THE PATHOLOGY OF NON-NEOPLASTIC LUNG DISEASE

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Herpes simplex virus infection

- Causes a necrotising tracheobronchitis with infected epithelial cells containing smudgy nuclear inclusions.
4 Conditions associated with Aspergillus

- Allergic reaction – Allergic Broncho-Pulmonary Aspergillosis (ABPA) and probably many cases of Bronchocentric granulomatosis (BG) – the organism may be very scanty indeed and not seen in the histology or cytology; of course precipitins will be helpful.

- Colonisation by Aspergillus – eg in bronchiectasis 5403/93 & 5753/96 with adjacent adenocarcinoma.

- Aspergilloma – 8383/94 – the very hyperplastic thick walled bronchial arteries in bronchiectasis and Aspergilloma make surgery on these lesions quite risky in terms of haemorrhage.

- Invasive Aspergillosis – generally heavy immunosuppression is responsible and this condition is untreatable. Angioinvasion and dissemination systemically is fatal.
Splendore-Hoepli phenomenon with squamous metaplasia of the wall of this cavity

Calcification typical of Aspergillus in this slide colonising a bronchiectatic cavity adjacent to an adenocarcinoma
The Spectrum of Granulomatous Lung Disease

- TB
- Sarcoid
- Rheumatoid
- Fungal infection
- Malignancy
- Granulomatous vasculitides & Bronchocentric granulomatosis
- Aspiration/obstruction
- Foreign body - iv drug abuse
- Interstitial lung disease
  - Extrinsic allergic alveolitis
  - Giant cell pneumonia
  - Desquamative interstitial pneumonia
  - Eosinophilic granuloma
Types of granulomatous inflammation

- Necrotising & caseating
- Necrotising with vasculitis
- Florid granulomas
- Poorly-formed granulomas
- Histiocytes only
Site of granulomas

- Airway
- Air space
- Parenchymal
- Vascular
- Lymphatics
- Pleural
Fungal infections

- Aspergillus
- PCP
- Cryptococcus
- Histoplasma
Granulomas & malignancy

- In draining lymph nodes
- Lymphoma or carcinoma
- Granulomas as part of lymphomatous mass
- Obstructive granulomatous/lipoid pneumonia
Granulomas present in very many lung diseases

Consider

- Type of inflammation
- Site & morphology of granulomas
- Organism stains
- Clinical & radiological findings
Classification of Granulomatous vasculitides

- Wegener’s
- Necrotising sarcoid
- Bronchocentric granulomatosis (probably allergic)
- Lymphomatoid granulomatosis (lymphoma)
- TB
Sarcoidosis

- Almost confluent non-caseating granulomas in a lymph node is highly suggestive of sarcoid but TB must be considered. In the lung, the granulomas of sarcoidosis follow the angiolympathics. There can be a lymphocytic alveolitis also and excess lymphocytes of CD4 subtype are present in BAL (excess CD8 lymphocytes are present in EAA). Finding granulomas in alveolar spaces and the presence of necrosis is much more suggestive of infection.

- Tuberculosis vs Rheumatoid granuloma
- This wedge excision of a nodule from a woman with rheumatoid arthritis and positive serology resembles a rheumatoid nodule but ZN shows many AAFBs which is obviously diagnostic.
NG04/4717 shows a granuloma in an FNA of a lymph node that also contains adenocarcinoma. Granulomatous reaction to a tumour is well recognised.

By contrast, pleural TB (PP EQA No5 Case 34) shows caseating necrosis and giant cell granulomas.
Wegener’s granulomatosis

- Three examples of WG with characteristic features: large geographic areas of necrosis with much nuclear debris mostly neutrophilic in origin in the centre of the necrotic zones. At the margins of the necrosis are a few ‘smudgy’ giant cells. Vasculitis may be seen in sections away from the necrotic areas but it is difficult to interpret damaged vessels within the inflamed areas. Limited Wegener’s may affect the lungs alone and the kidneys are normal. ANCA is an essential investigation for the clinician. The pathologist will perform stains for organisms; ZN, Grocott and Gram stains to exclude TB, fungal infection and lung abscess. Bad teeth infected with Strep milleri can cause lung abscesses that could look quite similar.
Lymphangioleiomyomatosis

- Women of reproductive age with chylous effusion and recurrent pneumothorax is the classical presentation. Can be related to tuberous sclerosis and angiomyolipomas in other regions such as the kidney. The lung cysts are scattered throughout the lungs giving characteristic radiology. Histology shows abnormal smooth muscle in the wall of the cysts that obstruct lymphatics. Actin and HMB45 stain the abnormal cells.
Lymhangioleiomyomatosis
Interstitial Lung Disease

- UIP / CFA
- NSIP
- AIP
- EAA / Hypersensitivity
- DIP / RB-ILD
- COP / BOOP
- (LIP)
Usual interstitial pneumonia (UIP / CFA) vs Non-specific interstitial pneumonia (NSIP)

- UIP is still often called cryptogenic fibrosing alveolitis in the UK. These 2 examples show much smooth muscle hyperplasia as well as other typical features, namely, fibroblastic foci, normal and diseased lung side by side, subpleural accentuation, chronic inflammatory cell infiltration of alveolar septae and fibrosis.

- ILD 39/00 is a putative case of NSIP with no variation in the type of inflammation throughout the biopsy. None of the other features of UIP are seen except perhaps some subpleural accentuation.
Extrinsic allergic alveolitis (EAA) vs Cryptogenic organising pneumonia (COP)

- These conditions show extensive inflammation of the lung parenchyma but both show a predilection for the airways and alveolar ducts. There are poorly formed granulomas and many cholesterol clefts in EAA and intra-alveolar fibroblastic tissue in COP. The latter is a disease that leads to shadows on X-ray that move around the lungs as it progresses then heals. Both will respond to steroid therapy.
Alveolar filling - Alveolar (lipo) proteinosis vs Pneumocystis

- Ground glass change on CT scan is evidence of alveolar filling that can be due to oedema or much less commonly PCP or alveolar proteinosis. Pneumocysts slightly refract and now are best demonstrated on immunostains as Grocott’s suffer from so much background staining. There may be very little cellular inflammation if the patient is immunosuppressed. The granular debris in alveolar proteinosis consists of surfactant that is not mopped up as the alveolar macrophages are not fully functional. EM of the debris shows the laminated ‘fingerprint’ appearance of surfactant.
Pneumocystis
Lipoid pneumonia
Desquamative interstitial pneumonia (DIP) vs Respiratory bronchiolitis interstitial lung disease (RB-ILD)

- Smoking unites respiratory bronchiolitis, RB-ILD, DIP and Langerhans cell histiocytosis. This case crosses the boundaries between DIP and RB-ILD. There would be much less extension of the lightly pigmented macrophages into the parenchyma with concentration around bronchioles in respiratory bronchiolitis. The infiltrate is extremely diffuse in DIP but there should be minimal fibrosis or alveolar septal inflammation. RB-ILD fits inbetween these 2 conditions but parenchymal fibrosis should still be lacking.

- Some authors have suggested new nomenclature for these conditions – macrophage pneumonias!

- Beware of alveolar malignancy as a mimic, because macrophages can appear very epithelial so not surprisingly a carcinoma could resemble sheets of macrophages – sometimes in sputum the same problem occurs.
Langerhans cell histiocytosis
(Eosinophilic granuloma)

Usually diagnostic radiology with multiple nodules. Histologically the lesions are at varying stages of cellularity and scarring. Stellate scars at low power and at high power there are groups of eosinophils with histiocytes in active lesions. These histiocytes stain with S100 and CD1a.

Similar histiocytic and eosinophilic infiltrate in the pleura is very unlikely to be LCH and usually is reactive eosinophilic pleuritis (18245/98) due to a pneumothorax. Air in the pleural space acts like a foreign body.
Reactive eosinophilic pleuritis
Giant cell interstitial pneumonia (GIP)

- Giant cells throughout the alveolar infiltrate of macrophages give this distinctive pattern of GIP which is related to occupations hard metal industry. Inhaling the hard metal produces a DIP-like picture but with giant cells, presumably because the metal is acting as a foreign body. Perhaps in a different clinical setting some viral pneumonias such as measles could look similar.
Acute interstitial pneumonia (AIP)/ Diffuse alveolar damage (DAD)

- There are hyaline membranes, intra-alveolar fibrin and haemorrhage. Epithelial cell regeneration appears atypical but this is normal. Fibrosis will soon follow and within a few days the process will either become irreversible and untreatable or recovery will start. The cause is often not apparent and the list of possible causes is long and includes: shock lung, infection and drug reaction.
Bronchial asthma

- The post-mortem histology shows mucus plugged bronchi with eosinophils in the mucus. There is epithelial sloughing and thickening of the ‘basement membrane’ (at EM it is actually beneath the BM). In acute asthma cytology shows Charcot-Leyden crystals, the crystalline product of eosinophil degranulation, and Creola bodies, the result of epithelial sloughing. The attachment of epithelial cells to the BM is impaired in asthmatic airways. Eosinophils on a Pap stain may look slightly greenish with bilobed nuclei slightly larger than neutrophils. Being degranulated makes them more difficult to recognize.
Mitral valve disease

- The effect of severe mitral valve disease produces dramatic effects on the lung. The vessel walls and alveolar walls become elastotic and encrusted with iron that is well seen on a Perls/EVG stain. Some calcification occurs too. Pulmonary hypertension occurs but does not produce the severe vascular changes of primary pulmonary hypertension such as angiomatoid lesions or dilatation lesions. However, medial hypertrophy and fibromuscular intimal thickening may be seen.
Amyloid in the lung

- Systemic amyloidosis due to ulcerative colitis and nodular amyloid are shown in these slides.
- Ulcerative Colitis is also known to be related to bronchiectasis.
Drug abuser’s lung

- First case is from a Methadone overdose and the second from Temazepam. Both show that intra-venous injection of particulate matter, starch filler in the case of Temazepam usage, has resulted in vascular occlusion and deposition of material with a florid giant cell reaction in the wall of vessels.
Primary pulmonary hypertension (PPH)

- Most PPH is put down to recurrent thrombo-embolic disease that is unproven. The most severe vascular changes are seen in this condition and angiomatoid lesions and dilatation lesions are seen. Onion-skinning and other changes are more obvious on an EVG stain. Radiologically the lungs may be apparently normal but the patient is breathless and requires lung transplantation.
Additional reading

- Corrin’s “Pathology of the Lungs”
- Katzenstein & Askin’s “Pathology of Non-neoplastic lung disease”

And now it’s time for dessert