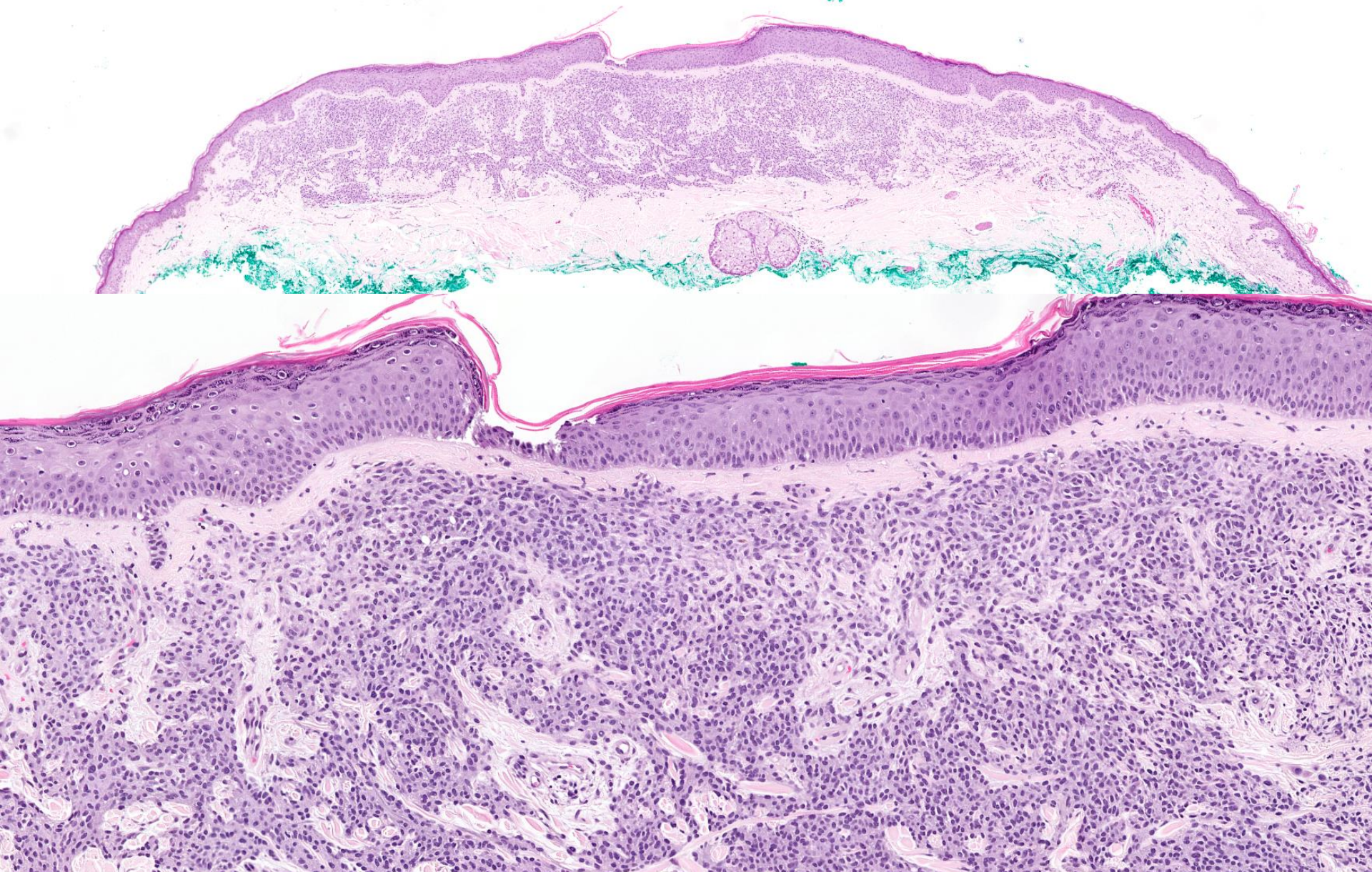


## Case 2

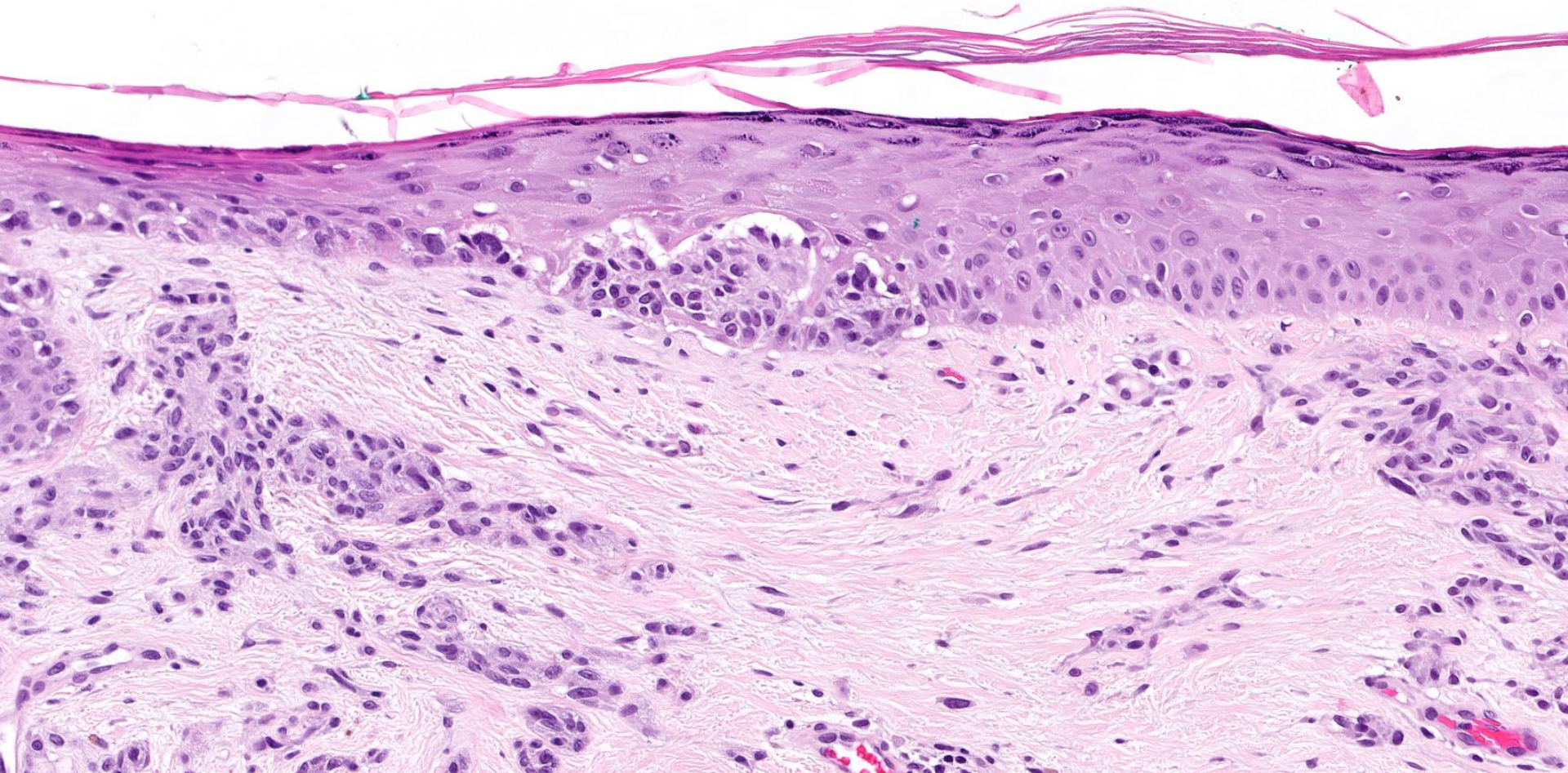
62 year-old man with left posterior shoulder papule.

Neoplasm of uncertain biological potential vs basal cell carcinoma.

# Histopathological Features

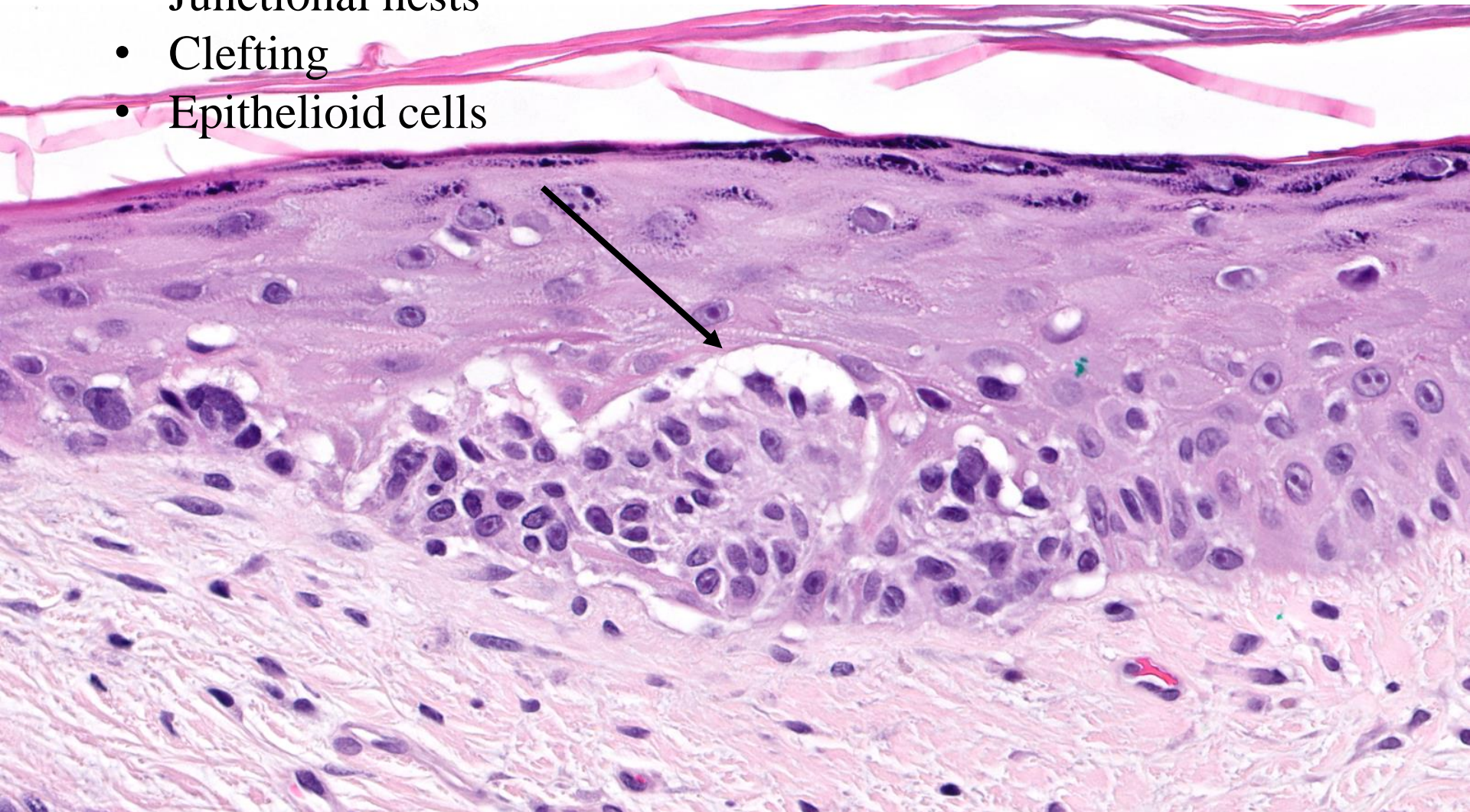


# Histopathological Features

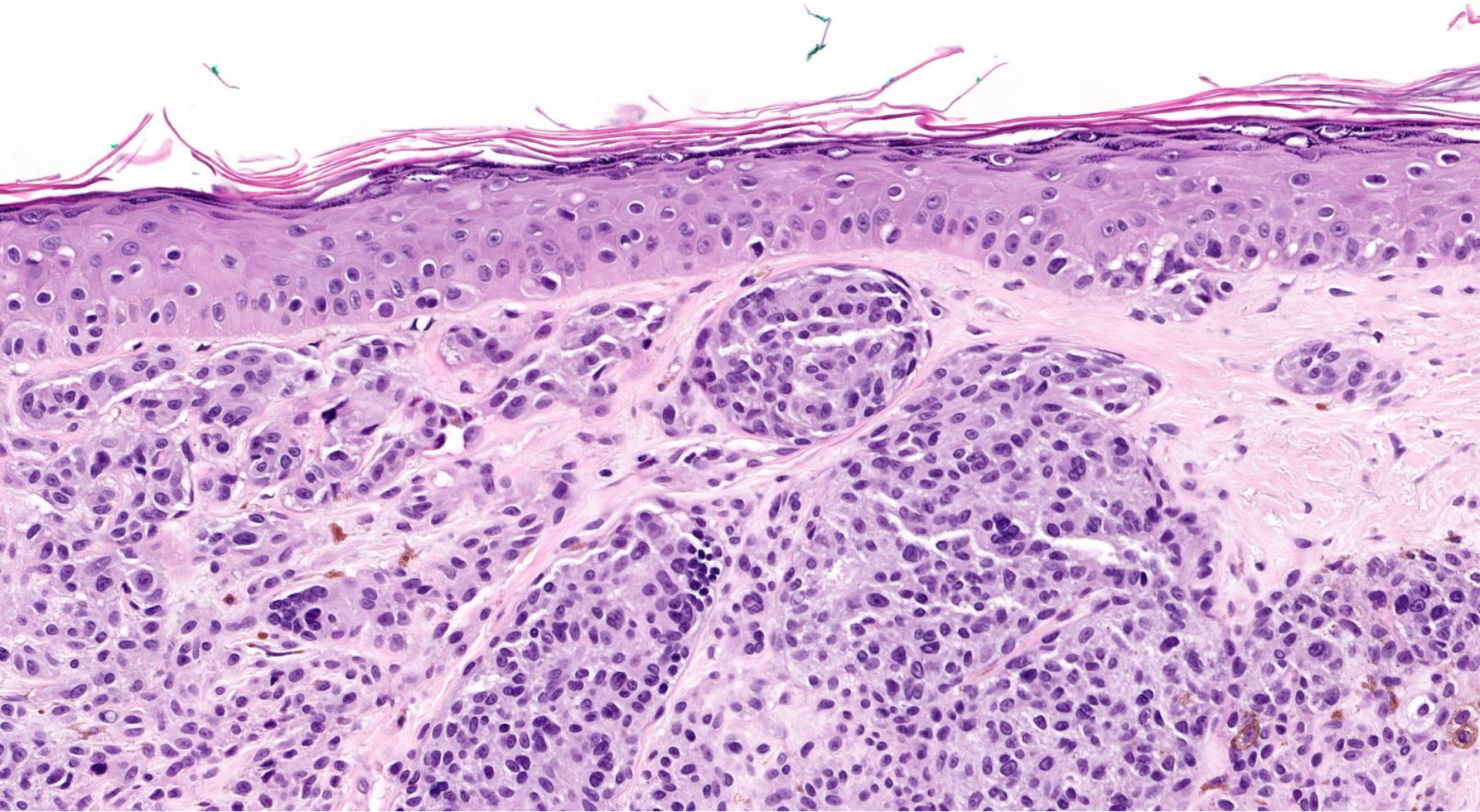


# Histopathological Features

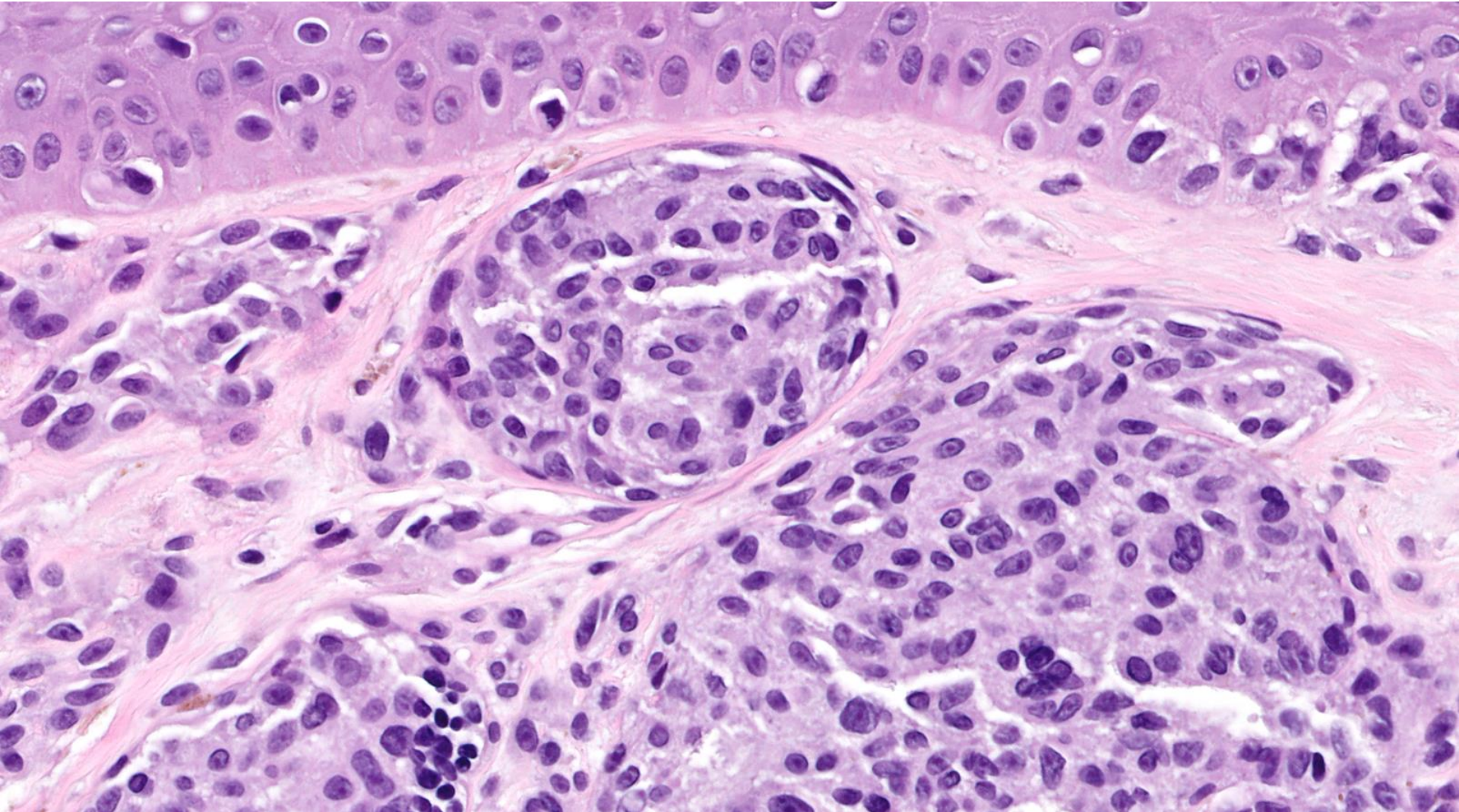
- Junctional nests
- Clefting
- Epithelioid cells



# Histopathological Features

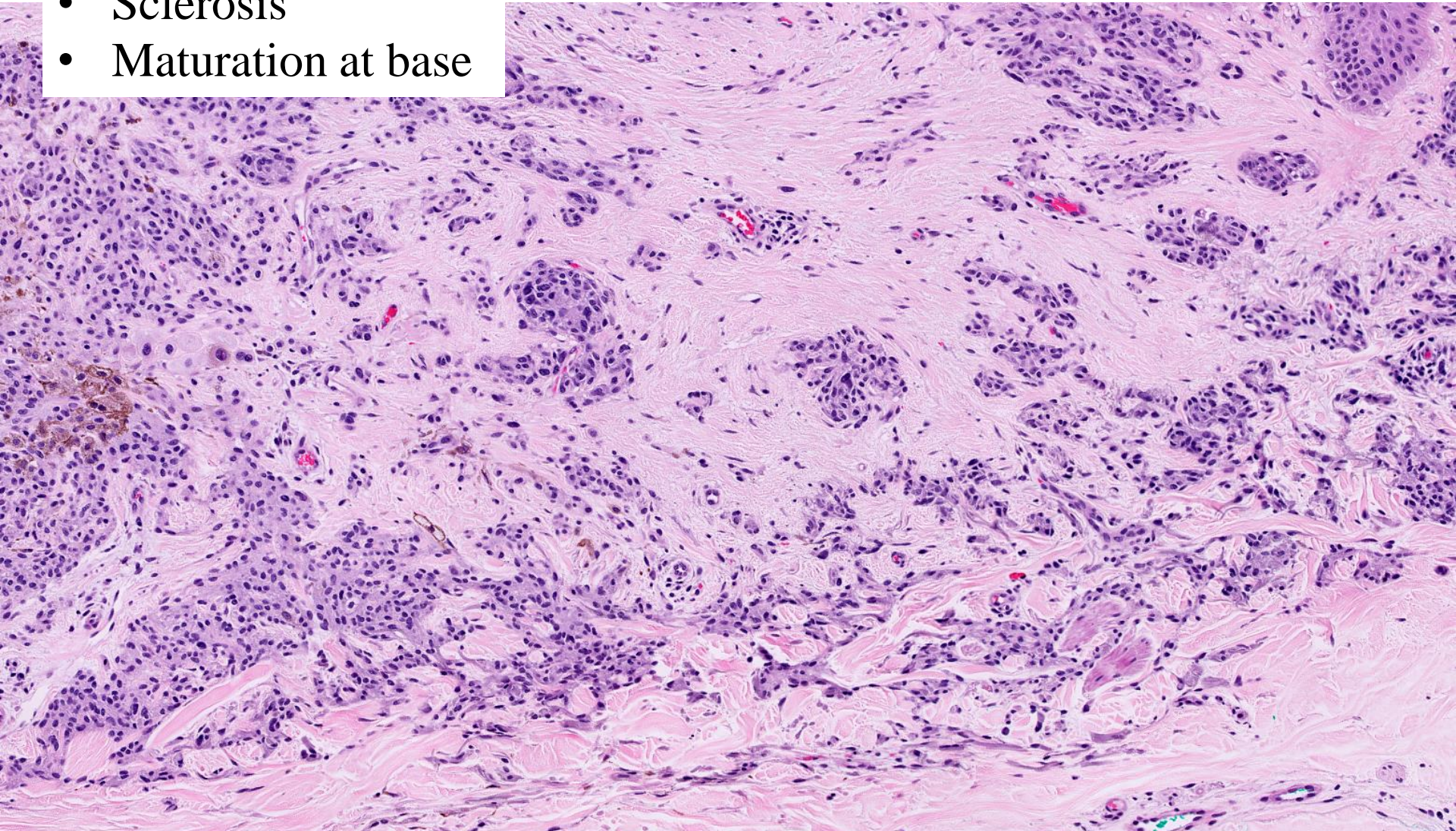


# Histopathological Features



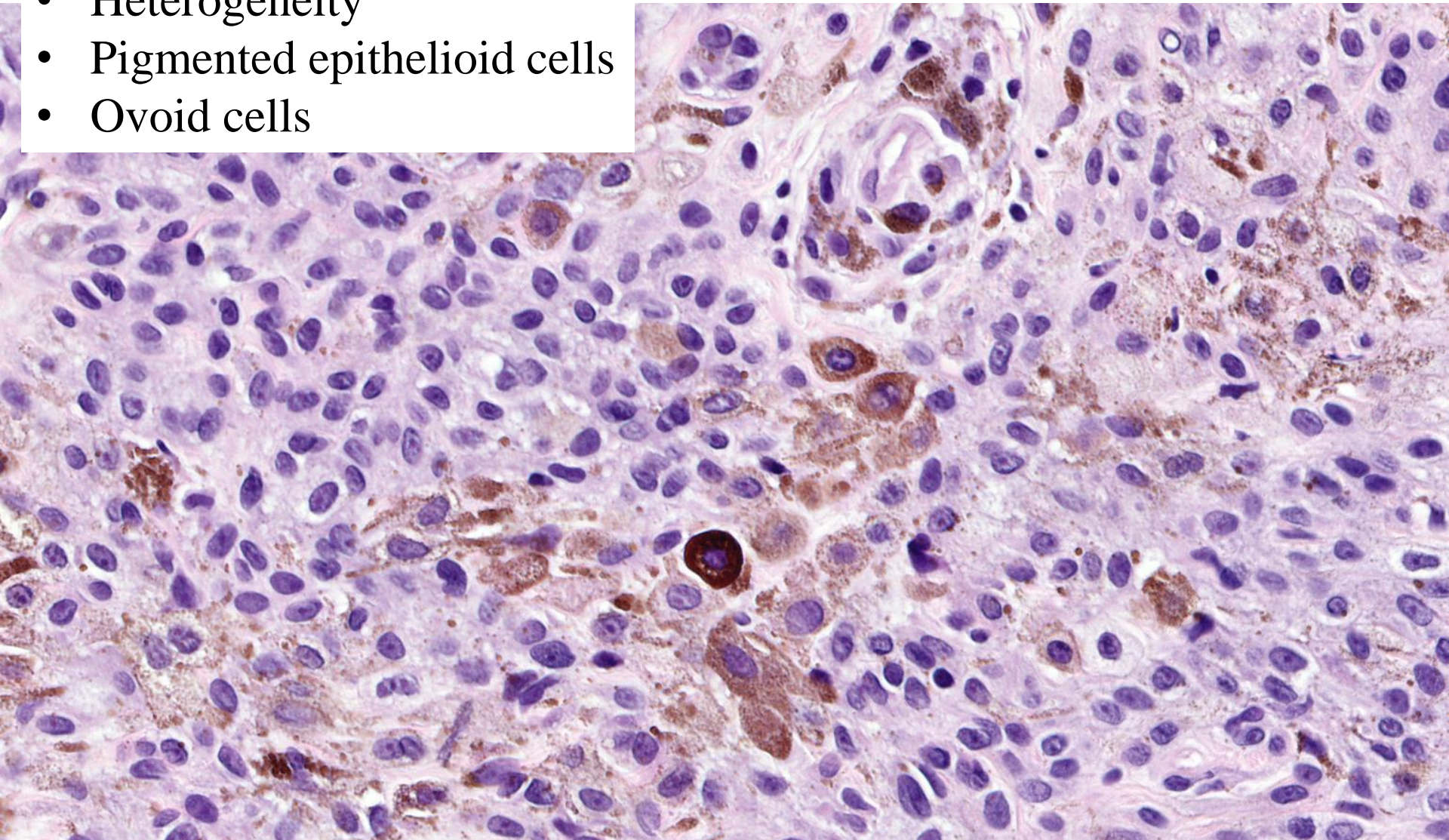
# Histopathological Features

- Sclerosis
- Maturation at base



# Histopathological Features

- Heterogeneity
- Pigmented epithelioid cells
- Ovoid cells



# Histopathological Features

- Diameter 6 mm\*
- Plaque-type configuration
- Well circumscribed
- Slight asymmetry
- Effacement of epidermis
- Thickness: 1 mm\*
- No ulceration\*
- Partial maturation
- Epithelioid, spindle, ovoid melanocytes
- Cytological atypia\*
- No involvement subcutaneous fat\*
- 1 mitosis per mm<sup>2</sup>\*

1. What is the most likely preliminary diagnosis?

- a. Spitz nevus/tumor
- b. Atypical spitzoid melanocytic neoplasm
- c. Melanocytoma
- d. “Spitzoid” melanoma

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2. What immunohistochemistry might be of value?

- a. BRAF V600E
- b. p16
- c. PRAME
- d. All of the above
- e. None of the above.

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a. BRAF V600E

b. p16

c. PRAME

d. **All of the above**

e. None of the above.

# Immunohistochemistry

- Melan-A, SOX10, BAP1, p16 +
- PRAME < 50% +
- $\beta$ -catenin, BRAF V600E --

3. What molecular study might be of most value?

- a. Routine FISH
- b. Next generation sequencing panel
- c. Array comparative genomic hybridization
- d. None of the above needed for this case.

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# Molecular Analysis

- Mutations in BRAF V600K, KMT2A, NFE2L2, PIK3CA, SMARCA4, TERT promoter hot spot
- High mutation burden
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- Mutations in BRAF V600K, KMT2A, NFE2L2, PIK3CA, SMARCA4, TERT promoter hot spot
- High mutation burden
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## 4. What is the most likely diagnosis?

- a. Spitz nevus/tumor
- b. Atypical dermal spitzoid melanocytic neoplasm with uncertain malignant potential. Treat as melanoma pT1b
- c. Melanocytoma
- d. “Spitzoid” melanoma

## 4. What is the most likely diagnosis?

- a. Spitz nevus/tumor
- b. Atypical dermal spitzoid melanocytic neoplasm with uncertain malignant potential.  
Treat as melanoma pT1b**
- c. Melanocytoma
- d. “Spitzoid” melanoma

# Clinical Course

- Wide excision: No residual tumor
- New patient, no evidence of disease.

# Histopathological and Other Features

## Criteria for melanoma

- Age 62
- Slight asymmetry
- Cytological atypia
- Solar elastosis
- TERT promoter mutation\*

## Criteria against melanoma

- Diameter 6 mm\*
- Thickness: 1 mm\*
- No ulceration\*
- Mitotic rate: 1 per mm<sup>2</sup>\*
- Partial maturation
- p16 retained\*
- PRAME < 50%
- Well-circumscribed

# Summary

- Morphological features argue against clear-cut melanoma
- BRAFV600K-mutated spitzoid tumors are reported.
- In conventional melanomas, BRAFV600K mutation is associated with a more aggressive course than BRAFV600E mutated melanomas.
- TERT promoter mutations may be seen in nevi and ASTs