Pulmonary Hypertension - Challenges in Pathology

Peter Dorfmüller
Pathologist
Marie Lannelongue Hospital, Paris South University
and
INSERM Unit 999 "Pulmonary Hypertension: Pathophysiology and Novel Therapies"
Le Plessis Robinson, France
Disclosures

• None
Diagnostic classification of pulmonary hypertension
(Updated ESC/ERS guidelines 2015)

1 Pulmonary arterial hypertension

1' Pulmonary veno-occlusive disease / pulmonary capillary hemangiomatosis

1” Persistent pulmonary hypertension of the newborn

2 Pulmonary hypertension due to left heart disease

3 Pulmonary hypertension due to lung diseases and/or hypoxia

4 Chronic thrombembolic pulmonary hypertension and other PA obstructions

5 PH with unclear multifactorial mechanisms

Diversity of lesions in PAH: Variation of the prevailing cell type

Dorfmüller P, Humbert M.

‘Characteristic’ lesions

Arteries

‘Morphometric’ lesions

Arterioles/Interstitium

Sample images are presenter’s own.
Pathology of pulmonary hypertension

No true correlation can be seen between typical pulmonary artery remodeling and hemodynamics in PAH.

mPAP, mean pulmonary arterial pressure; PVR, pulmonary vascular resistance.
Lungs from a patient with HIV-associated PAH (Group 1)

HIV, human immunodeficiency virus. Images are presenter’s own.
Plexiform lesion (1)

Arterial branch with two plexiform lesions

Image is presenter's own.
Plexiform lesion (2)

EC, endothelial cell. Image is presenter’s own.
Note the para-arterial position of the lesion and its connection to the adventitia.

IPAH displaying plexiform lesions in bronchial vessels

IPAH, idiopathic pulmonary arterial hypertension. Image is presenter’s own.
Intrapulmonary Bronchopulmonary Anastomoses and Plexiform Lesions in Idiopathic Pulmonary Arterial Hypertension
hPAH: Atypical, large (millimetric) fibrous lesions comprising several blood vessels (1)

SiMFis: **S**ingular **m**illimetric **f**ibrovascular **l**esions

hPAH, hereditary pulmonary arterial hypertension.

hPAH: Atypical, large (millimetric) fibrous lesions comprising several blood vessels (2)

SiMFis: Singular millimetric fibrovascular lesions

Association of SiMFis presence and hypertrophy of systemic (bronchial) vessels

43.5% of BMPR2+ (carriers) = SiMFis
9.5% of BMPR2- (non-carriers) = SiMFis

BMPR2, bone morphogenetic receptor type II; SiMFis, singular millimetric fibrovascular lesions.

CTEPH (Group 4, peripheral disease)


CTEPH, chronic thromboembolic pulmonary hypertension.
Microvascular disease in CTEPH


= Pulmonary vein/venule
Anastomosis of a bronchial artery (b) and pulmonary arteriole (p) at an alveolar capillary loop

In PAH systemic (bronchial) vessel hypertrophy correlates positively with pulmonary venous remodeling. 

IMPACT OF HYPERTROPHIC SYSTEMIC VASCULATURE IN PAH

- Systemic Vascular Plexus
- Bronchopulmonary Anastomoses
- Pulmonary Artery with Constricting Lesion
- Muscular Hyperplasia and Intimal Fibrosis
- Pulmonary Vein
- Bronchiolar Microvessels
- Bronchial Haemorrhage
- Systemic Vascular Plexus
Typical vascular lesions in PVOD (Group 1‘) (1)

PVOD, pulmonary veno-occlusive disease. Images are presenter’s own.
Typical vascular lesions in PVOD (Group 1') (2)

Nossent et al., submitted, 2016
Typical vascular lesions in PVOD (Group 1’)
Conclusions

Pathology is an observational and descriptive discipline…

But it is also an important non-abstract (real) visual of the disease, the morphological correlate of what causes disease

We might have arrived at a turning point of PH pathology – same old lesions, but rebooting interpretation:

• It might be that, in the past, we were too focused on ‘the classic arterial lesions’ and have neglected the role of the microvasculature (arterioles and venules)

• The systemic lung vasculature appears to play an important role in different forms of PH, even if its part in disease evolution has yet to be elucidated

• All levels of the pulmonary vasculature (arteries, capillaries, veins) are involved in most forms of PH

• From pathology’s standpoint of view a clear-cut categorization into pre- and post-capillary PH / vascular remodeling appears more and more difficult: perhaps rather different conditions in one large spectrum of disease?