

INTRODUCTION

- Metaplastic thymoma (MT) is a rare, biphasic thymic epithelial neoplasm, historically termed “thymoma with pseudosarcomatous stroma”
- It is characterized by anastomosing islands of bland epithelial cells admixed with bland spindle cells
- WHO-recognized entity since 2004, with fewer than 40 cases reported to date
- The median age at-diagnosis is approximately 50 years with slight female predominance (M:F ≈ 1:1.5)
- Most patients are asymptomatic, with the tumor detected incidentally as an anterior mediastinal mass
- Association with myasthenia gravis is rare
- MT harbors a recurrent YAP1–MAML2 gene fusion, distinguishing it from type A/AB thymoma, which carries the GTF2I c.74146970T>A mutation
- Here, we report two cases confirmed by YAP1-MAML2 FISH, with a review of the literature

METHODS

- Retrospective clinicopathological and molecular review of two cases of metaplastic thymoma diagnosed at our institution
- Histopathological review (H&E) of the surgical resection specimens
- Immunohistochemistry: pan-cytokeratin, p63, PAX8, TdT, vimentin
- Fluorescence in situ hybridization (FISH) for YAP1-MAML2 rearrangement
- Structured literature review of previously reported case series and case reports
- Comparative analysis of clinicopathological and molecular features

DISCUSSION AND CONCLUSION

- Both our cases were younger than the composite literature average (5th to 6th decade) and presented at an early age (pT1) similar to as seen across the literature
- Female predominance or near-equal sex distribution reported across most series, mirrored in our cases
- Association with myasthenia gravis is rare
- Key histopathology and molecular notes:
- Recognize the characteristic biphasic architecture and immunophenotype (keratin/p63+ epithelial islands with keratin-negative, vimentin-positive spindle stroma) to avoid misdiagnosis as sarcoma or carcinosarcoma
- Confirm with YAP1-MAML2 FISH
- FISH analysis requires particular caution because YAP1 and MAML2 are located on the same chromosome (chromosome 11), resulting in narrow split
- MT carries an excellent prognosis after complete surgical excision. Thus, accurate recognition avoids unnecessary aggressive therapy.

- Future Direction for Research
- Larger multi-institutional molecular cohorts are needed to define the full spectrum of YAP1-MAML2 fusion partners, progression to aggressive histotypes and any prognostic correlates

REFERENCES & ACKNOWLEDGEMENTS

1. Suster S, Moran CA, Chan JK. Thymoma with pseudosarcomatous stroma. Am J Surg Pathol. 1997;21(11):1316-23.

2. Vivero M, Davinini P, Nardi V, Chan JK, Sholl LM. Metaplastic thymoma: a distinctive thymic neoplasm characterized by YAP1-MAML2 gene fusions. Mod Pathol. 2020;33(4):560-5.

3. Zhao J, Zhao R, Xiang C, Shao J, Guo L, Han Y. YAP1-MAML2 fusion as a diagnostic biomarker for metaplastic thymoma. Front Oncol. 2021;11:692283.

4. Wang M, Xu H, Han Q, Wang L. Significance of YAP1-MAML2 rearrangement and GTF2I mutation in the diagnosis and differential diagnosis of metaplastic thymoma. Ann Med. 2023;55(2):2237040.

5. Kang G, Yoon N, Han J, Kim YE, Kim TS, Kim K. Metaplastic thymoma: report of 4 cases. Korean J Pathol. 2012;46(1):92-6.

6. WHO Classification of Tumours Editorial Board. Thoracic Tumours. 5th ed. Lyon: IARC; 2021.

Acknowledgements: The authors thank the Department of Pathology, AIIMS New Delhi, for institutional support.

RESULTS

- Two cases of metaplastic thymoma, both confirmed by **YAP1-MAML2 FISH**:
- Case 1 (24y, F): incidental anterior mediastinal mass; complete excision; well-encapsulated, no necrosis/atypia/increased mitoses; stage pT1a; YAP1-MAML2 rearrangement in the majority of tumor nuclei
 - Case 2 (34y, F): 9-month progressive dyspnea; large mass (15×15×8.3 cm) abutting the great vessels; total thymectomy (17×16×6 cm, 1062 g); pT1a, R0 resection; YAP1-MAML2 rearrangement confirmed
 - Immunophenotype in both cases: epithelial islands diffusely positive for cytokeratin and p63 (focal PAX8); spindle-cell stroma negative for cytokeratin/p63.
 - Both patients achieved complete resection with an excellent expected prognosis and no indication for adjuvant therapy.

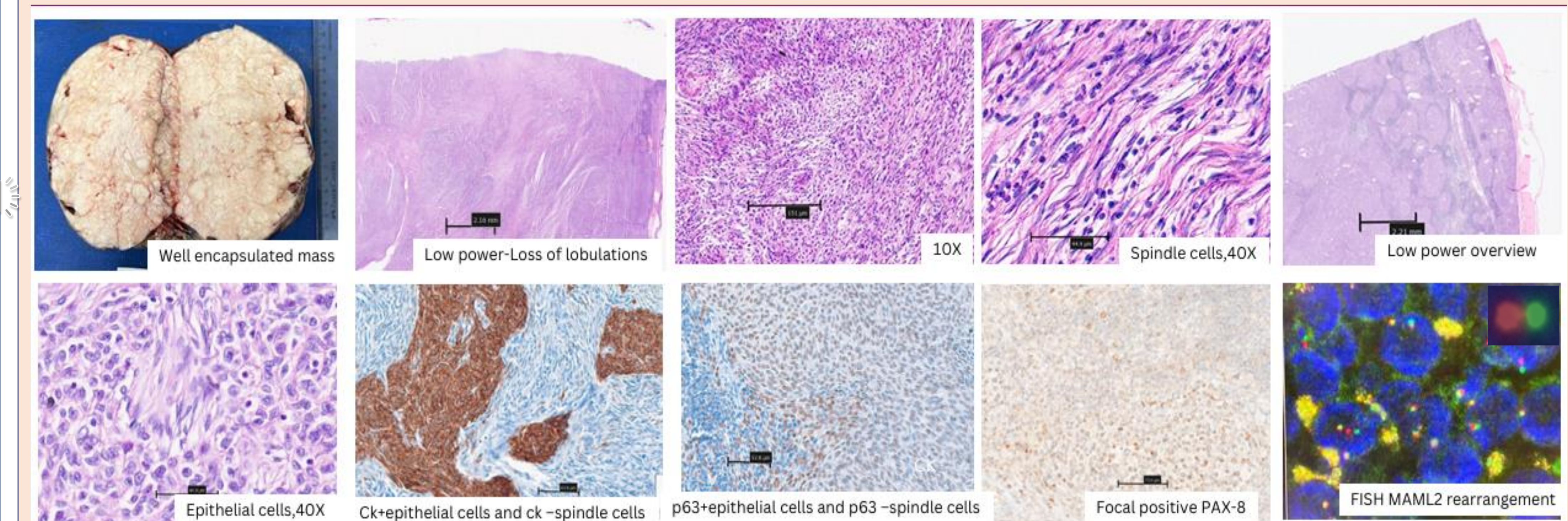


Figure 1. Composite histopathology, immunohistochemistry, and FISH findings: (top row) well-encapsulated gross specimen, loss of normal lobulation at low power, biphasic epithelial/spindle-cell morphology at 10×, spindle-cell component at 40×, low-power overview; (bottom row) epithelial cells at 40×, cytokeratin positivity restricted to epithelial cells, p63 positivity restricted to epithelial cells, focal PAX-8 positivity, and FISH demonstrating YAP1-MAML2 rearrangement.

TABLE: SUMMARY OF REPORTED METAPLASTIC THYMOMA CASE SERIES AND THE PRESENT STUDY					
STUDY	NO. OF CASES	AGE/SEX	MYASTHENIA GRAVIS ASSOCIATION	YAP1-MAML2	OUTCOME
Suster et al. 1997	6	28–70y (4M:2F)	Absent	Not performed	All alive & disease-free, 5–20y
Yoneda et al. 1999	5	44–71y (4M:1F)	Absent	Not performed	4/5 alive without disease; 1 recurrence, re-resected
Kang et al. 2012	4	43–56y (mean 49.5y)	1/4 (25%) – first reported	Not performed	All alive & disease-free
Vivero et al. 2020	8	29–66y (median 55y)	1/8 (12.5%)	6/6 tested (100%)	All alive & well, no recurrence
Zhao et al. 2021	17	29–71y (9M:8F)	Absent (1 possible)	13/17 (76.5%)	All alive without recurrence
Wang et al. 2023	5	36–74y	Absent	5/5 (100%)	All alive without disease
Present study – Case 1	1	24y, F	Absent	Positive	Recent case; not yet available
Present study – Case 2	1	34y, F	Absent	Positive	R0 resection; no recurrence reported