Angiogenesis Inhibition and AAA
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ABSTRACT

Background: Abdominal Aortic Aneurysm (AAA) is a frequent disease of the older population, especially among smokers. Rupture is associated with morbidity and mortality rates and remains a leading cause of death. Currently only surveillance and surgical treatment upon a threshold of 50mm are available. No medical growth inhibition or even prophylaxis are known.

Methods: Having identified angiogenesis as a distinct feature of AAA pathogenesis occurring in the hypoxic, thickened aneurysm wall in previous studies we investigate inhibition of neovessel formation as a potential target for growth inhibition. The PFE mice aneurysm model is applied to test the effect of an already clinically approved multitargeted kinase inhibitor used in cancer therapy on AAA growth. Therefore male Balb/c mice were operated by local elastase perfusion. 7 days later each systemic oral treatment on a daily basis was started – or mice were re-operated for a single local intravasculary drug application (a.i. simulating endovascular treatment). Ultrasound was used to follow AAA diameter. IHC, PCR and mouse transcription assays were used for mechanistic studies.

Results: Both treatments significantly reduced AAA diameter in terms of inhibiting aneurysm growth. The number of CD34+ vessels was reduced compared to standard PFE animals. Apoptosis was not observed. VEGF receptor signaling is blocked and collagen gene expression is up-regulated. Fibrosis is seen on morphologic analysis.

Conclusions: Angiogenesis inhibition can be a valuable target for AAA growth alteration. Additionally, drug repurposing, hence the use of clinically approved drugs in other diseases and indications is worth investigation for AAA disease.

BACKGROUND

epidemiology
- most frequent aneurysm
- prevalence (age 60)
- cases per year (Blanding): ca. 30%
- prevalence: 2.15%
- cases per year: ca. 15,000

surgical repair
- surveillance (ID) 50mm
- CTA (ID)

Research Question

Is angiogenesis a target to alter aneurysm growth?

no AAA growth inhibition
no AAA prophylaxis

Introduction

angiogenesis – human AAA

CD34

angiogenesis – mouse AAA

porcine pancreatic elastase PPE

RESULTS

- Angiogenesis is a distinct feature of AAA pathogenesis most prominent in the thickened media.
- It is driven by VEGF and the number of CD34+ vessels correlates with vascular inflammation independent of AAA diameter.
- The PFE mouse model shows a similar pattern of angiogenesis.
- Local and systemic treatment with a multitargeted kinase inhibitor stabilize aneurysma growth from 7 days after AAA induction.

CONCLUSION

- Angiogenesis and vessel density can be used to discriminate individual disease.
- Local and systemic MTK treatment of mice with induced AAA significantly reduced AAA growth

DISCLOSURES

- I do not have any potential conflict of interest