neutralizing ADAs may decrease the therapeutic efficacy of biologic treatments by:

• Potential contributors include
  – Medication constitution
  – Mode or frequency of administration
  – Patient characteristics

Anti-drug antibodies in psoriasis

<table>
<thead>
<tr>
<th>Medication</th>
<th>Reported rates of ADAs</th>
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</thead>
<tbody>
<tr>
<td>Etanercept</td>
<td>0-18.3%</td>
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<tr>
<td>Adalimumab</td>
<td>5.4-43.6%</td>
</tr>
<tr>
<td>Infliximab</td>
<td>8.8-44.8%</td>
</tr>
<tr>
<td>Ustekinumab</td>
<td>3.8-5.4%</td>
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</tbody>
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- Patients with one anti-drug antibody (ADA) are more likely to develop additional ADAs


- New treatment option rationale:
  - Clear neutralizing ADA and repeat trial of infliximab
Rituximab to decrease antidrug antibodies
• Rituximab administered
  – RA dosing
    • (1000 mg x2, day 1 and 15)
  – Had progression of cutaneous disease during treatment
  – Worsening joint pain with effusions
  – Partially relieved with
    • Intralesional steroid injections
    • Low dose prednisone taper
    • Narcotic pain medicine
Restored response to infliximab

- Infliximab start at 5 mg/kg IV
- Rapid improvement after 1st infusion
- Virtual resolution of all lesions after 2nd infusion
Restored response to infliximab after treatment with rituximab to decrease ADAs in psoriasis

Rituximab may be effective in reducing ADAs

Restored efficacy of TNFα inhibitors and other targeted biology treatments

This case exemplifies the ways by which advances in basic science and immunology can guide treatment decisions and ultimately benefit patients
References

Thank you!