Differentiated Thyroid Cancer: Diagnostic Biomarker Aids and Monitoring Controversies

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Disclosure

Nothing to disclose

2015 ATA Guidelines

[C4] What are the appropriate methods for following patients after initial therapy?

[C5] What is the role of serum Tg measurement in the follow-up of DTC?

RECOMMENDATION 92

(A) Serum Tg should be measured by an assay that is calibrated against the CRMA7 standard. Thyroglobulin antibodies should be quantitatively assessed with every measurement of serum Tg. Ideally, serum Tg and anti-Tg antibodies should be measured simultaneously in the same laboratory and using the same assay for a given patient.

(Strong recommendation, High-quality evidence)

Haugen et al. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer. Thyroid 26 (1) (2016).
Tg Testing Methods

Immunometric Assay (IMA)
- Valid in TgAb- patients only!

Radioimmunoassay (RIA)
- Less prone to TgAb interference
- May result occasionally in falsely elevated Tg levels
- TAT ~6 days

LC-MS/MS
- Completely resistant to TgAb BUT may not pick up some Tg variants
- Concern in patients w/structural disease
- TAT ~2 days

Tg IMA Assays available in the US

First Gen: Siemens Immulite Tg Assay (~100 US Labs)
Functional Sensitivity: 0.9 ng/mL

2G-Tg IMA: Beckman Access/DxI Tg Assay (150 US Labs)
Functional Sensitivity: 0.05-0.1 ng/mL
Used in most laboratories: Mayo, ARUP, LabCorp and MUSC

Can be used on Tg Ab – patients ONLY!
TgAb+ DTC Patient Monitoring

TgAbs present in 25-30% patients with DTC

IMA Bias in TgAb+ Patients

J Clin Endocrinol Metab. 2015; 100(8): E1074-E1083.
TgAb Interference in Defined Tg/TgAb Mixtures

Mass Spectrometry

Potential Tg Trypsinization Sites: Major isoform, 2768 aa
Mass Spectrometry

Mayo Clinic Tg LC-MS/MS Method

The Effect of Tg Heterogeneity on Tg Assays

N = 37  N = 52

ROC Curves and Clin Sens/Spec: IMA, RIA, MS


J Clin Endocrinol Metab 2015; 100(8): E1074-E1083.
TgAb as a Surrogate Tumor Marker

TgAb Trends in TgAb+ Patients

Not all TgAb assays are created equal!

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Funct Sens (LOD)</th>
<th>Assay</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beckman</td>
<td>1.8 (0.9)</td>
<td>Immunometric</td>
</tr>
<tr>
<td>Roche</td>
<td>20</td>
<td>Competitive</td>
</tr>
<tr>
<td>Siemens Immulite</td>
<td>20</td>
<td>Immunometric</td>
</tr>
<tr>
<td>Abbott Architect</td>
<td>0.3</td>
<td>Immunometric</td>
</tr>
</tbody>
</table>

Significant method differences exist!
Monitor trends within a single method
For effective TgAb monitoring critical to use a sensitive method with <15% imprecision
MUSC Testing Strategy

Thyroglobulin Antibody (TgAb)

- TgAb Negative (<1.0 IU/mL)
  - Tg by IMA (Sensitivity: 0.1 ng/mL)
    - Turnaround Time: 2-3 Days
  - Performed in-house

- TgAb Positive (1.0 IU/mL or higher)
  - Tg by LC/MS-M5 (Sensitivity: 0.2 ng/mL)
    - Turnaround Time: 4-6 Days
  - Tg by RIA (Sensitivity: 0.5 ng/mL)
    - Turnaround Time: 6 Days

Last but not Least….Biotin!

Pt taking Biotin

<table>
<thead>
<tr>
<th>Biotin (ng/mL)</th>
<th>Tg Expected</th>
<th>Tg Measured</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>15.3</td>
<td>9.6</td>
</tr>
<tr>
<td>400</td>
<td>60.7</td>
<td>61.6</td>
</tr>
</tbody>
</table>

*May be seen in pts on mega doses of biotin (100-300 mg/d), e.g. MS

Nondestructive tissue analysis for ex vivo and in vivo cancer diagnosis using a handheld mass spectrometry system


"The Write Tool for the Job"
MasSpec Pen system and operation

MasSpec Pen analysis of PTC and normal thyroid tissue sections
Nondestructive molecular analysis of human tissue samples using the MasSpec Pen

Effect of MasSpec Pen tip diameter on the mass spectra obtained

Thank you!