



Sebaceoma with *GRHL* fusions: Expanding the clinical and morphological spectrum in a series of 3 cases

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Disclosures

I do not have any relevant financial relationships to disclose

Background

- Sebaceoma is a benign adnexal neoplasm with sebaceous differentiation, composed predominantly of immature basaloid cells and variable mature sebocytes.
- A subset of cases has been associated with mismatch repair (MMR) deficiency.
- Recent work (Legrand et al. 2025) has identified recurrent *GRHL1* and *GRHL2* gene fusions in a subset of molecularly distinct sebaceomas.
- Grainyhead-like (*GRHL*) gene encodes conserved transcriptional factors that regulate key processes in embryogenesis and, when dysregulated, contribute to tumorigenesis.

Objectives:

- To describe clinical, histopathologic, and molecular features of 3 additional cases of sebaceoma with *GRHL* fusions.
- To highlight the utility of molecular testing in accurately classifying adnexal neoplasms with overlapping or ambiguous histologic features.

CASE#1

A 41-year-old male presented with a 1.1 cm nodule on the lower lip.

CASE#1

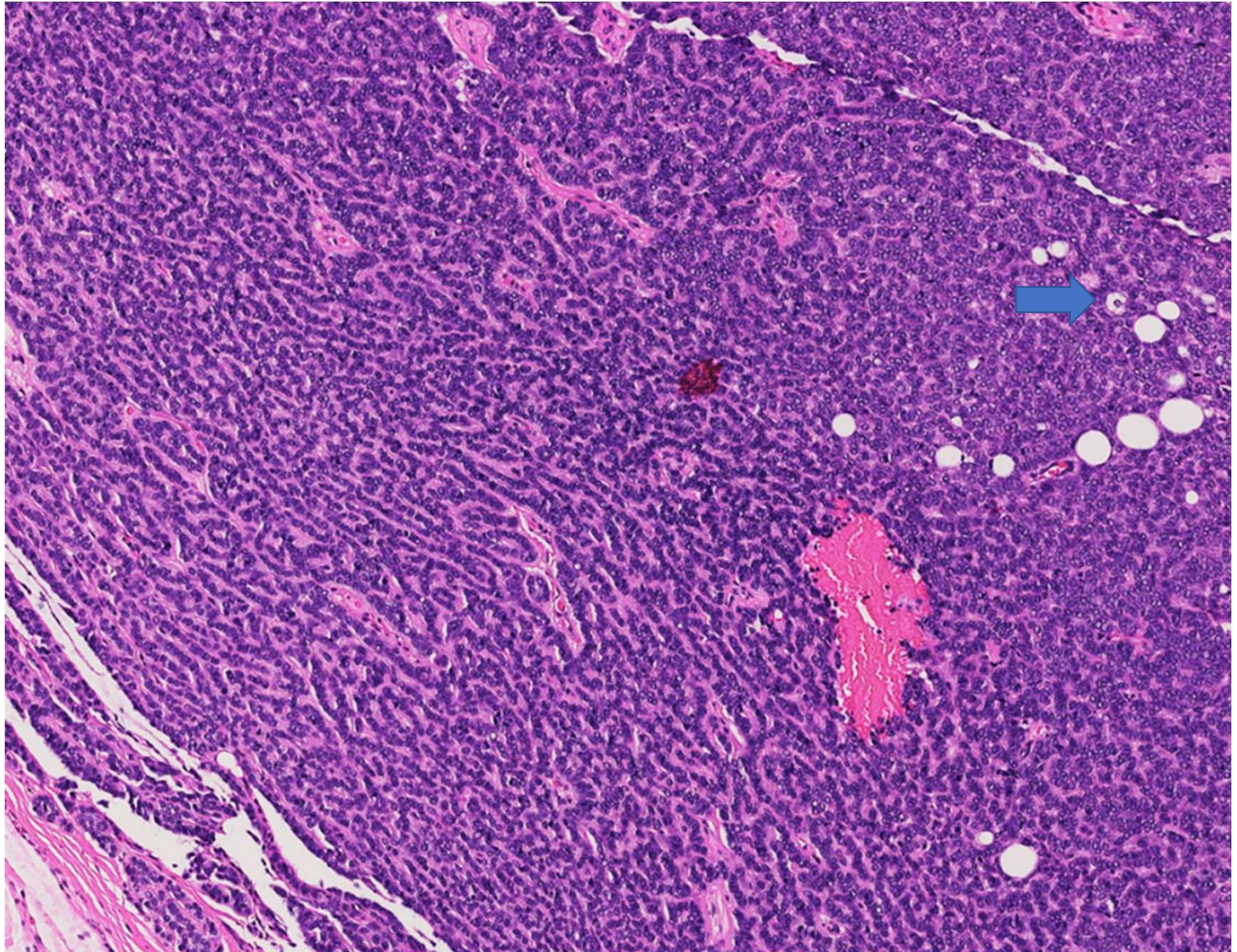
Well circumscribed dermal
nodule



1x

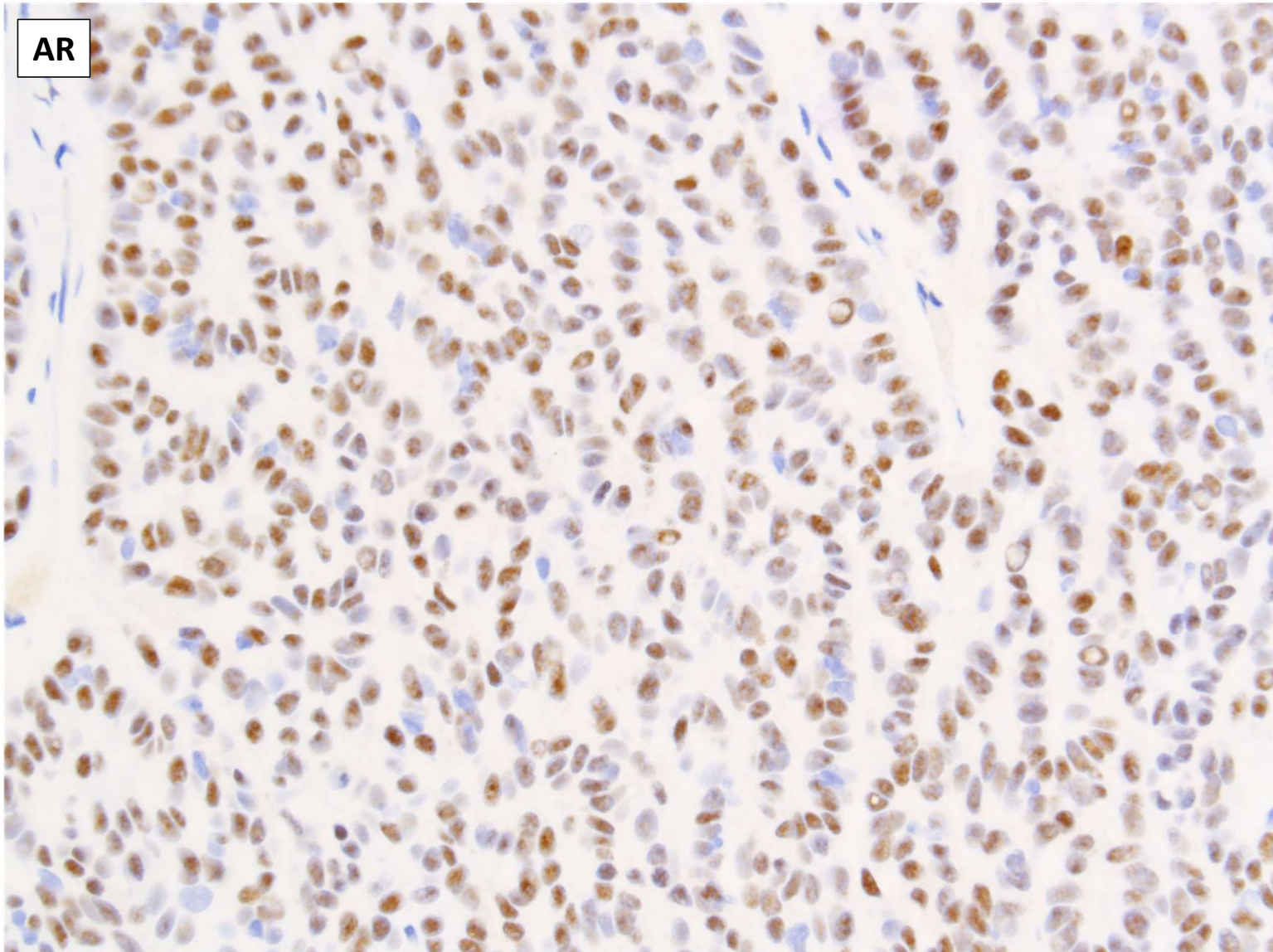
CASE#1

Basaloid tumor with
“rippled” growth pattern
and focal sebocytes



10x

AR



40x

CASE#1

Histopathology

- Well-circumscribed dermal nodule composed of basaloid tumor cells exhibiting rippled growth pattern with scattered mature sebocytes.

Immunohistochemistry

- Strong nuclear positivity for androgen receptor (AR).

Molecular studies (Next generation sequencing)

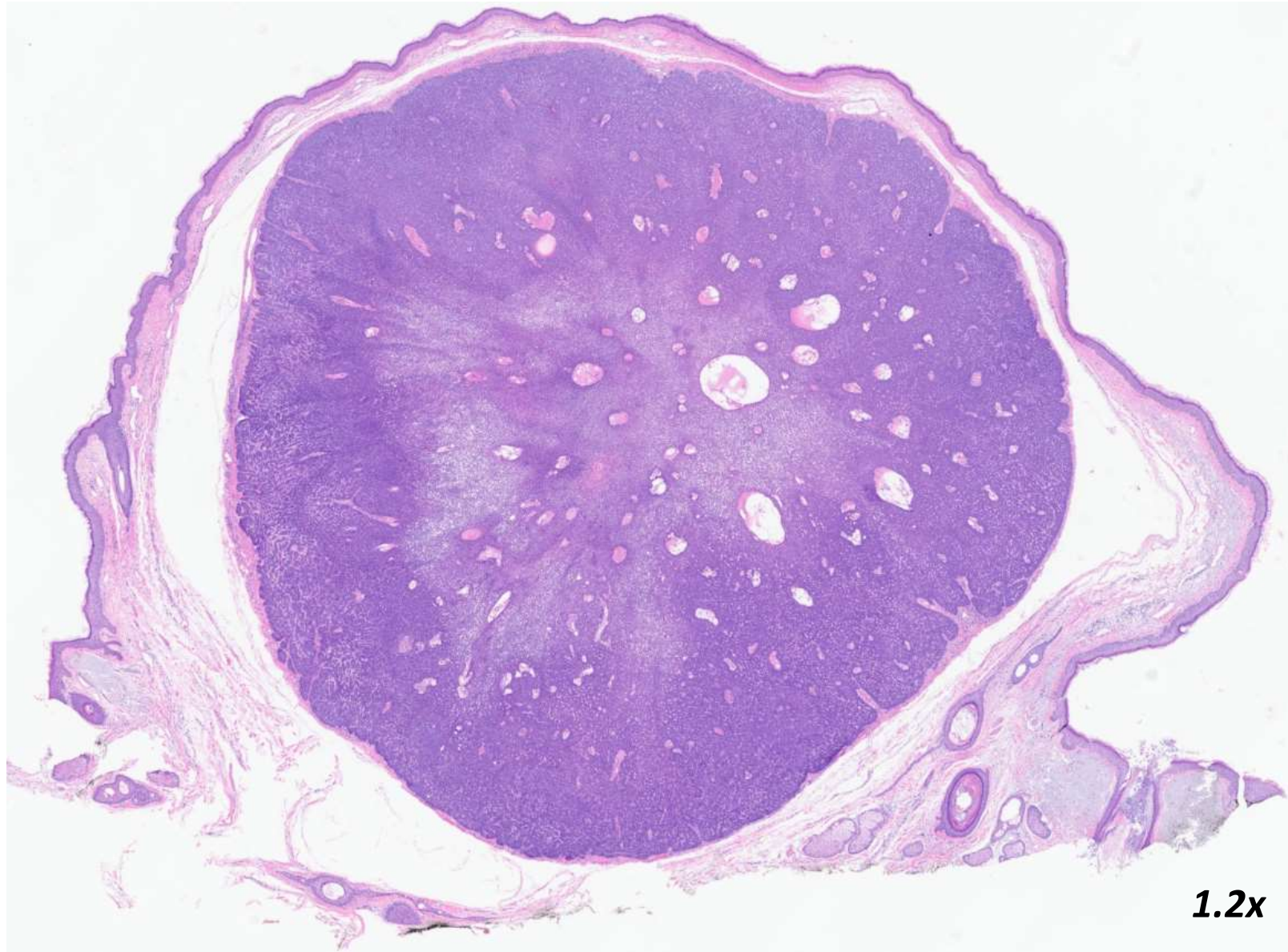
- *RCOR1::GRHL2* fusion.

CASE#2

An 84-year-old male presents with a smooth, pedunculated, flesh-colored 1.0 cm papule on the cheek.

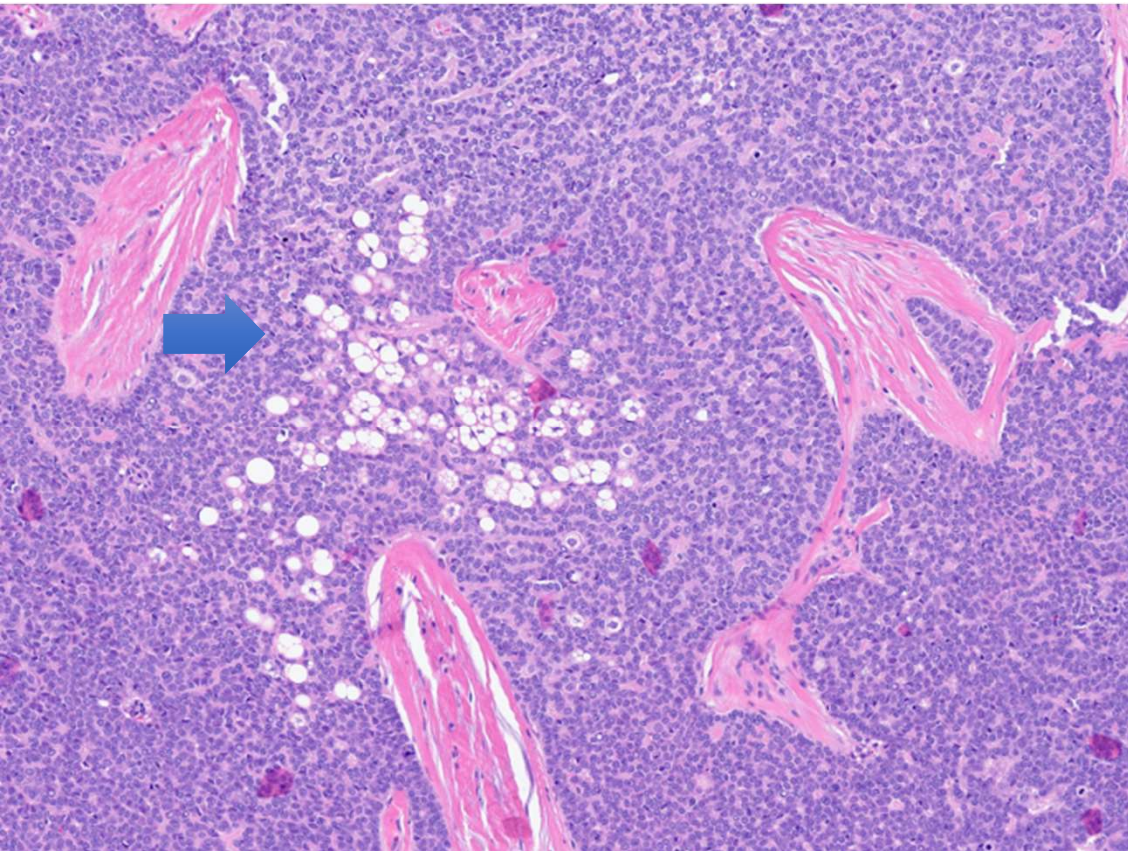
CASE#2

Sharply circumscribed
dermal tumor
composed of basaloid
cells

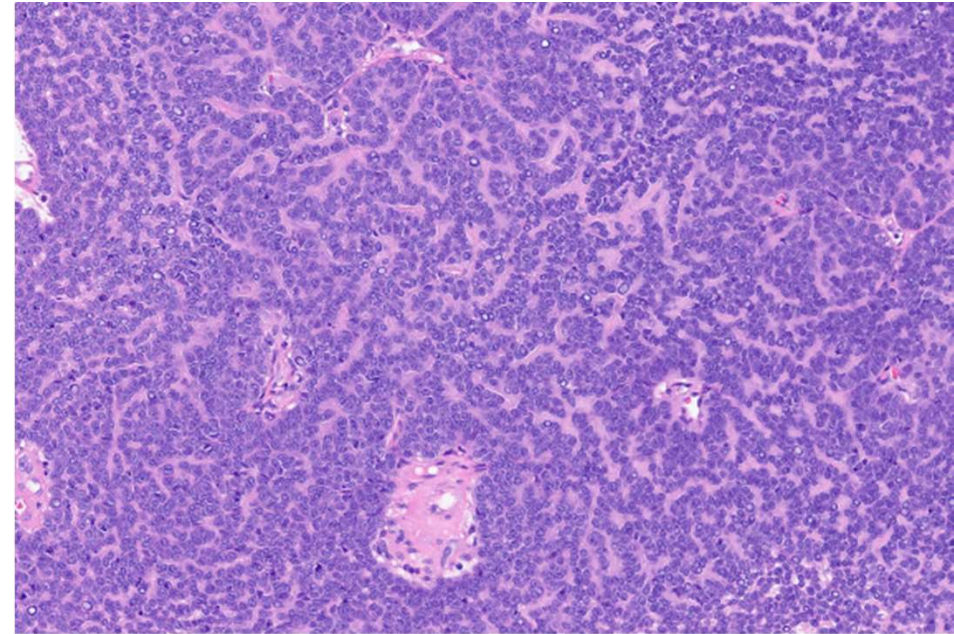


1.2x

CASE#2



11x

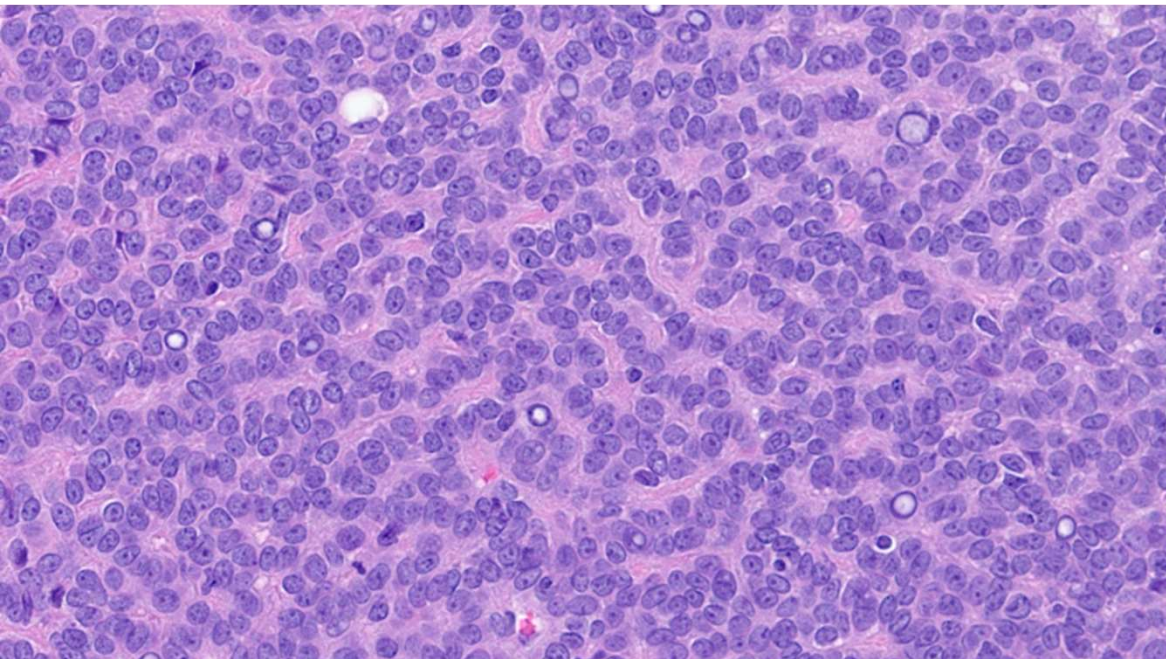


14x

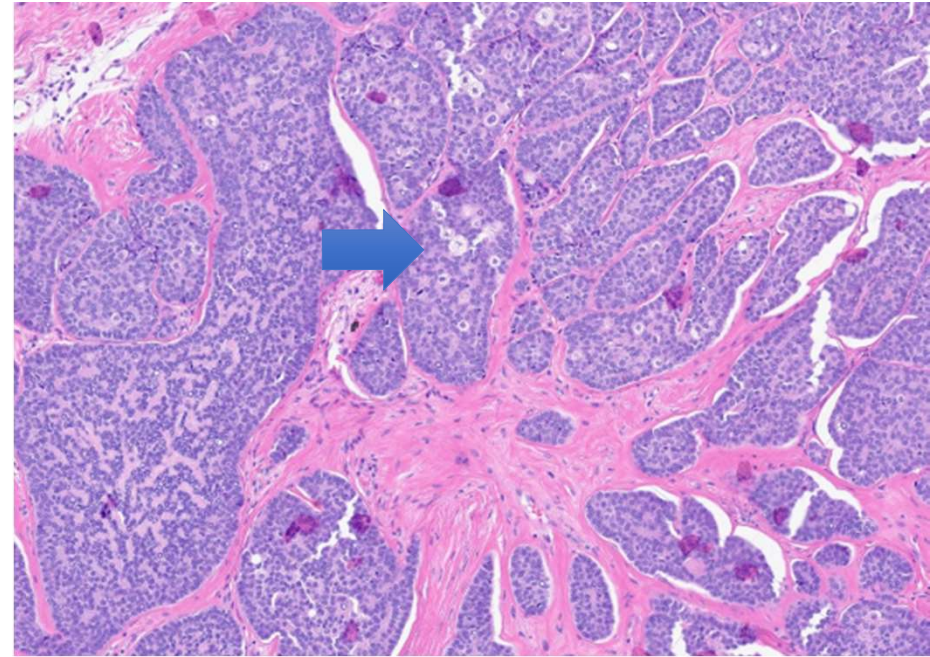
Focal palisaded or "rippled" pattern
Aggregates of mature sebocytes

CASE#2

Stromal hyalinization



40x



10x

CASE#2

Histopathology:

- Sharply circumscribed dermal tumor composed predominantly of basaloid cells with scattered mature sebocytes.
- Palisaded cords of tumor cells exhibit a subtle rippled pattern.
- No significant atypia.

Immunohistochemistry

- Not performed.

Molecular studies (Next generation sequencing)

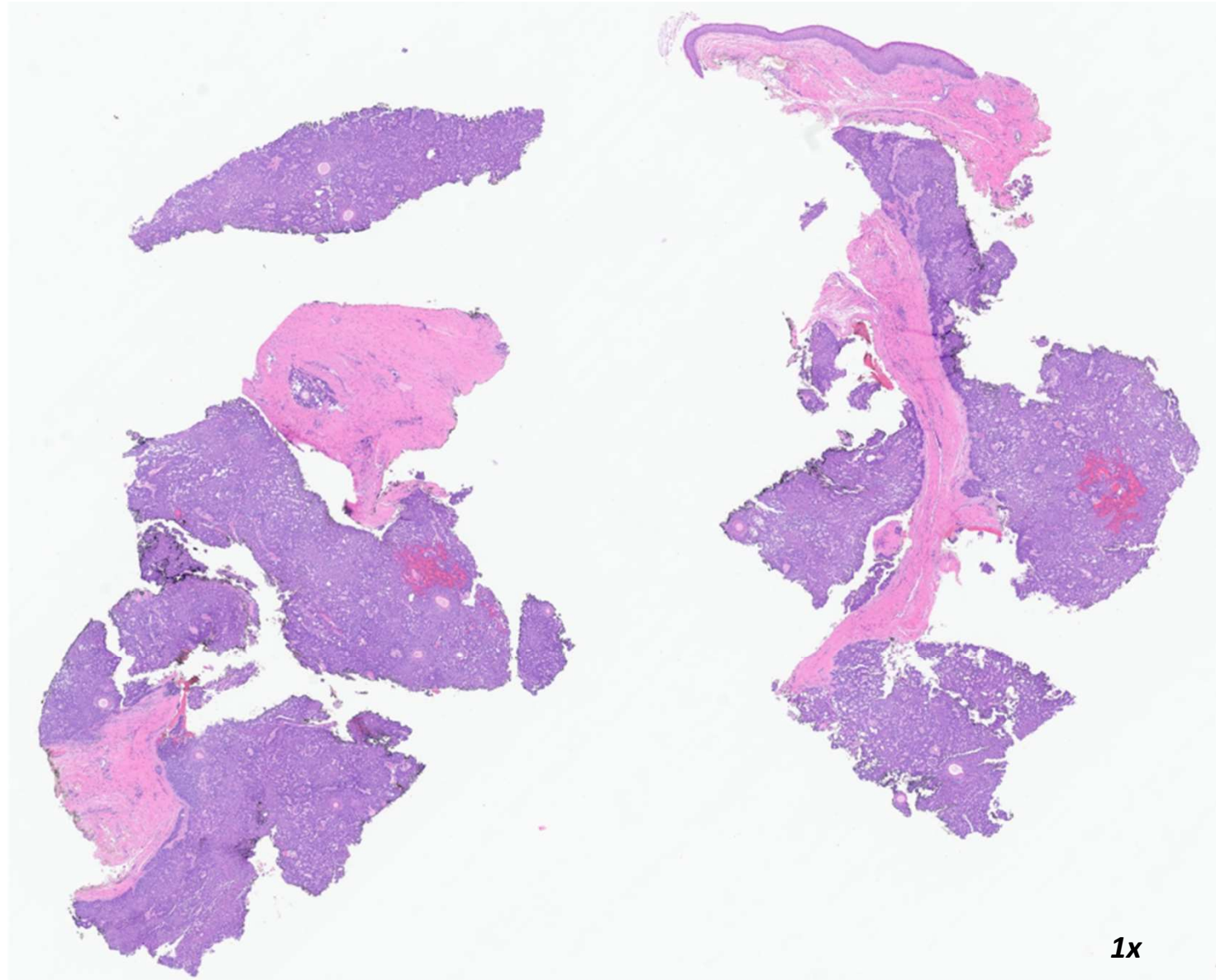
- *RCOR1::GRHL2* fusion.

CASE#3

A 40-year-old male presented with a 3.0 cm axillary nodule.

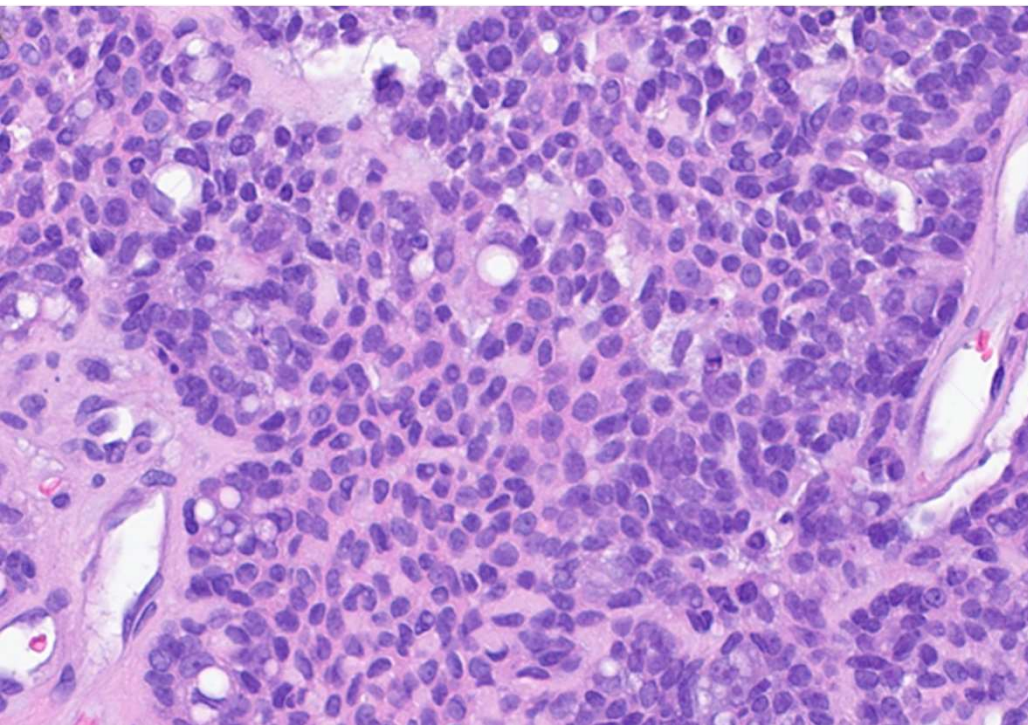
CASE#3

Intradermal tumor with
prominent fibrous septae

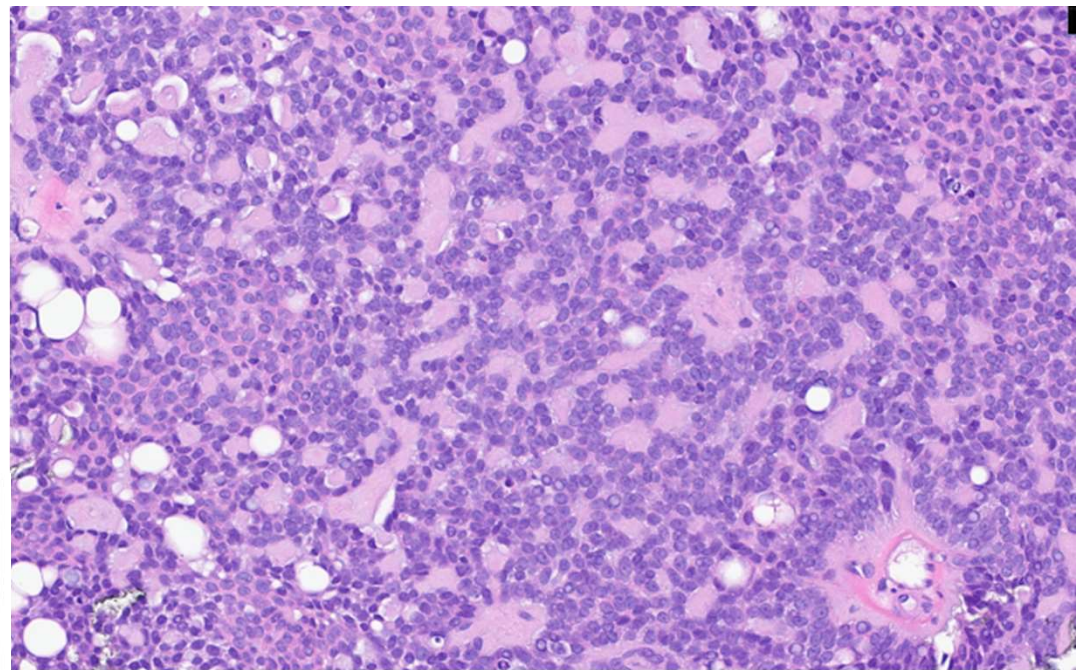


1x

CASE#3

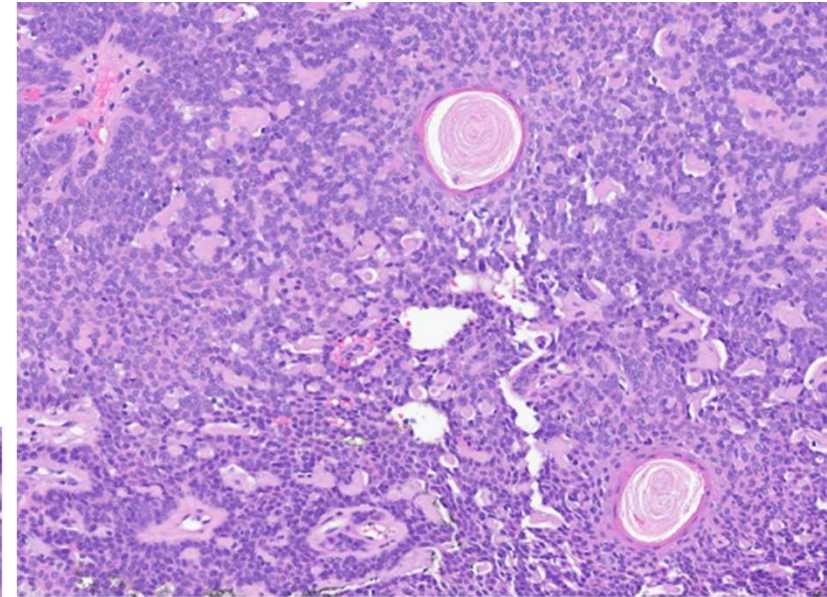
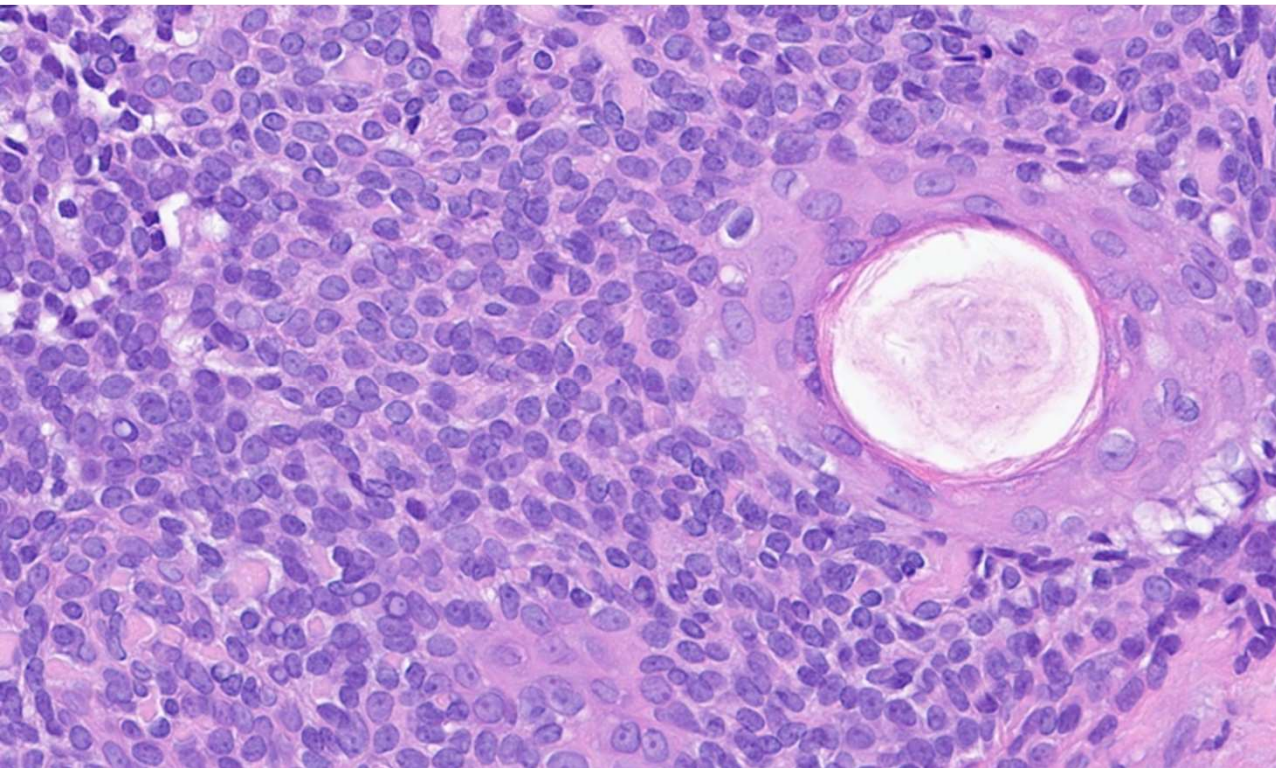


30x



21x

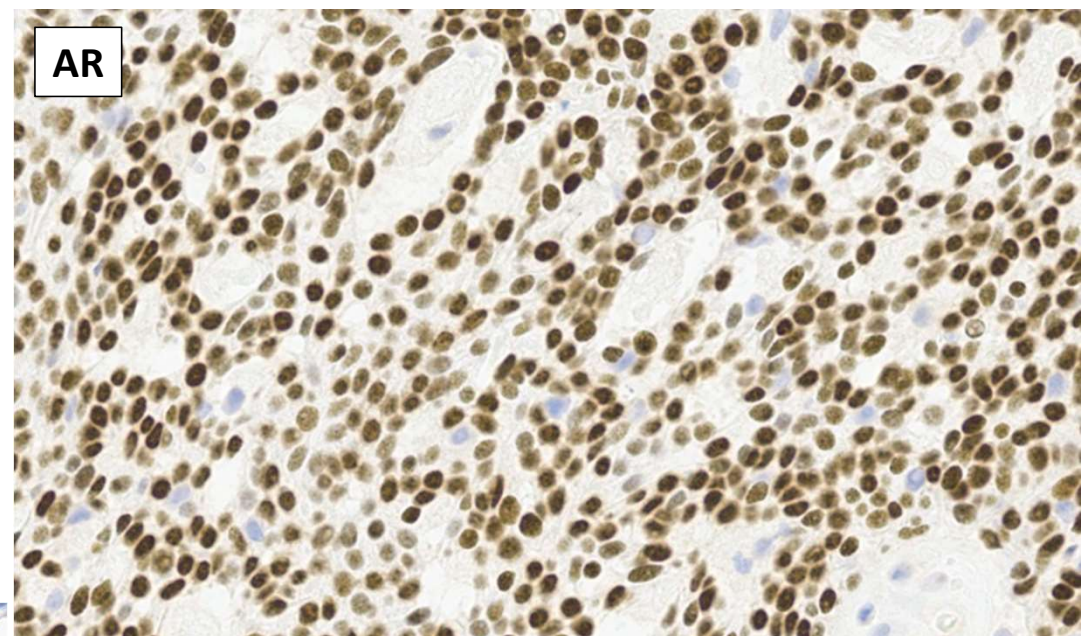
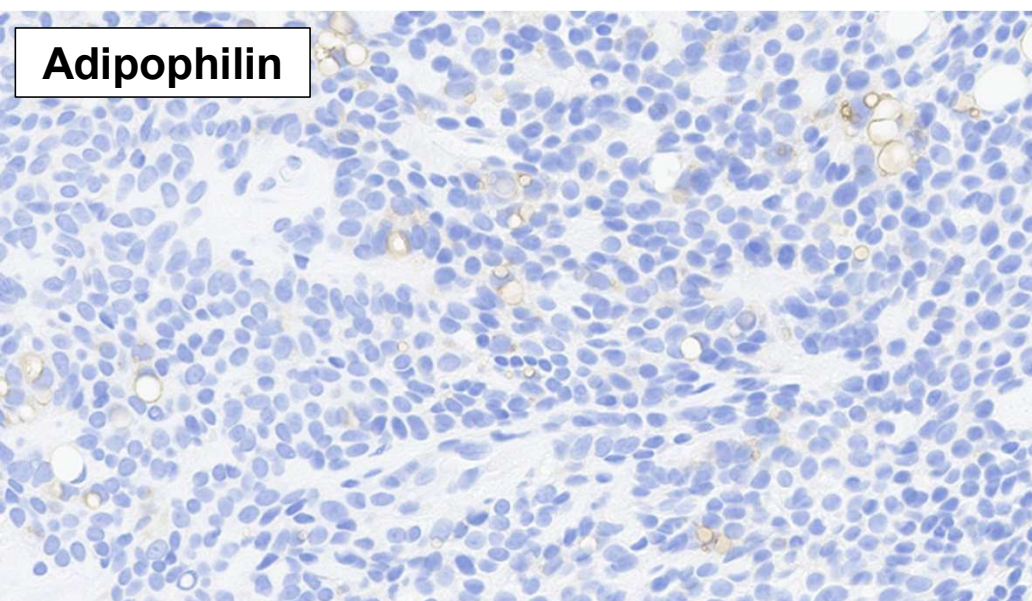
Follicular differentiation



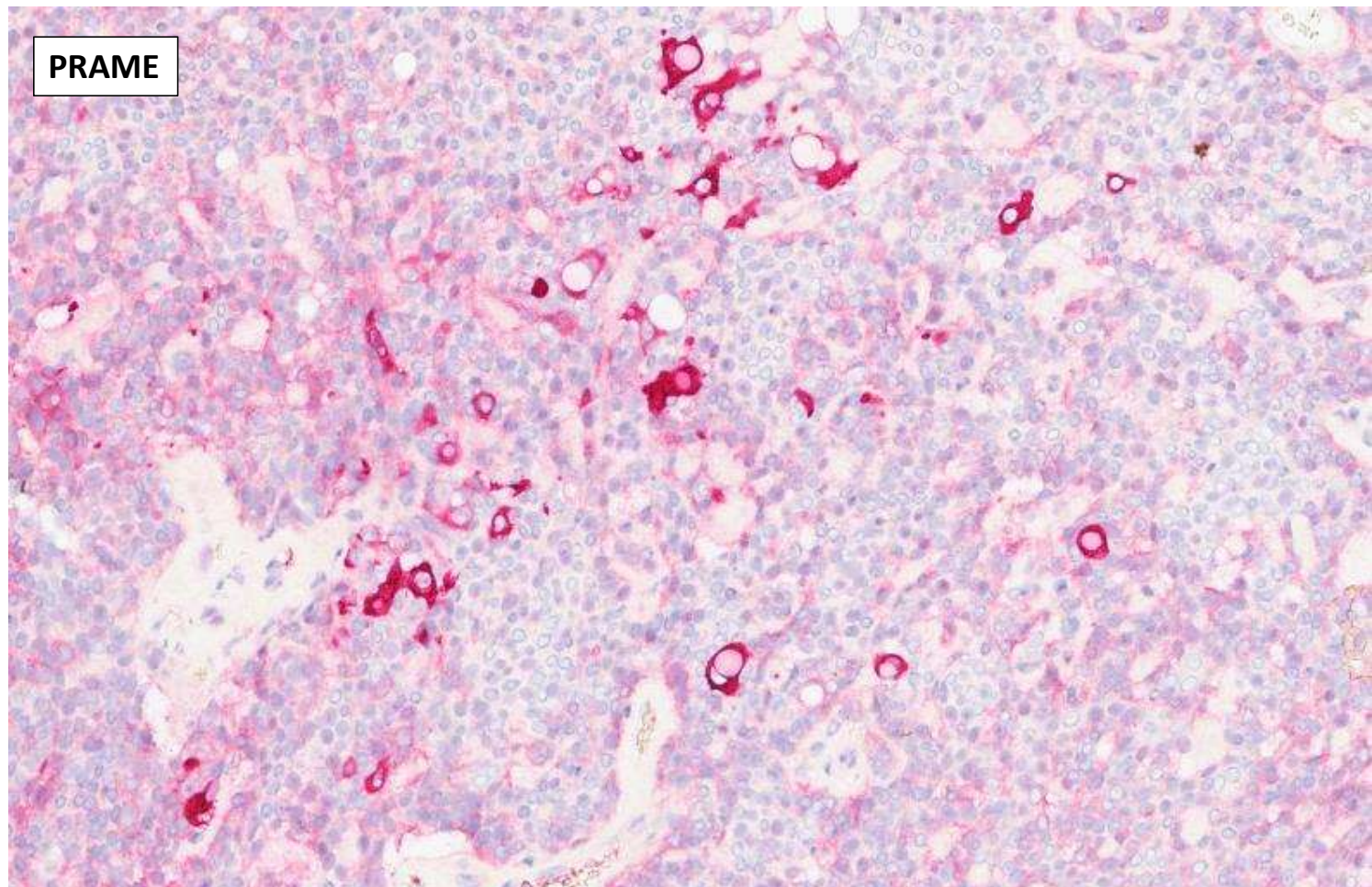
14.5x

40x

CASE#3



CASE#3



21x

CASE#3

Histopathology

- Dermal adnexal tumor with fibrous septa, uniform basaloid cells with bland nuclei and pale eosinophilic cytoplasm.
- Scattered cytoplasmic vacuoles, suggestive of mature sebocytes.
- Infundibulocystic differentiation.
- No significant cytologic atypia or mitotic activity.

Immunohistochemistry

- Strong and diffuse positivity for AR.
- Patchy adipophilin and PRAME.

Molecular Studies (Next generation sequencing)

- *RCOR1::GRHL2* fusion.

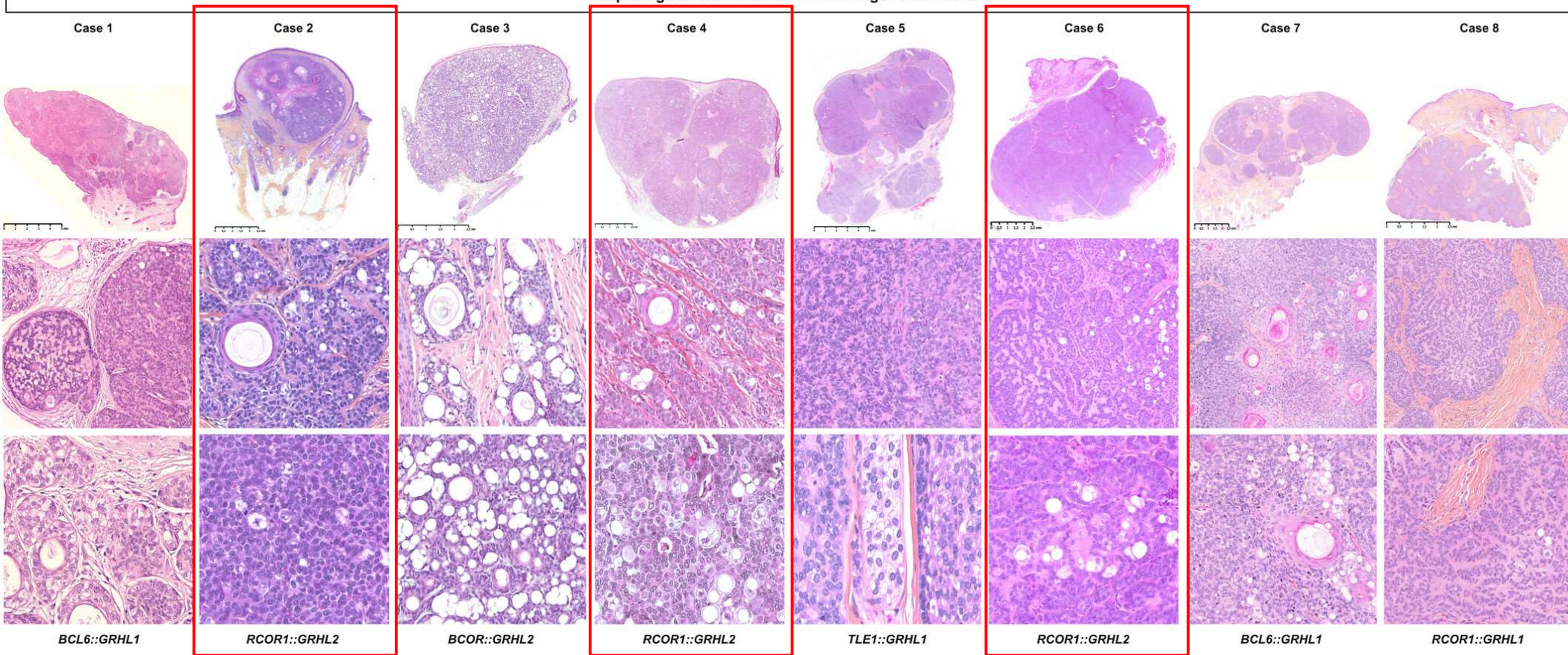
Summary of clinical, histopathological, and molecular findings

Case	Age	Sex	Site	Size (cm)	Histopathology	IHC findings	Fusions (Breakpoints)
1	41	M	Lower cutaneous lip	1.1	Rippled pattern	AR+	<i>RCOR1::GRHL2</i> , Exon 11; Exon 3
2	84	M	Right cheek	1.0	Rippled pattern	Not performed	<i>RCOR1::GRHL2</i> , Exon 11; Exon 3
3	40	M	Axilla	3.0	Follicular differentiation	AR+ Adipophilin+ (focal) PRAME+ (patchy)	<i>RCOR1::GRHL2</i> (Exon 11; Exon 3)

Discussion

- *GRHL* fusions define a subset of sebaceomas with diverse morphologic features.
- Among these include a "rippled" pattern, and tumors with infundibulocystic differentiation.
- Tumors can arise outside of the head and neck, including axilla (case 3).
- Findings align with prior reports of *GRHL*-fusion sebaceomas.
- Immunohistochemical markers of adipocytic differentiation (such as AR, adipophilin and PRAME), may be helpful in supporting the diagnosis.

Morphological features of *GRHL*-rearranged sebaceomas

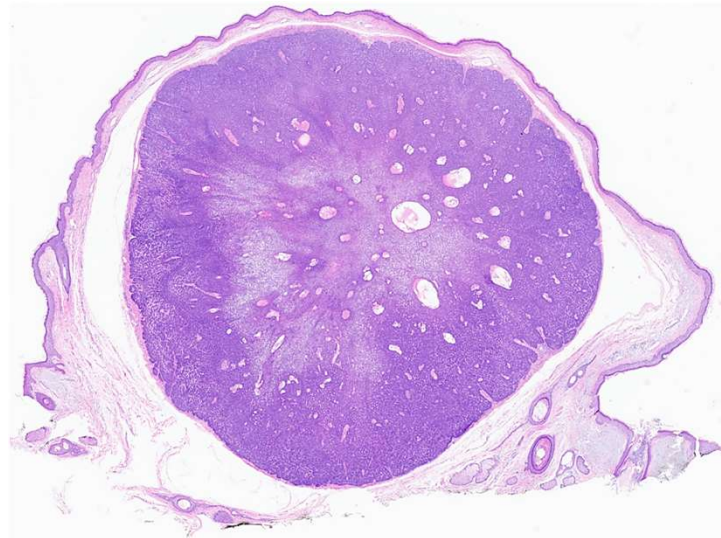


Legrand M, Louveau B, Macagno N, et al. Recurrent *GRHL* fusions in a subset of sebaceoma. *Histopathology*. 2025;86(4):571–584.

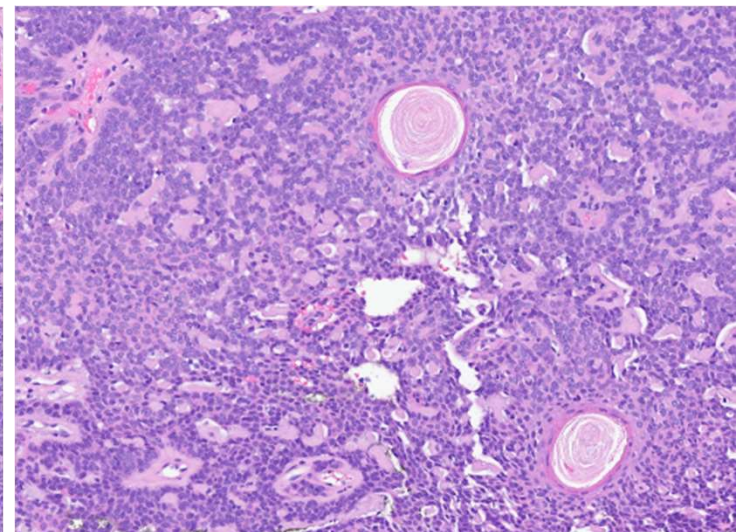
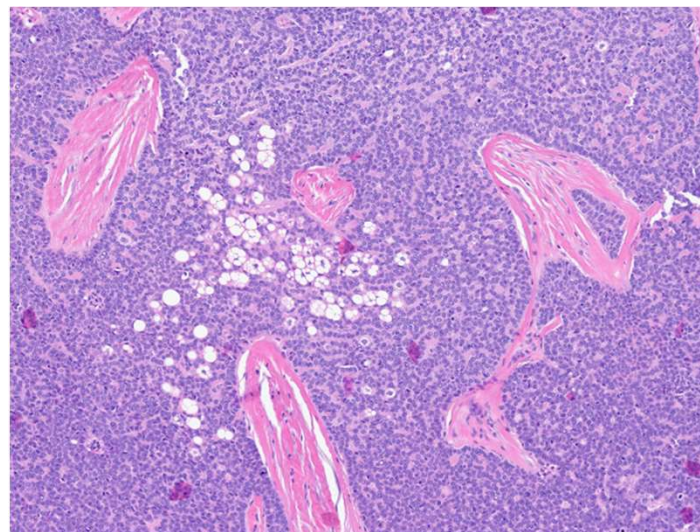
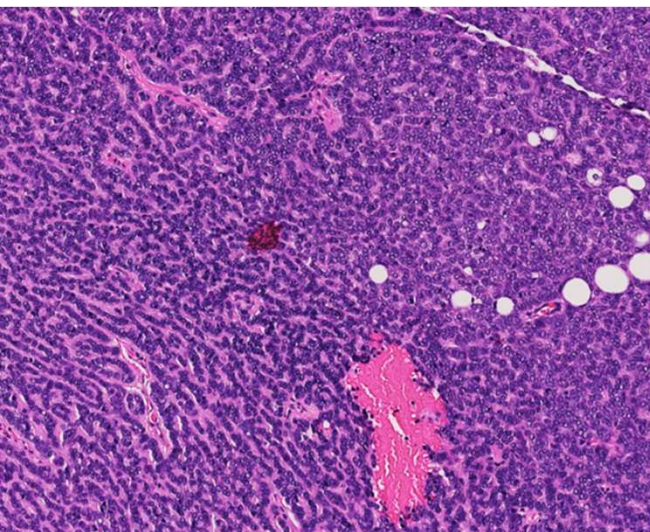
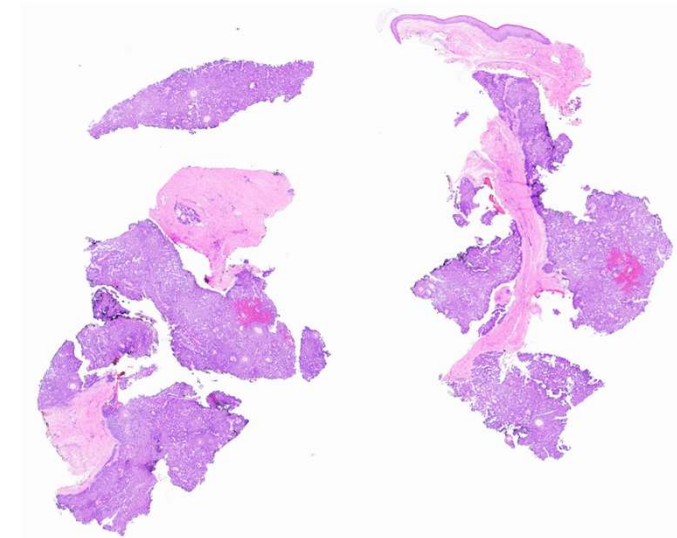
Case 1



Case 2



Case 3



Conclusion

- *GRHL*-rearranged sebaceomas show a broad morphologic spectrum, including follicular differentiation and rippled/organoid growth pattern
- Recognition can be challenging, particularly in tumors with focal mature sebocytes or prominent infundibulocystic features, which may increase the risk of misclassification.
- Heightened awareness of this emerging entity, combined with targeted fusion testing, can aid in establishing accurate diagnosis in diagnostically ambiguous cases.

References:

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QUESTIONS
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