BEYOND ANGIOGENESIS: UNVEILING VESSEL CO-OPTION AND VASCULOGENIC MIMICRY IN HIGHLY MALIGNANT CANINE TUMORS

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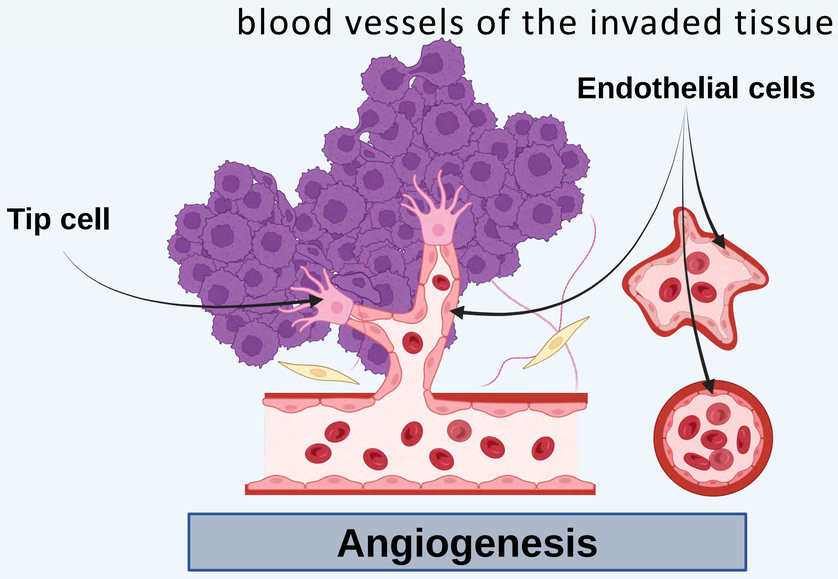
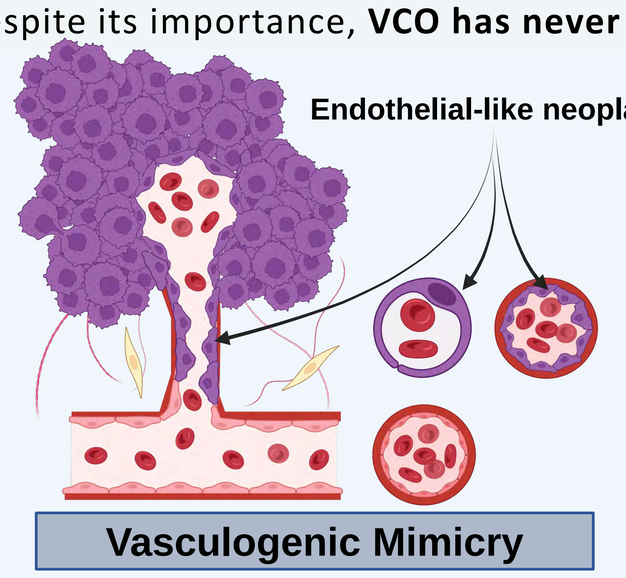
Background

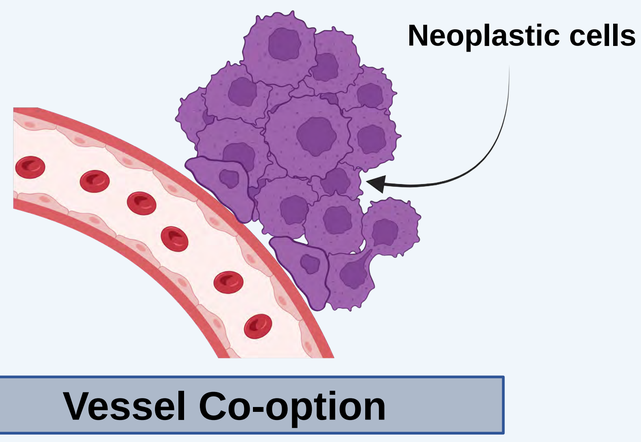
Angiogenesis is essential for tumor progression and metastasis. The alternative and poorly known forms of tumor nutrition named **vasculogenic mimicry (VM)** and **vessel co-option (VCO)** are related to poorer prognosis and anti-angiogenic treatments resistance in human oncology. In **VM**, highly malignant tumor cells line newly formed vascular-like channels, while in **VCO** cells survive by hijacking pre-existing blood vessels of the invaded tissue. Despite its importance, **VCO has never been described in Veterinary Medicine**



Angiogenesis



Vasculogenic Mimicry



Vessel Co-option

Materials and Methods

1- Retrospective inclusion of cases

Necropsies of dogs with metastatic tumors (n=98)

2- Histopathology (H-E)

Compatible with **VM** or **VCO** in primary or metastatic tumors

3- Special Stains

PAS
Reticulin Stain
Masson's trichrome
CD31 IHC

Results

Vessel Co-option

Metastases	Primary tumor
(n=11/98, 11% VCO)	(n=0/98, 0% VCO)

Brain metastasis (n=1/2, 50% VCO)

→ Perivascular pattern

Liver metastasis (n=1/7, 14% VCO)

→ Perivascular pattern

Lung metastases (n=9/33, 27% VCO)

- Alveolar pattern (7/9)
- → Lepidic pattern (1/9)
- Interstitial pattern (1/9)

Vasculogenic Mimicry

Primary tumor and metastases (n=19/98, 20% VM)

PAS	Masson's trichrome	Reticulin stain	CD31 (endothelium)

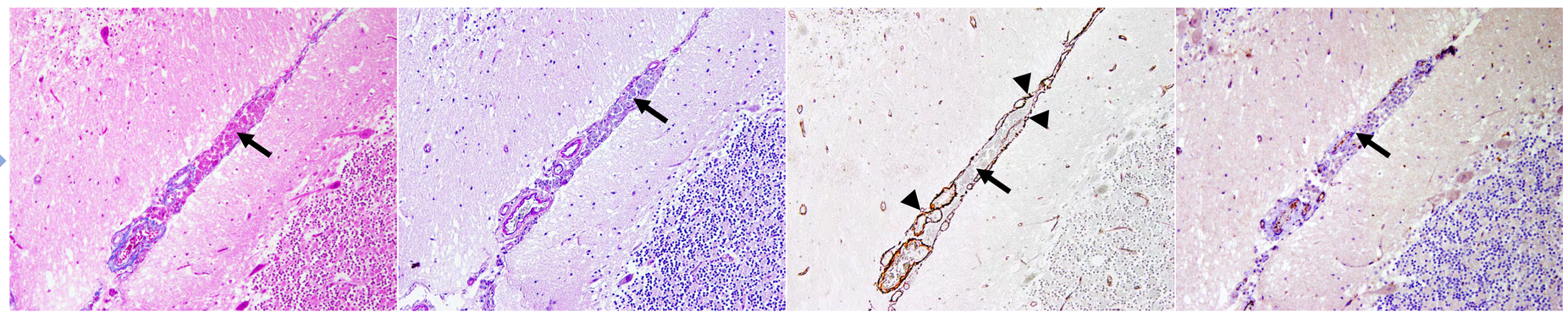


Fig. 1. Vessel co-option in brain metastasis in a perivascular pattern. Neoplastic cells co-opt brain vessels by growing in a perivascular location (arrow), without disrupting the basement membrane or the reticulin framework (arrowheads). Endothelial immunolabeling (CD31) does not show the formation of new blood vessels.

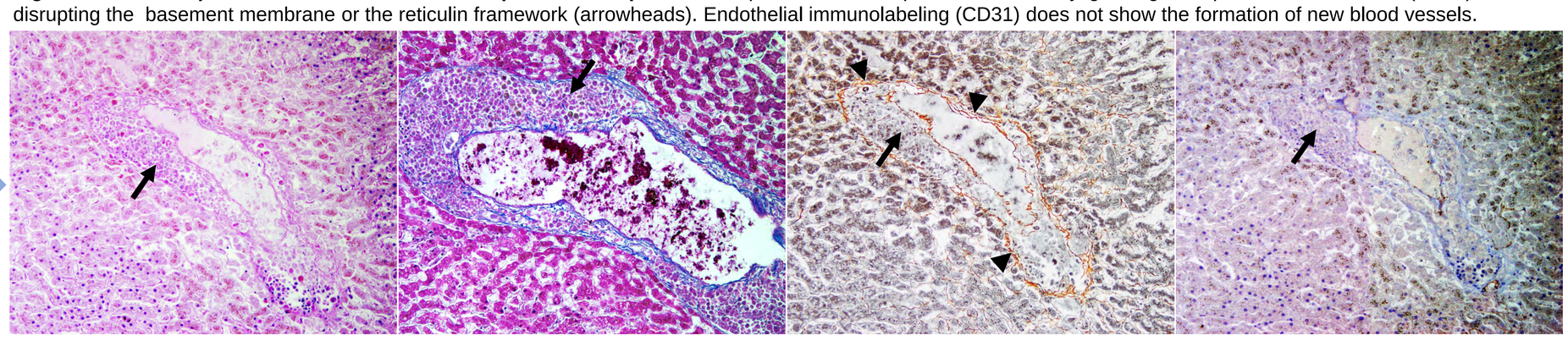


Fig. 2. Vessel co-option in liver metastasis in a perivascular pattern. Neoplastic cells hijack the preexistent vasculature by expanding the perivascular space (arrows). Periodic acid of Schiff, Masson's and Reticulin staining demonstrate the conservation of the basement membranes and reticulin framework (arrowheads) from both, the vasculature and the hepatic cords.

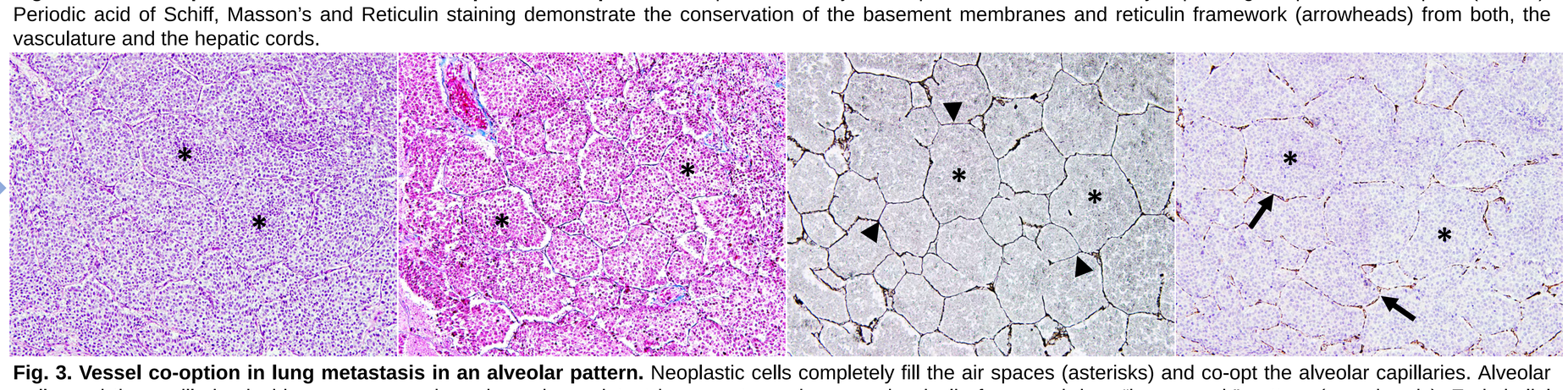


Fig. 3. Vessel co-option in lung metastasis in an alveolar pattern. Neoplastic cells completely fill the air spaces (asterisks) and co-opt the alveolar capillaries. Alveolar walls, and the capillaries inside, are preserved as shown by an intact basement membrane and reticulin framework in a "honeycomb" pattern (arrowheads). Endothelial immunolabeling (CD31) exhibit the conserved alveolar capillaries (arrows) and does not show the formation of new blood vessels.

Hematoxylin and eosin

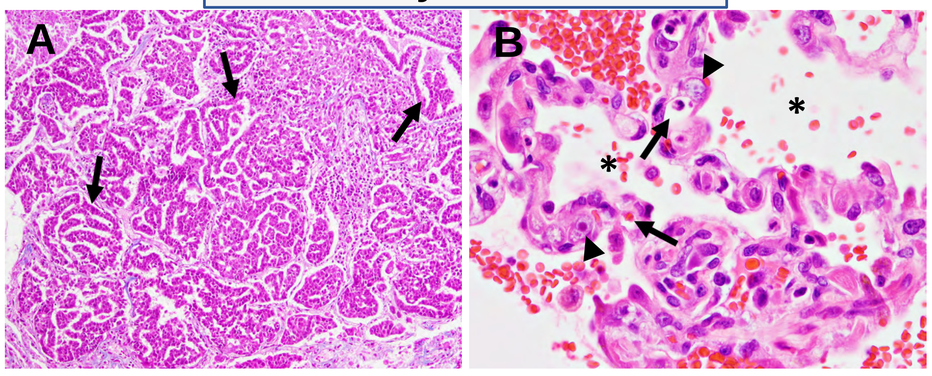


Fig. 4. Vessel co-option in lung metastasis in lepidic (A) and interstitial (B) patterns. In the lepidic pattern (A), neoplastic cells (arrows) grow by replacing non-malignant pneumocytes and remain adhere to the basement membrane without completely filling the air space. In the interstitial pattern (B), cancer cells (arrowheads) grow within alveolar wall by infiltrating through the lung interstitium and co-opting the alveolar capillaries (arrows). The air space (asterisks) is free of neoplastic cells and contains extravasated erythrocytes (hemorrhage).

Conclusion

This study describes for the first time in Veterinary Medicine, the presence of VCO. Although the significance of VCO remains obscure, its observation should be considered in the pathology reports.