Vasculogenesis in Hemangioblastomas associated with von Hippel-Lindau Disease

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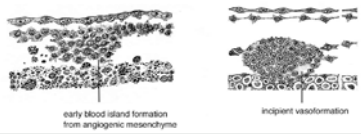
Introduction

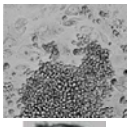
Arvid Lindau Proceedings of the Royal Society of Medicine (1931)
hemangioblastoma tissue may be derived from a "congenital anlage"
The histological picture reveals an "... embryological type of the tumor cells"

Stein et al. J Neurosurg (1960)
angiomesenchymal origin of hemangioblastoma based on developmental biologic observations



Introduction

Choi et al. Development (1998)
Identification of the hemangioblast:
A common precursor for hematopoietic and endothelial cells.



Huber et al. Nature (2004)
Hemangioblast is a subpopulation of mesoderm that co-express SCL, Brachyury and FLK-1

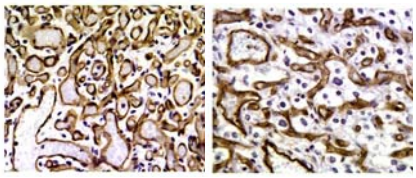
Methods

Material
- 60 VHL disease-associated hemangioblastomas
- Investigate vascular differentiation

Methods
- Histomorphology
- Immunohistochemistry (CD31, NSE)
- Microdissection-based genetic analysis
- HIF

Results

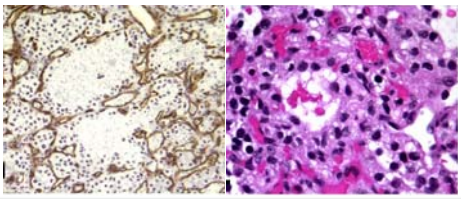
- In 47/60 tumors no evidence of vasculogenesis or hematopoiesis
- Tumor cells scattered between reactive angiogenetic vessels or arranged in solid clusters



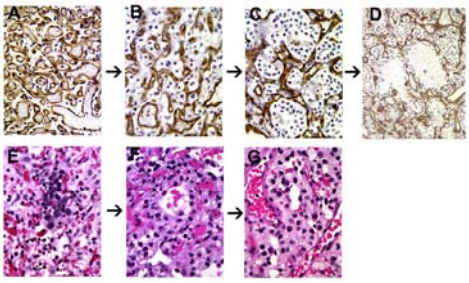
CD31

Results

- 13/60 tumors epithelial vasoformation
- lined by cuboidal or flat cells
- frequently contained red blood cell precursors or mature red blood cells



Histomorphological progression

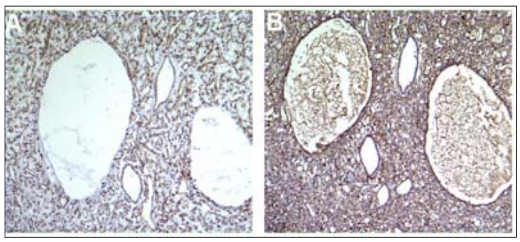


CD 31

H&E

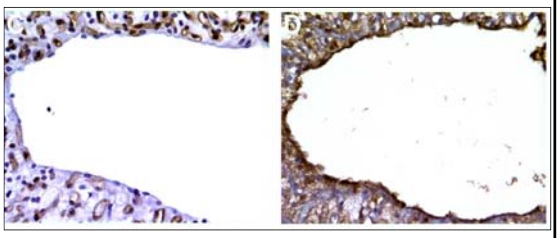
Vasculogenetic elements

CD 31 NSE

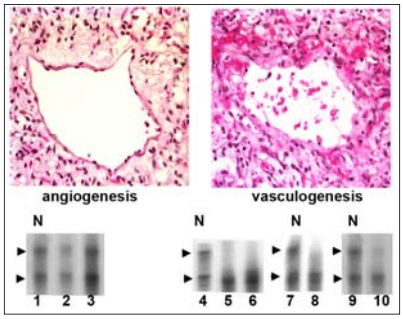


Vasculogenetic elements

CD 31 NSE

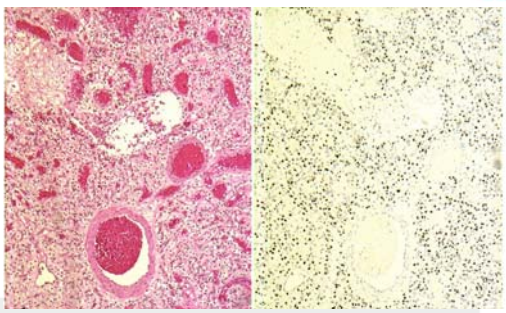


Microdissection



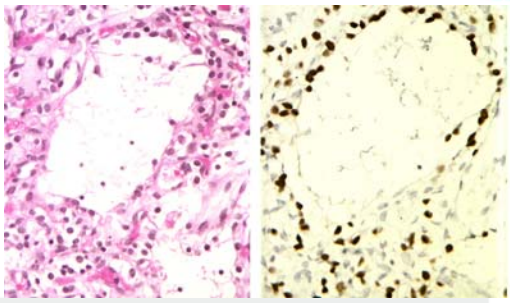
HIF2 expression

H&E HIF2



HIF2 expression

H&E HIF2



Conclusion

- Hemangioblastomas show two types of vascularization:
  1. intense mature capillary network as result of VEGF-driven reactive angiogenesis
  2. vasculogenesis by the neoplastic "stromal" cells
- Both processes next to each other without transition or connection
- Hemangioblastomas resemble the process of vasculogenesis accompanied by extensive angiogenesis