CASE OF THE MONTH

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- A 2 year old girl presented with a gradually progressive swelling in right upper arm since 7 months

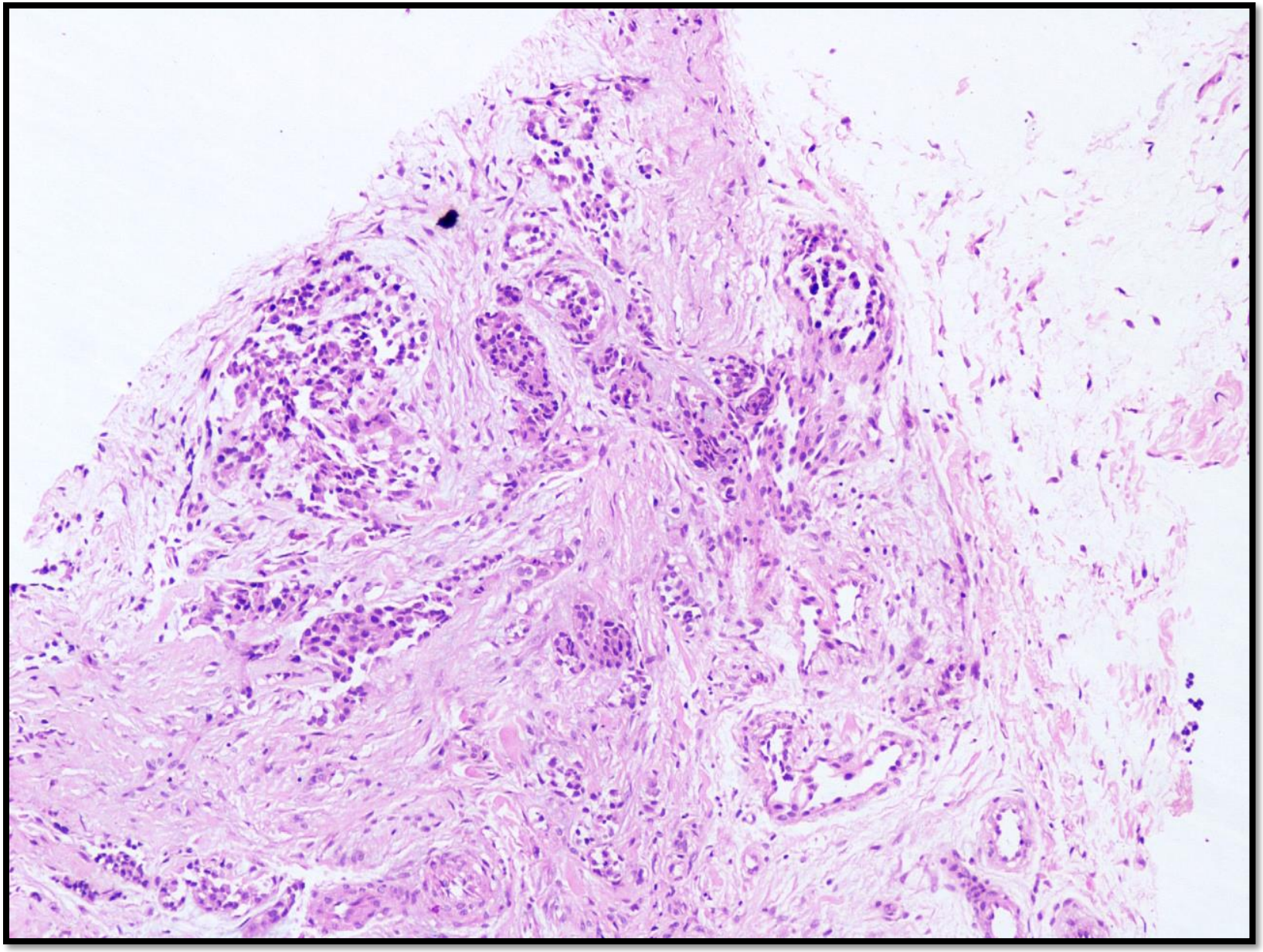
- Examination revealed a hard mass measuring 10 x 8 cm over arm and forearm along with a palpable lymph node

- MRI, right elbow revealed well defined lobulated lesion of 9.8 x 4.4 x 3.6 cm involving volar muscular and intermuscular plane of arm and elbow. Multiple reticular hypointensities and hyperintense locules were noted within the mass. Lower humerus showed bony changes. Bilateral lung fields revealed multifocal lobulated hyperintensities.

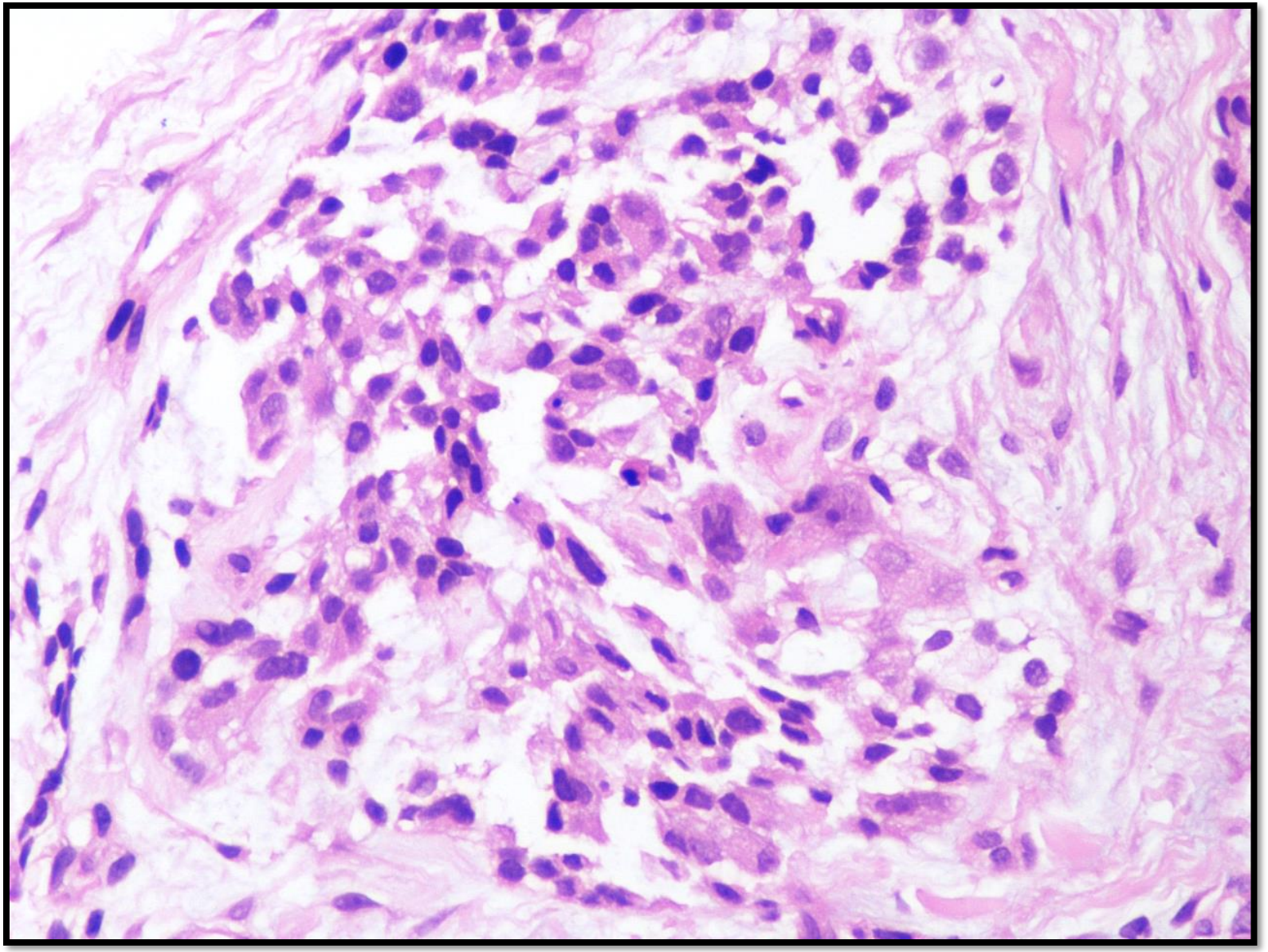
- Provisional diagnosis: Rhabdomyosarcoma with bilateral pulmonary metastasis

- Trucut needle biopsy from the mass was performed and subjected to histopathological examination

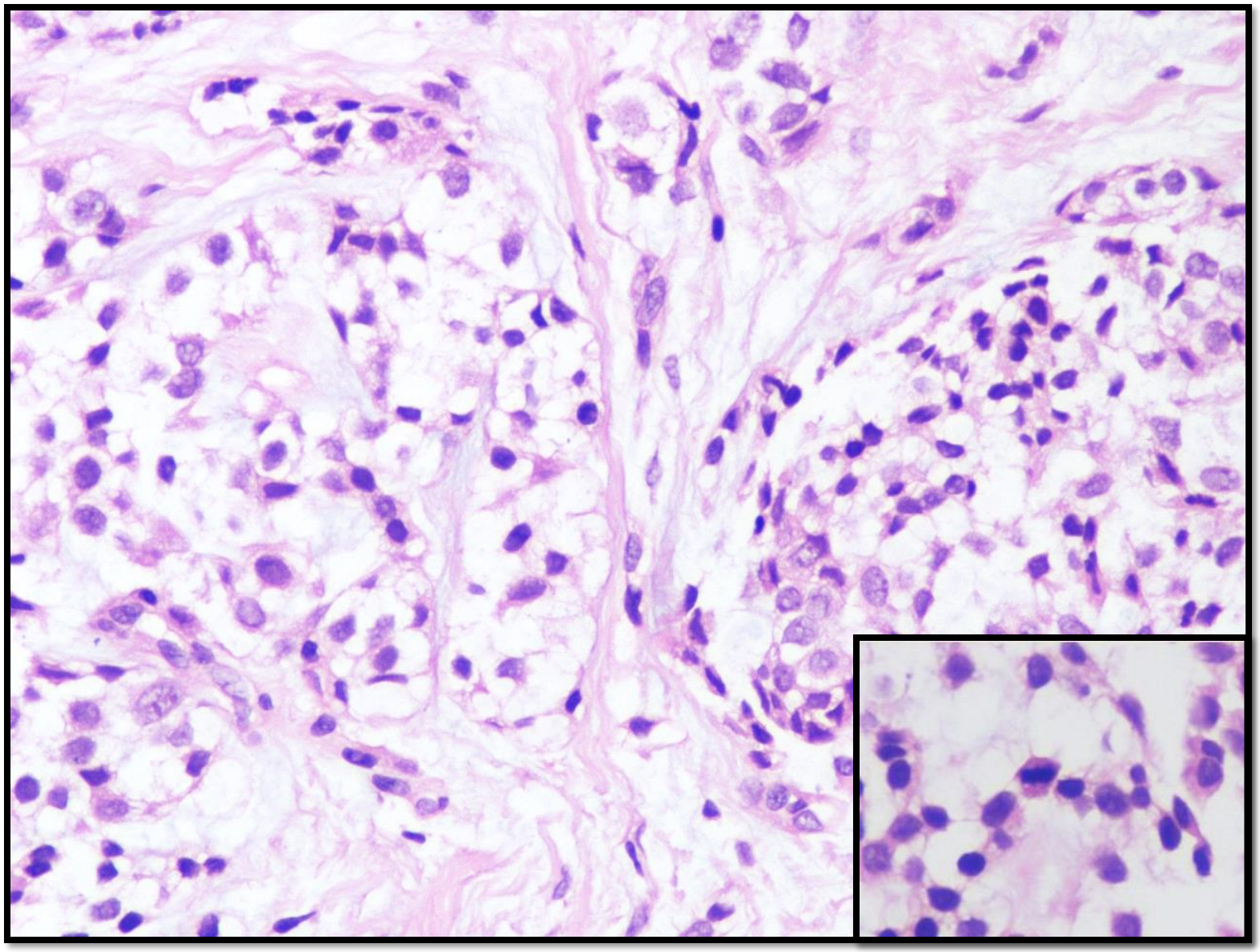
Histopathological examination



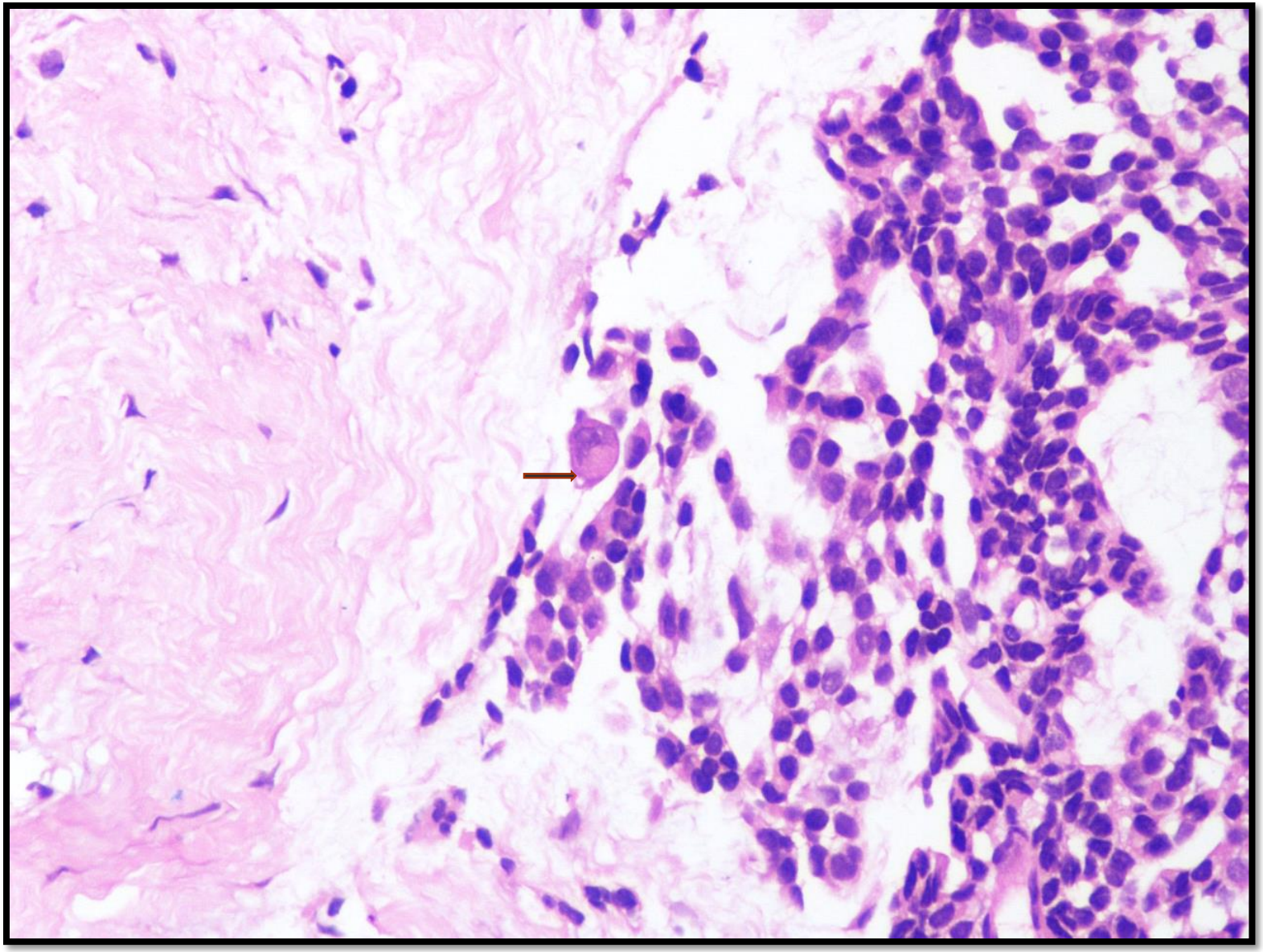
Tumor exhibited varied growth patterns in the form of nesting, trabecular and reticular with prominent myxoid stroma (H & E, 100X)



Tumor cells ranged from epithelioid to plump oval with mildly pleomorphic nuclei and eosinophilic to clear cytoplasm on a myxoid stroma without any significant mitosis (H & E, 200X)



Tumor cells showing prominent cytoplasmic vacuolation (H & E, 200X) . Few mitosis seen (Inset, H & E, 400X)



Tumor cells in a reticular growth pattern, few cells showing plasmacytoid appearance. Occasional cell showed hyaline cytoplasmic inclusion (arrow) (H & E, 400X)

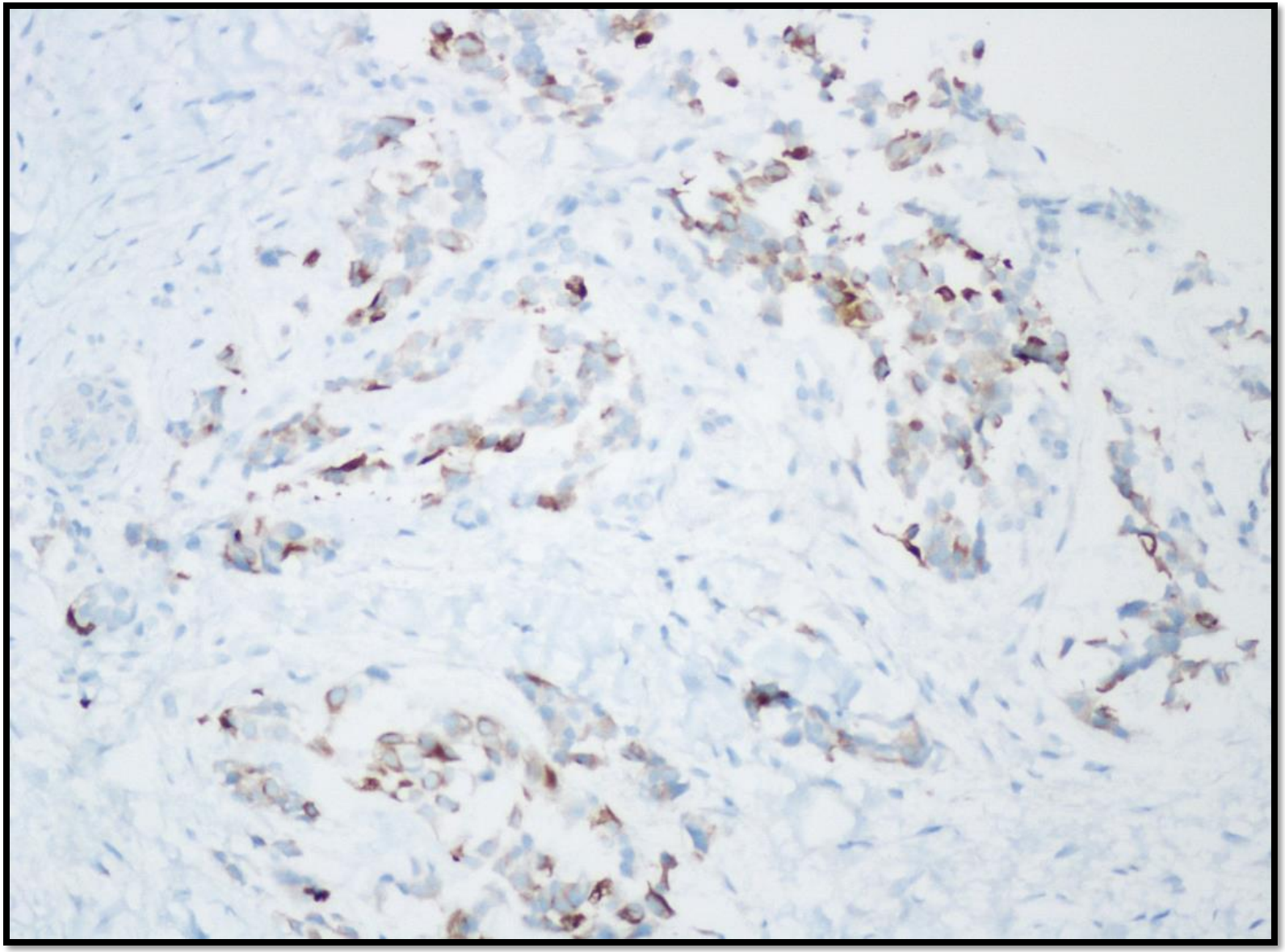
Summary of histopathological findings

- The tumor exhibited varied growth patterns in the form of nesting, trabecular and reticular with prominent myxoid stroma. Focal areas of hyalinized stroma were seen.

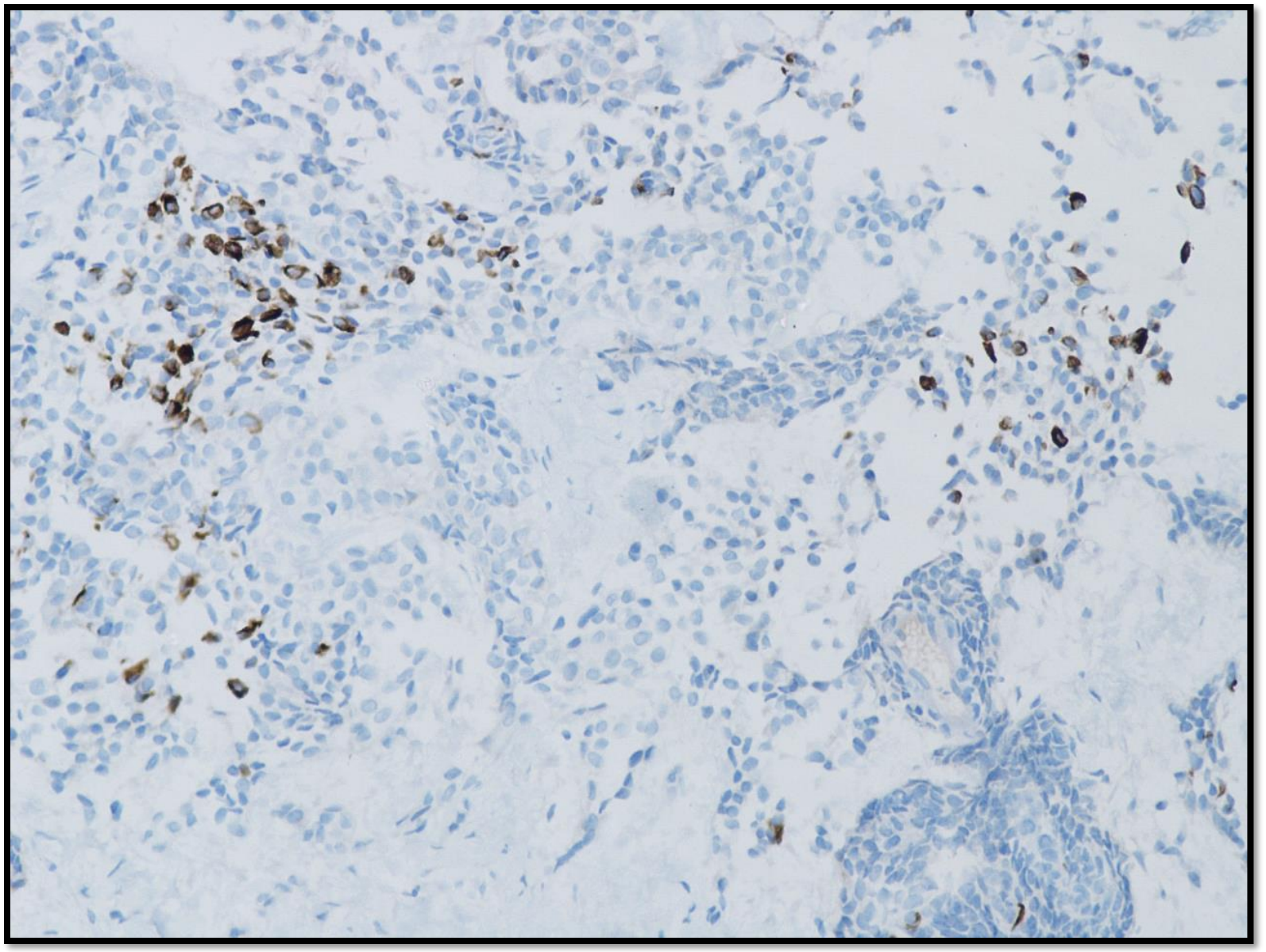
- Tumor cells ranged from epithelioid to plump oval with uniform nuclei and eosinophilic to clear cytoplasm. Few cells had plasmacytoid appearance with an occasional cell showing hyaline cytoplasmic inclusion. Few mitotic figures noted.

- No significant cytologic atypia, necrosis or brisk mitotic activity was noted.

Immunohistochemistry



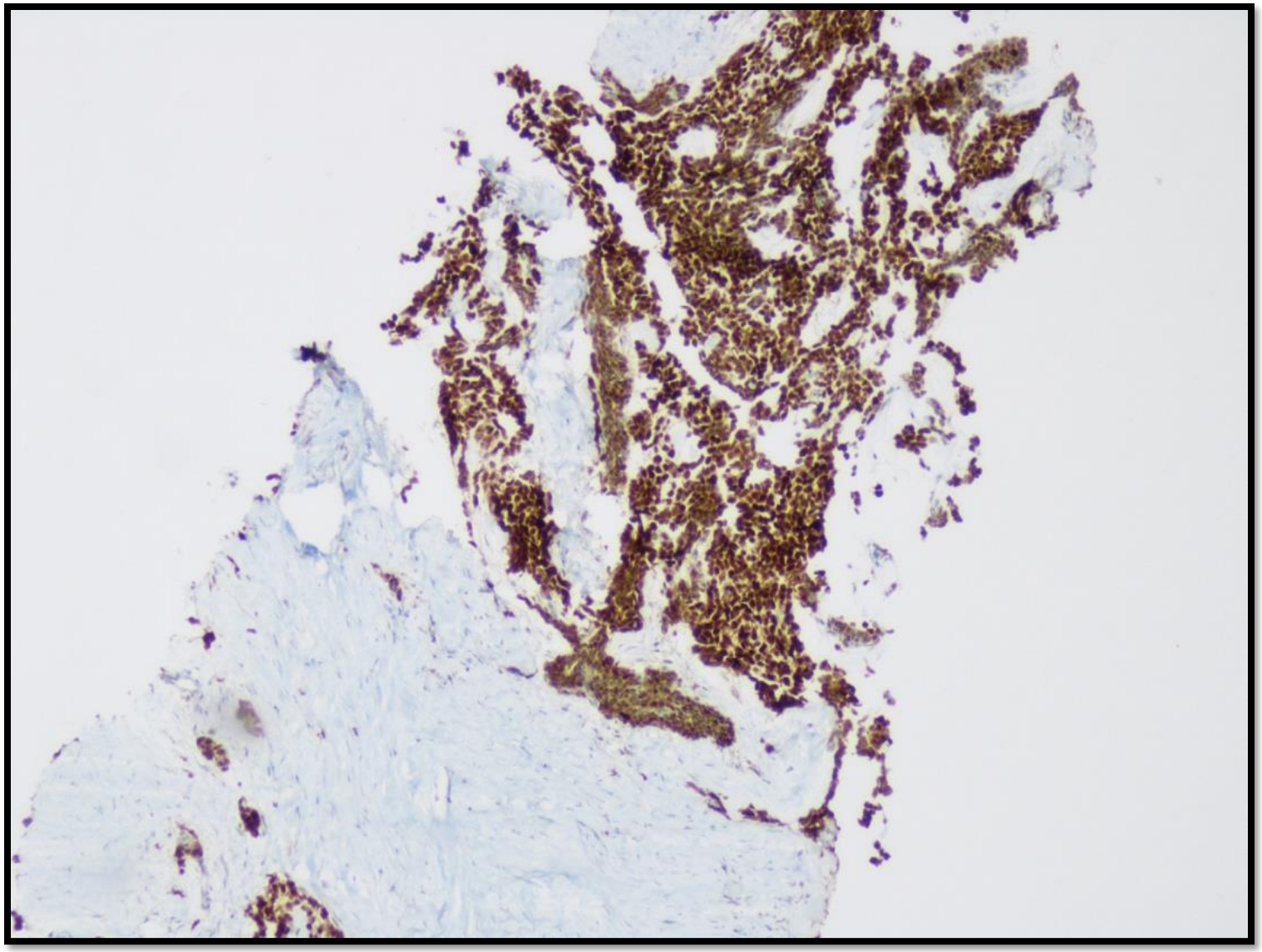
Tumor cells were focal positive for Pancytokeratin (200X)



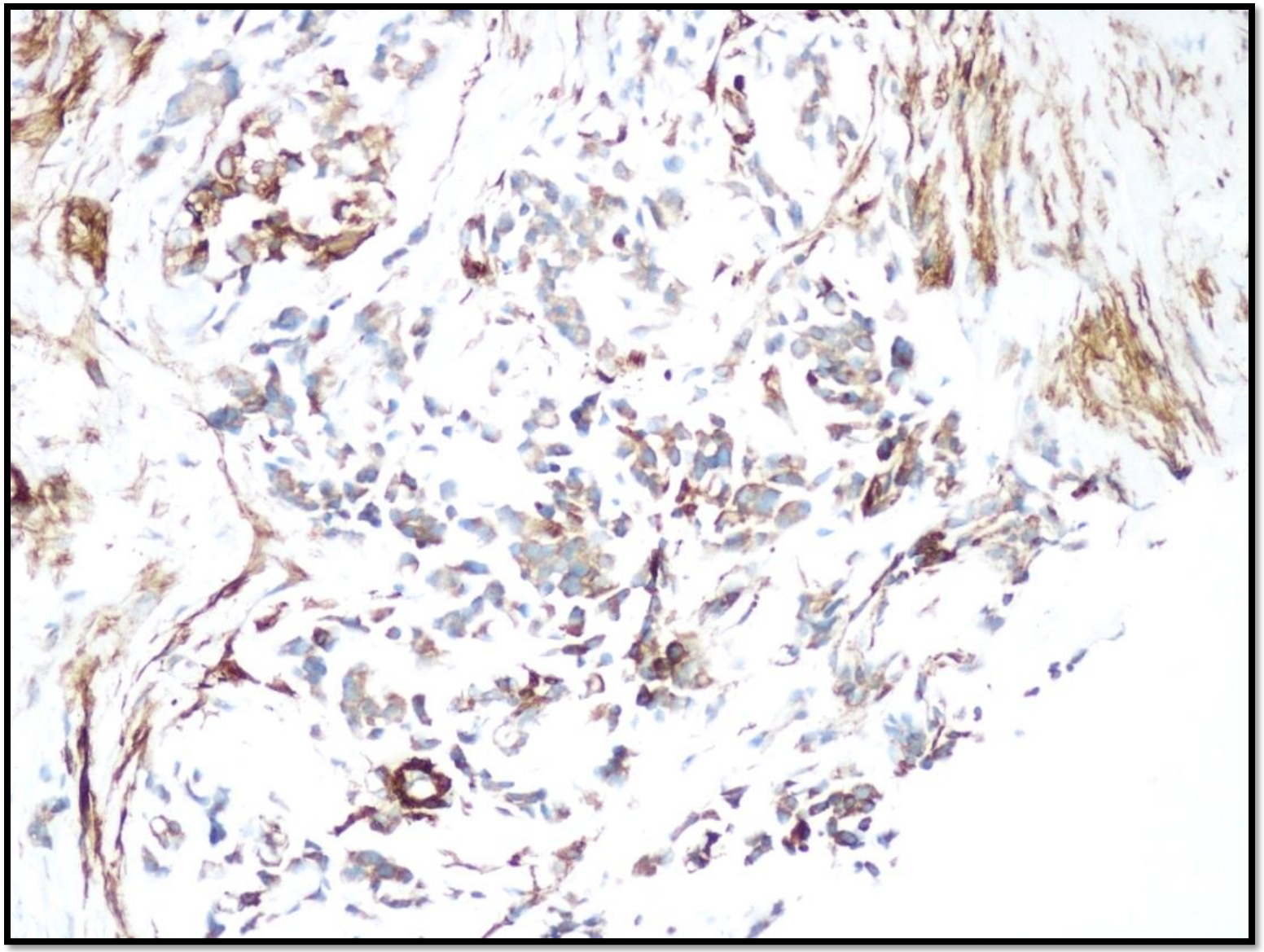
Tumor cells were focal positive for Desmin (200X)

Tumor cells were negative for Myogenin, Myo-D1, NKX2.2, WT-1.

On subsequent IHC:-



Tumor cells were diffuse and strong positive for S-100 (100X)



Tumor cells were focal positive for SMA (200X)

Tumor cells were negative for EMA, GFAP, p63, Calponin, synaptophysin

Immunohistochemistry

- To summarize IHC findings, tumor cells showed co-expression of CK and S-100 /SMA. Desmin was focally positive also.

- Ki-67 proliferation index = 15%

Final Diagnosis

- In view of histomorphology and coexpression of CK and S-100, **features were suggestive of myoepithelial tumor of soft tissue.**

- However, ***in view of radiological evidence of large infiltrative mass and bilateral pulmonary infiltration***, a possibility of **myoepithelial carcinoma of soft tissue** was suggested.

Discussion

- **Myoepithelial tumors of soft tissue are uncommon** but have been increasingly characterized over the past decade by morphologic, immunohistochemical, and genetic means.

- Myoepithelial tumors of soft tissue are known to occur over a wide age range with a peak in the 3rd - 5th decade, both sexes affected equally, and approximately **20 % of cases occur in pediatric patients**.

- They occur in a **broad anatomic distribution**, frequently on the **extremities** and proximal limb girdles. Others being trunk, viscera, and head/neck.

- Most commonly they arise as subcutaneous nodules but can occur in subfascial or intramuscular location.

Discussion

- While having many morphologic and immunophenotypic similarities to their salivary gland counterparts, they are distinct in their histologic criteria for malignancy and characteristic genetic aberrations.

- **Tumors are classified as mixed tumor/chondroid syringoma, myoepithelioma, and myoepithelial carcinoma**.

- Mixed tumor and myoepithelioma show a benign clinical course, with recurrence in up to 20 % (typically secondary to incomplete excision), and do not metastasize.

- **Myoepithelial carcinoma shows more aggressive behaviour with recurrence and metastasis in up to 40–50 % of cases.**

- Sites of metastasis are lungs/pleura, lymph node, bone, soft tissue, liver, brain, skin.

Discussion

- This is a case report of myoepithelial carcinoma of soft tissue in a child who presented with a large infiltrative mass in the extremity and bilateral pulmonary metastasis.

- The literature shows **a higher proportion of myoepithelial tumors of soft tissues being malignant as compared to salivary gland tumors**.

- **In the largest study published, it has been shown that those arising in children were more likely to be malignant than in adults, approximately 65%.**

- The studies have shown that large deep-seated lesions, often have a rapidly progressive clinical course while smaller superficial soft tissue tumors have an initial indolent behavior but a final tendency to metastasize.

Discussion

- Grossly, myoepithelial tumors of soft tissue are often well circumscribed but unencapsulated and have infiltrative margins. Mostly <5cm , but may be large also.

- Myoepithelial tumors of soft tissue show a wide range of architectural and cytological features both within and between different tumors.

- **The criteria for malignancy in myoepithelial tumors of soft tissue is defined strictly by cytologic atypia (moderate to severe atypia with vesicular nuclei and prominent nucleoli) rather than invasive growth pattern**

- Mitosis and necrosis are not the reliable predictors of aggressive behaviour

Discussion

- On IHC, **majority coexpresses epithelial antigens and S-100 protein.** The rate of positivity of other markers are EMA(60-65%), GFAP (50%), Calponin (80-90%), SMA (30-40%), p63 (20-25%), desmin (0-20%).

- Though literature reports desmin negativity in most of the cases, this case showed focal positivity for Desmin. However, Myogenin, Myo-d1 and WT-1 were negative.

- **SMARCB1/INI1 expression is lost in a subset of myoepitheliomas and myoepithelial carcinomas (9–22%)**.

- Up to 45 % of myoepithelial **tumors harbor EWSR1 gene rearrangement** (and rarely alternate FUS rearrangement)

- Documented fusion partners include POU5F1 (6p21), PBX1(1q23), ZNF444 (19q23), ATF1 (12q13) and PBX3 (9q33)

- A study has shown that EWSR1-POU5F1 fusion had the distinctive appearance of nested epithelioid cells with clear cytoplasm.

- To conclude, although carcinomas are extremely rare in children, myoepithelial carcinoma of soft tissue is disproportionately common in the pediatric population.

- ***The wide spectrum of architectural and cytological features that coexist within the same lesion and the coexpression of IHC markers CK and S100 have been proved as a useful adjunct in clinching an accurate diagnosis, as was seen in this case***

- Though, the criteria for malignancy is yet not clearly established but relying on cytologic atypia and clinicoradiologic correlation helps in reaching a particular diagnosis of this rare entity.