Case #136

NAME Educational Activities Committee

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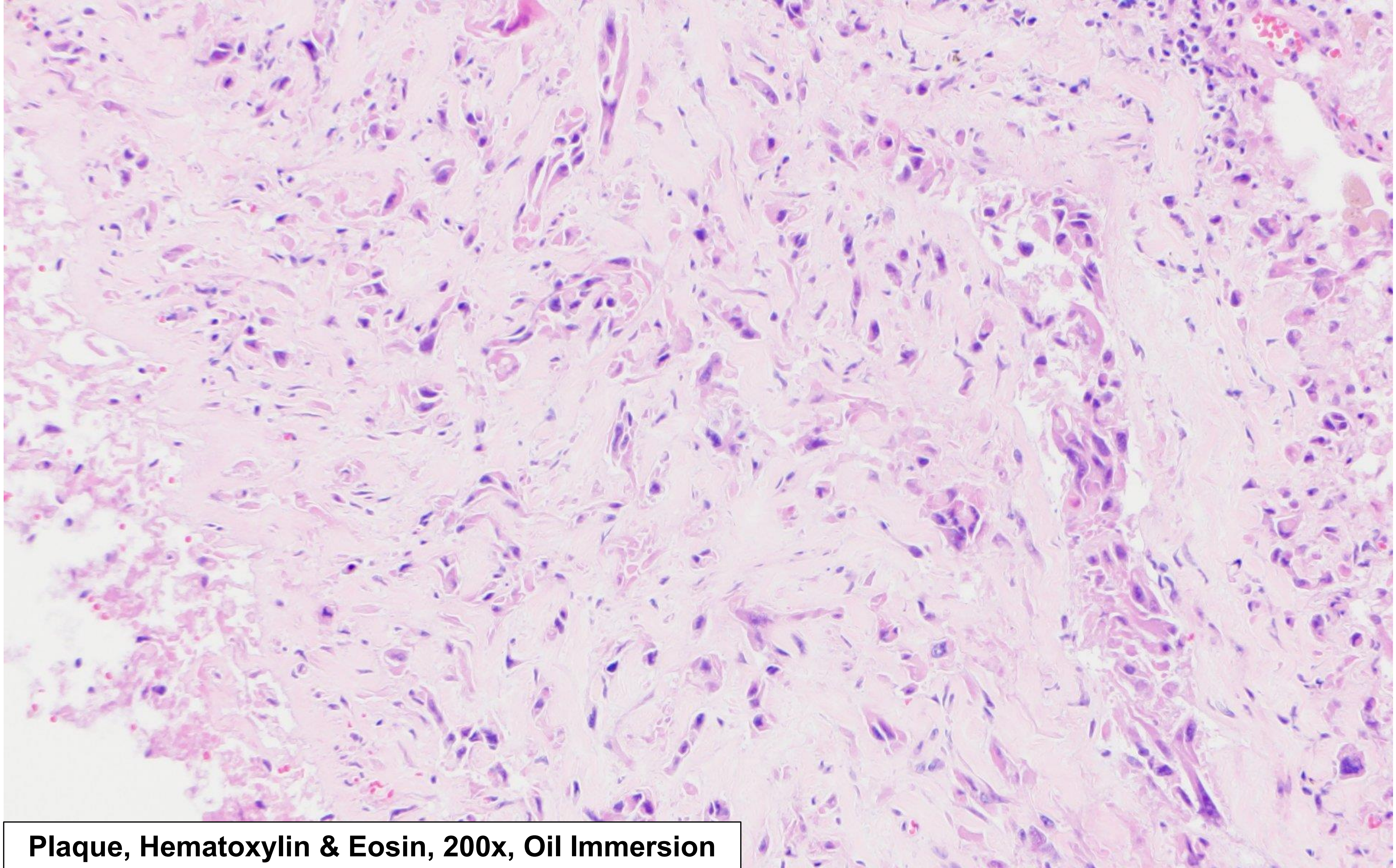
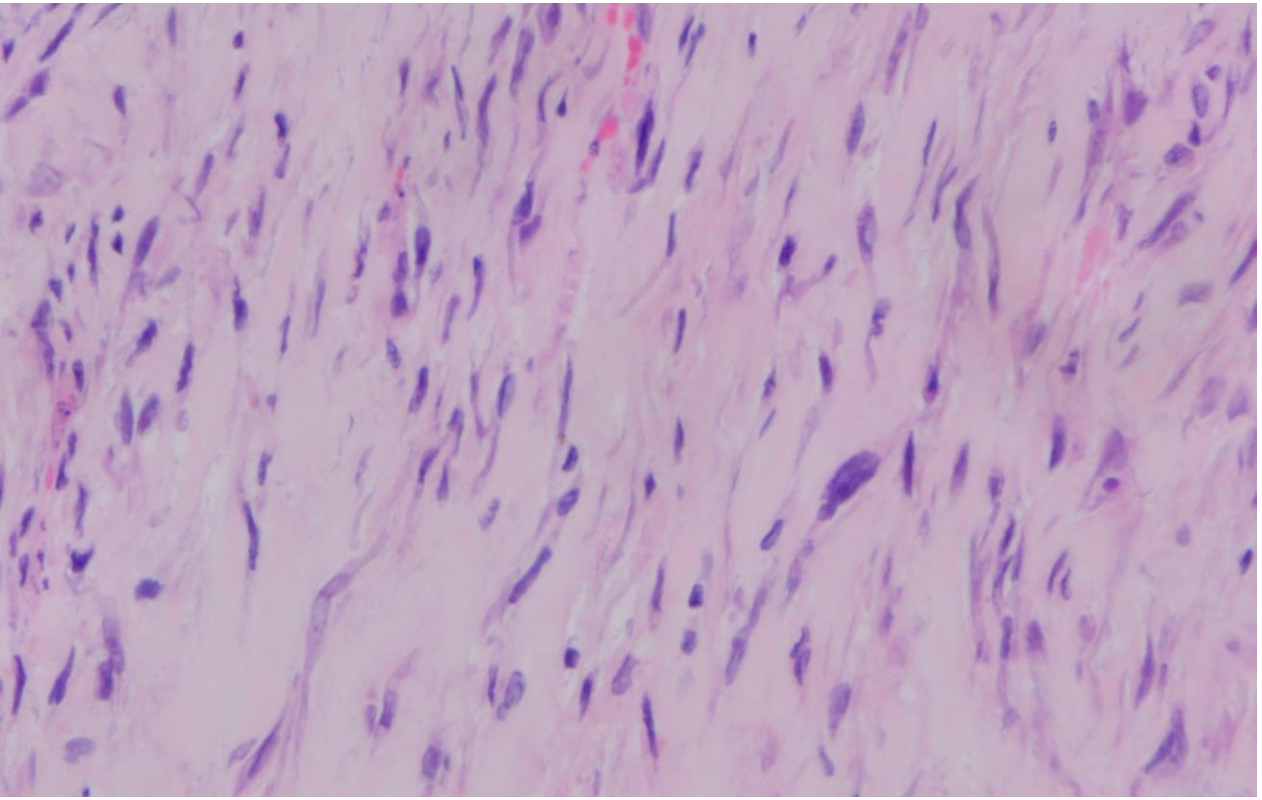
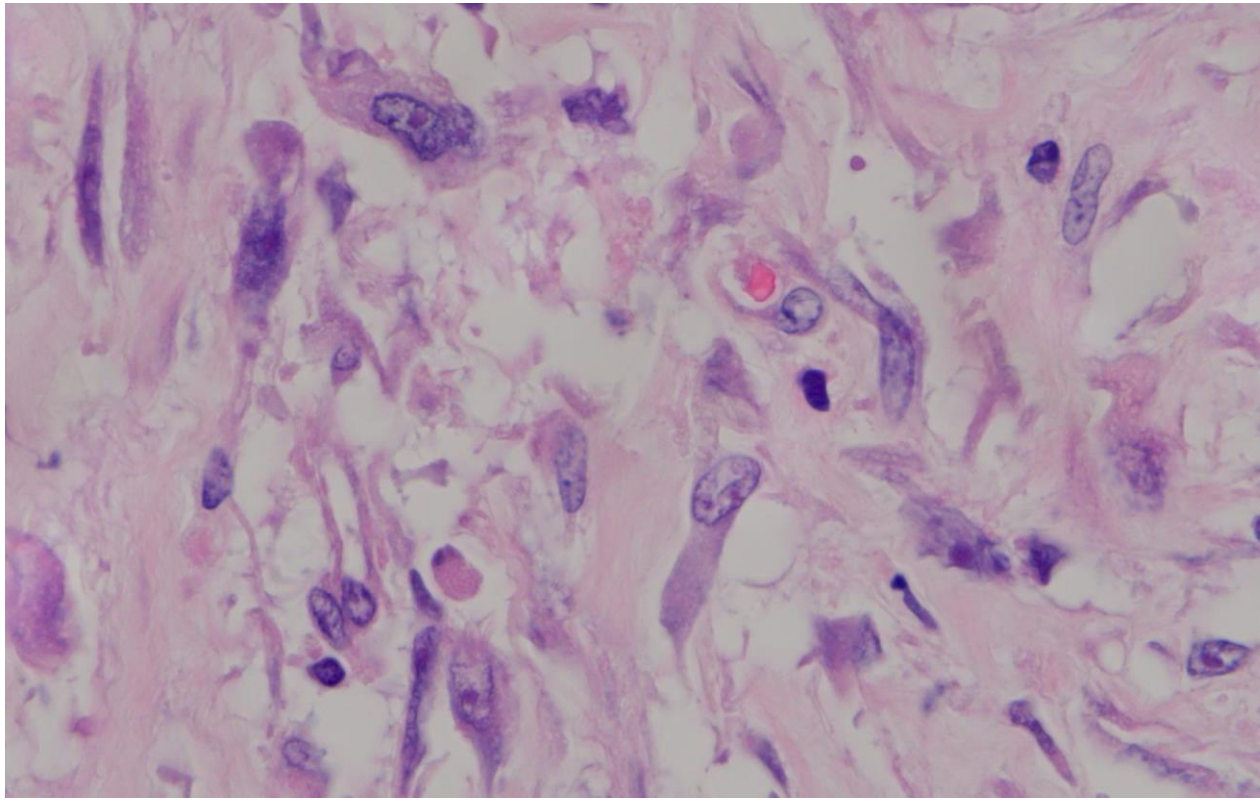
Kidney, Gross



Plaque, Hematoxylin & Eosin, 200x, Oil Immersion





Plaque, Hematoxylin & Eosin, 500x (Left) & 1000x (Right), Oil Immersion

1. The decedent is a male in his in his 60s with a history of urothelial cancer, status post partial colectomy and Bacillus Calmette-Guérin (BCG) immunotherapy, who presented with intractable right flank pain and died after a complicated month-long hospital course. Six months prior, he had a right renal mass found on imaging. Biopsy at that time showed atypical spindle cell proliferation with crush artifact and non-specific immunostaining. A month before admission, multiple new peritoneal nodules with spindle cells were identified and confirmed intraoperatively. Repeat biopsy of the renal mass during admission raised suspicion for a reactive versus neoplastic process. The patient went into shock and respiratory failure soon after, requiring critical care, but his condition worsened, and he passed away.

Autopsy showed abnormal plaques and nodules on the visceral pleura, diaphragm, omentum, abdominal/pelvic wall, and multiple peritoneal organs. A representative gross image of his right kidney with plaque, and representative medium-to-high power histology images of plaque are provided.

What is the most likely etiology behind this decedent's presentation?

- ◯ Benign neoplastic process
- ◯ Disseminated infection
- ◯ Drug reaction
- ◯ Malignancy

Answer...

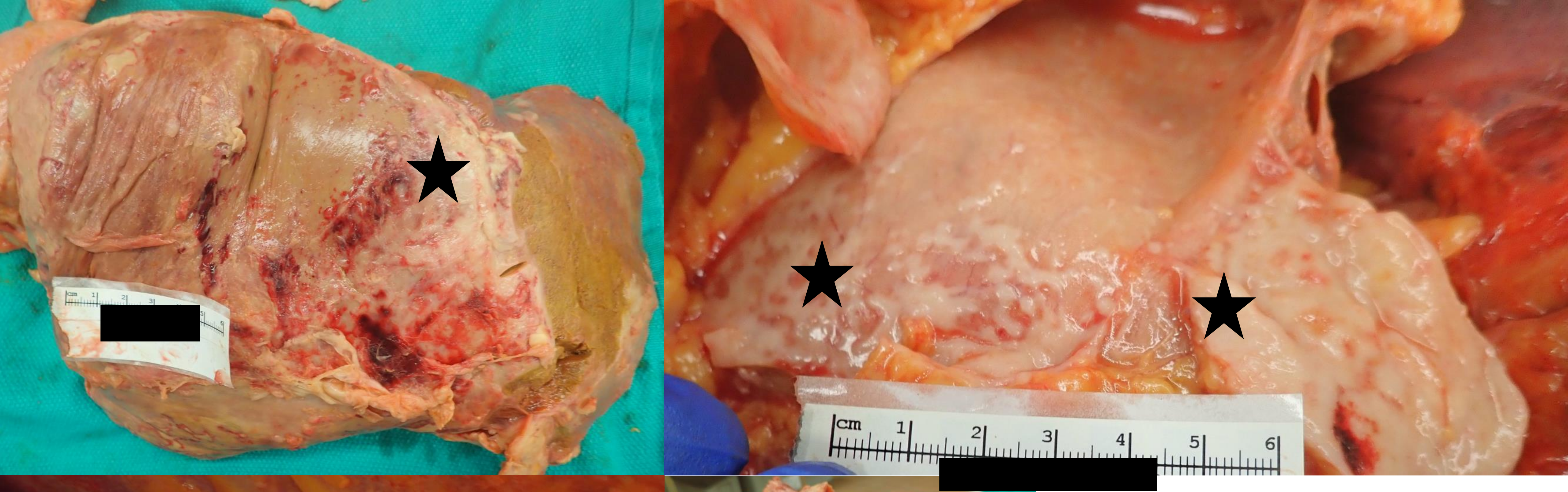
D. Malignancy (CORRECT ANSWER, 55.02% of responses)

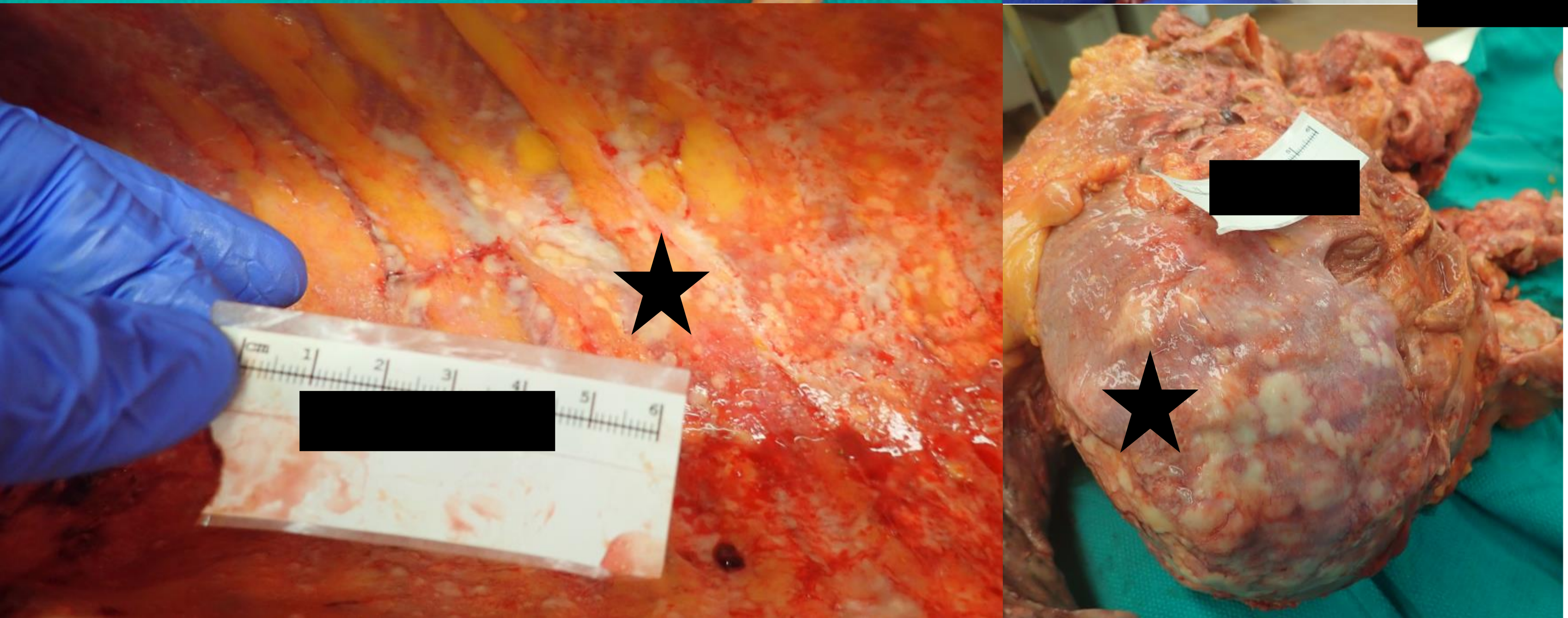
Sarcomatoid (or spindle cell) mesothelioma is a rare and aggressive variant, accounting for approximately 10-20% of diagnoses. It has a poor prognosis, with an average survival rate of five to twelve months and is predominately caused by **asbestos** exposure. Pleural disease is more common (98%) than peritoneal (2%), with fewer than fifty cases of the latter reported. The spindle cells in these tumors can appear cytologically bland and may not express mesothelial markers, leading to diagnostic challenges.

In our case, plaques and nodules were also observed on the visceral pleura, diaphragm, omentum, abdominal/pelvic wall, and multiple peritoneal organs (see next slides), markedly distorting local anatomy. Histology of plaques showing a spindle-cell proliferation with notable cytologic atypia on hematoxylin and eosin stain. These atypical cells had **partial retention of BAP1**, were **negative for claudin-4**, and **strongly expressed both CAM 5.2 and D2-40** (see next slides).

Additionally, molecular analysis of the renal plaque (resulted post-autopsy) showed a **homozygous CDKN2A deletion** and was negative for USP6 rearrangement.

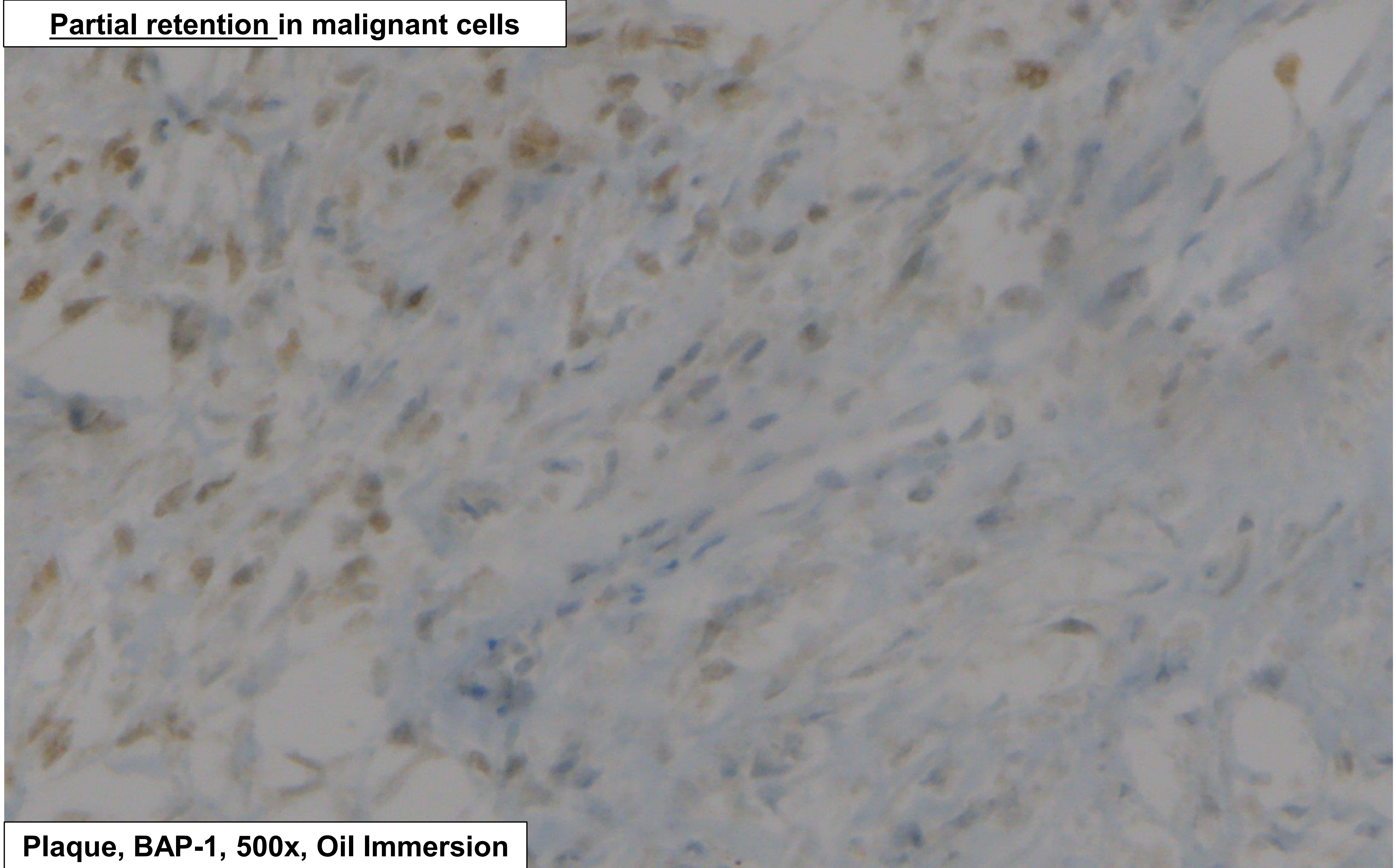
Taken altogether, these findings support a diagnosis of **sarcomatoid mesothelioma**.



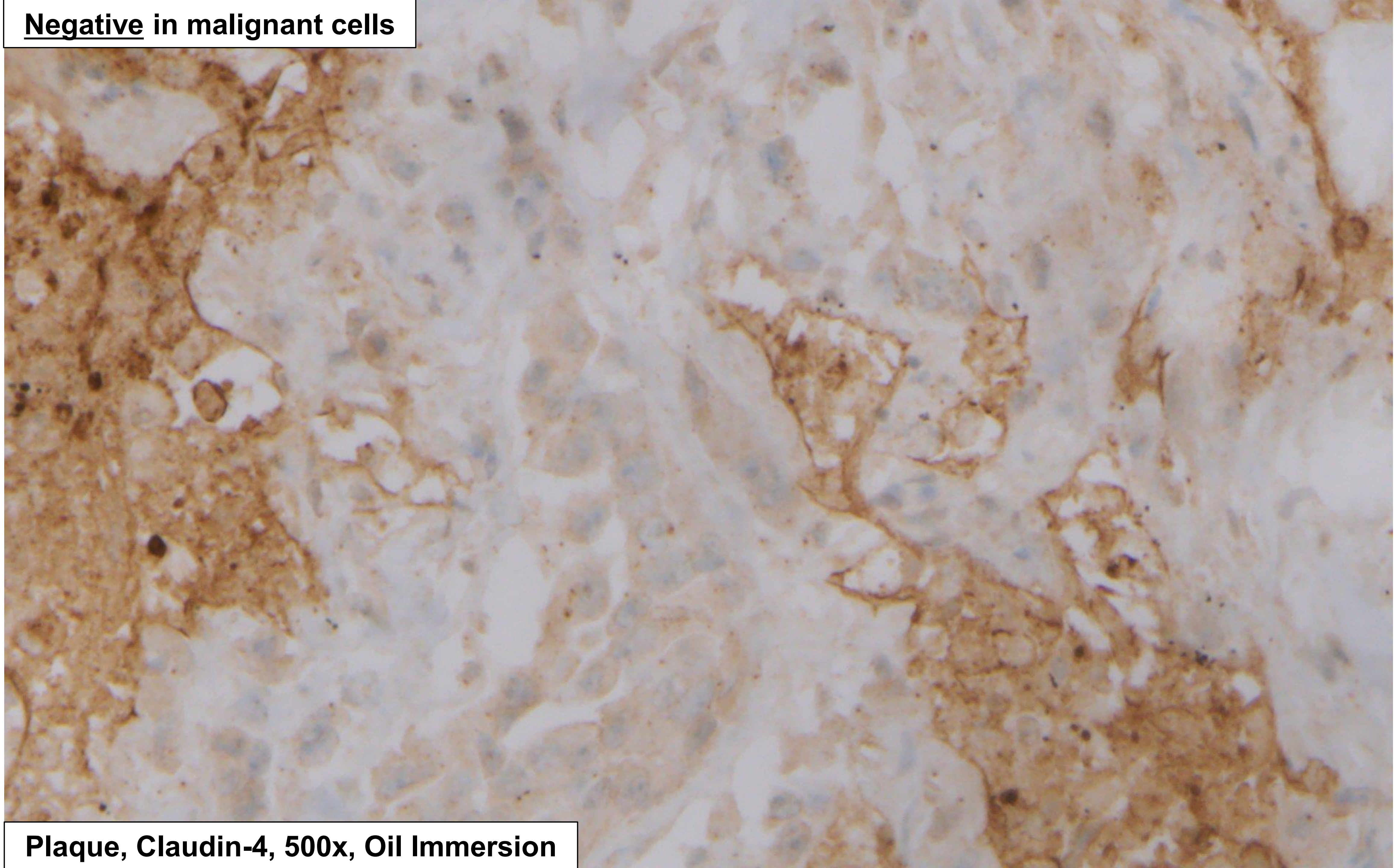


Representative gross images of abnormal plaques and nodules (**5-point stars**) on various visceral, omental, pleural, and peritoneal surfaces.

Partial retention in malignant cells



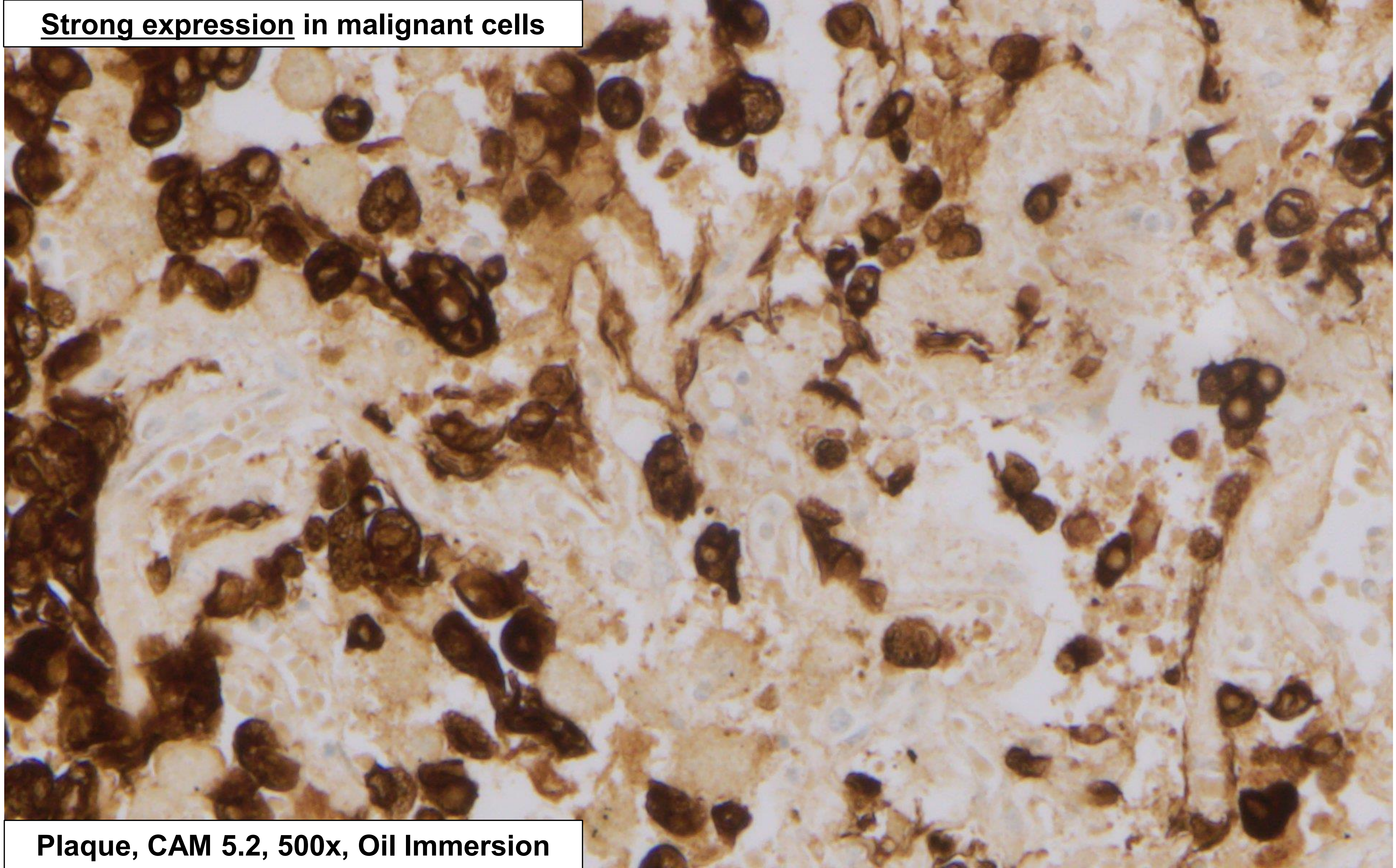
Plaque, BAP-1, 500x, Oil Immersion



Negative in malignant cells

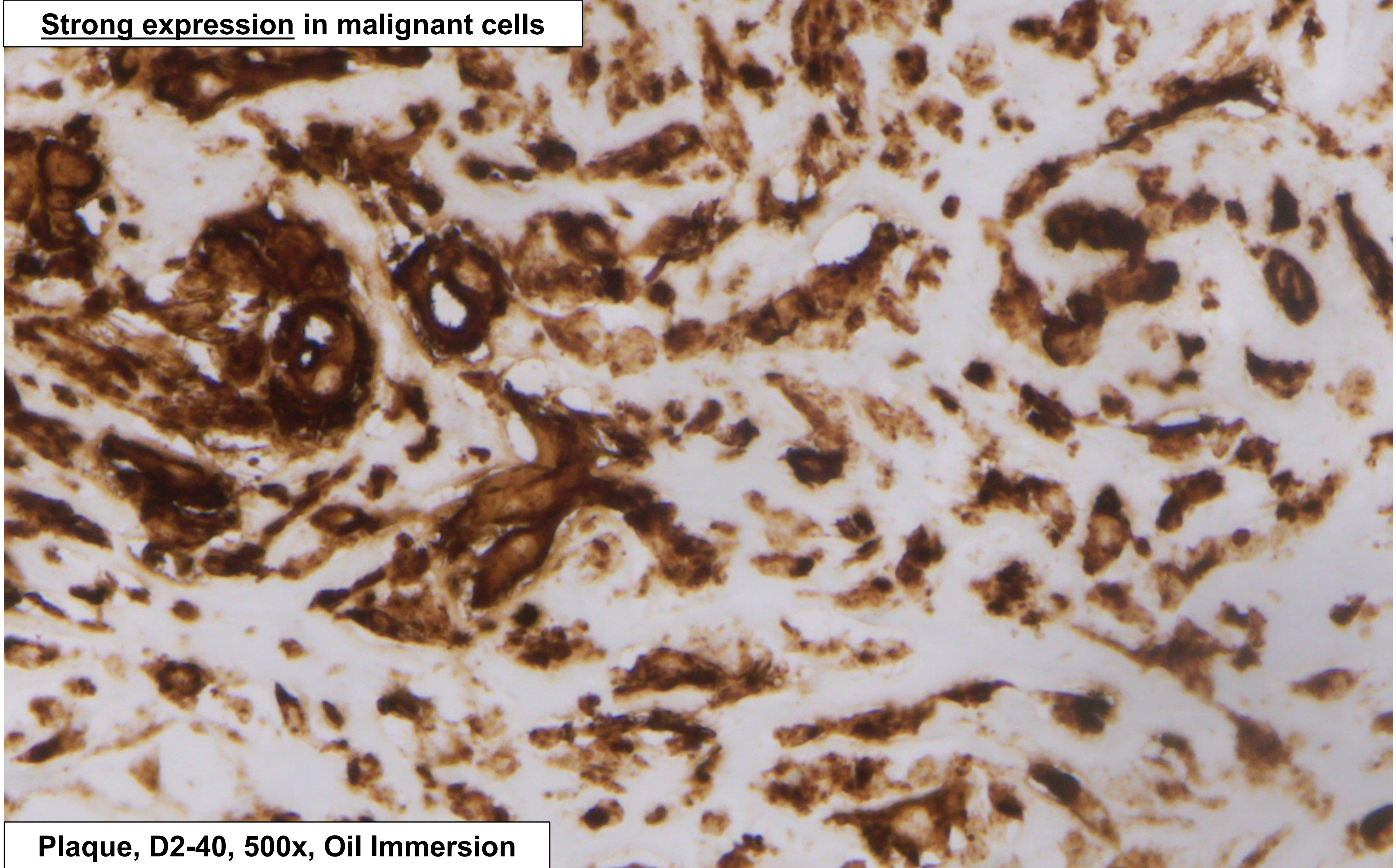
Plaque, Claudin-4, 500x, Oil Immersion

Strong expression in malignant cells



Plaque, CAM 5.2, 500x, Oil Immersion

Strong expression in malignant cells



Plaque, D2-40, 500x, Oil Immersion

Other responses…

A. Benign neoplastic process (12.11% of responses)

Other differentials for this presentation include non-malignant spindle cell proliferations such as **nodular fasciitis**. However, this is less likely given the diffuse presence of the decedent's neoplastic process, marked cytologic atypia, and supportive immunohistochemistry for sarcomatoid mesothelioma (BAP-1 partial retention, claudin-4 negativity, and CAM 5.2 and D2-40 strong expression). Additionally, negative **USP6** argues against nodular fasciitis.

B. Disseminated infection (16.61% of responses)

The decedent had a history of urothelial cancer and underwent intravesical BCG immunotherapy, which is a live-attenuated-strain of ***Mycobacterium bovis****.* BCG immunotherapy is a well-known (and frequently well-tolerated) treatment for superficial urothelial cancer. However, **approximately 1/15,000 patients may develop life-threatening infection** soon after the procedure, a condition colloquially termed "**BCG-osis**". No **granulomatous** lesions were identified on evaluated histologic sections (numerous samples were taken), arguing against this diagnosis.

C. Drug reaction (16.26% of responses)

Drug reactions often present as **multi-inflammatory lesions** with or without extensive **necrosis** in afflicted tissues following the administration of certain medications. The presence of atypical spindle cells would be highly uncommon and non-explanatory for this differential.

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