Melanomas with spindle cell differentiation: a review of clinical, pathological and molecular characteristics

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In this presentation there is nothing to disclose
Introduction: *Spindle cell melanoma*

- Rare subtype
- Atypical and spindled malignant melanocytes
- Partially overlapping features with desmoplastic melanoma
- Collagen content helps to distinguish these entities:
  
  \[
  \begin{align*}
  \text{<10\%} & \rightarrow \text{Spindle cell melanoma} \\
  10 - 90\% & \rightarrow \text{Mixed spindle/desmoplastic melanoma} \\
  >90\% & \rightarrow \text{Desmoplastic melanoma}
  \end{align*}
  \]
- Classic melanocytic immunohistochemical markers could be negative
- Molecular profile is not well known: *BRAF* mutations the most frequent ones (31% vs 40-50%)
Aims

To perform a retrospective review of the clinical and pathological characteristics, the immunohistochemical (IHC) and molecular profiles as well as the prognosis of a series of melanomas with predominantly spindle cell differentiation
Methods

10 cases (2005 to 2019) of melanomas with predominantly fusiform growth pattern were included

- Evaluation of clinical and histopathological features and prognostic factors
- Immunohistochemical techniques (MelanA, HMB45, S100 and SOX10)
- Ultrastructural studies (5 cases)
- Mutational status: BRAF V600E, NRAS and c-KIT
  Sanger sequencing and Idylla system
### Results I

<table>
<thead>
<tr>
<th><strong>Age</strong></th>
<th><strong>Sex</strong></th>
<th><strong>Location</strong></th>
<th><strong>Size</strong></th>
</tr>
</thead>
</table>
| - **Median:** 78 yo  
  - **Range:** 54-86 yo | - **Men** (n = 8)  
  - **Women** (n = 2) | - **Head & Neck** (n = 5)  
  - **Trunk** (n = 2)  
  - **Mucosal** (n = 2)  
  - **Nail** (n = 1) | - **Median:** 20 mm  
  - **Range:** 4-40 mm |
### Results II: Clinical presentation

<table>
<thead>
<tr>
<th>Description</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dermal nodule in the head + supra/adjacent pigmented macula</td>
<td>n = 3</td>
</tr>
<tr>
<td>Purely dermal nodule in the head</td>
<td>n = 2</td>
</tr>
<tr>
<td>Pink exophytic lesion with ulceration</td>
<td>n = 2</td>
</tr>
<tr>
<td>Acromic exophytic mucosal lesion</td>
<td>n = 2</td>
</tr>
<tr>
<td>Destruction of the nail plate + lesion with an underlying vascular appearance</td>
<td>n = 1</td>
</tr>
</tbody>
</table>
Results III: Histopathological features

Exclusively dermic (n = 7)  Dermic and Hipodermic (n = 3)

Without epidermic contact (n = 7)  With epidermic contact (n = 3)
Results III: Histopathological features

- Pure spindle cell (n = 6)
- Fusocellular + Epithelioid (n = 4)
- Storiform pattern (n = 1)
- Keloid pattern (n = 1)
Results III: Histopathological features

- **Vascular invasion (n = 1)**
- **Perineural invasion (n = 4)**
- **Ulceration (n = 4)**

**Breslow Index:** 6.55 mm

**Mitotic Index:** 4.55/mm²
Results III: **Histopathological features**

- Sclerosis <10% (n = 6)
- Sclerosis 10 - 90% (n = 4)
## Results IV: Immunohistochemical profile

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Positives</th>
<th>Negatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>MelanA</td>
<td>5/10</td>
<td>5/10</td>
</tr>
<tr>
<td>HMB45</td>
<td>5/10</td>
<td>5/10</td>
</tr>
<tr>
<td>S100</td>
<td>10/10</td>
<td></td>
</tr>
<tr>
<td>SOX10</td>
<td>10/10</td>
<td></td>
</tr>
</tbody>
</table>

[Images of tissue sections for each antibody]
Results V: Molecular profile

BRAF V600E
NRAS
C-KIT

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\[ \text{NRAS} \text{ c.182A>G; p.(Gln61Arg)} \]
\[ \text{c-KIT} \text{ c.2464A>T; p.N822Y} \]
\[ \text{c-KIT} \text{ c.1964A>G; p.N655S} \]
Results VI: Electron microscopy

Aberrants Melanosomes (5/5)
Results VII: Follow up

1. Full resection
   -
   -
   -
   LOCOREGIONAL RECIDIVA
   Incomplete resection (deep margin)
   Local RT
   DEATH

2. Full resection
   SLNB -
   -
   -
   LOCOREGIONAL RECIDIVA

3. Full resection
   SLNB -
   -
   -
   LOCOREGIONAL RECIDIVA

4. Incomplete resection (deep margin)
   Full resection
   -
   -
   LOCOREGIONAL RECIDIVA
   Incomplete resection (all margins)
   SLNB +

5. Full resection
   -
   -
   -
   LOCOREGIONAL RECIDIVA
   DEATH

6. Full resection
   -
   -
   -
   LOCOREGIONAL RECIDIVA
   DEATH

7. Full resection
   -
   -
   -
   LOCOREGIONAL RECIDIVA
   DEATH

8. Incomplete resection (deep margin)
   SLNB +
   -
   Lymphadenectomy
   LOCOREGIONAL RECIDIVA AND DISTANCE
   DEATH

9. Full resection
   SLNB -
   -
   -
   LOCOREGIONAL RECIDIVA
   DEATH

10. Full resection
    -
    -
    -
    LOCOREGIONAL RECIDIVA
    DEATH
Results VII: Follow up

Overall survival
3 years and a month
Conclusions

- Spindle cell melanomas are a distinctive clinicopathologic melanoma subtype that may have important diagnostic challenges.

- Immunohistochemically, common melanocytic markers (MelanA and HMB45) are frequently negative, whereas SOX10 is very helpful in this setting.

- *BRAF, NRAS* and *c-KIT* mutations are often negative.

- Ultrastructural study to differentiate with tumors of neural lineage could be useful in some cases.

- Locoregional aggressiveness and elevated mortality rates are frequent.

- Future comparative studies with a larger number of cases are necessary.