Granulomatous lung diseases

An approach to the differential diagnosis
Reference
Granulomas are among the most commonly encountered abnormalities in pulmonary pathology. Granuloma is a compact aggregate of histiocytes (macrophages) which are described as epithelioid cells.

Aggregate of histiocytes is a minimum requirement of a granuloma regardless of whether the lesion also contains necrosis, lymphocytes, plasma cells or multinucleated giant cells.
Recommended step-by-step approach to pulmonary granuloma

1) Attempt to identify an organism.
2) Look for histologic features of noninfectious granulomatous disease.
3) If step 1 and 2 do not reveal a specific diagnosis, ensure that an adequate number of blocks have been stained with special stains and re-examine the special stains. If no organisms are found despite through reexamination, issue a descriptive diagnosis (necrotizing or non necrotizing).
Step 1: Identifying organisms

The organisms commonly found in pulmonary granuloma are

**Mycobacteria**

**Fungi**

Histoplasma

Cryptococcus

Coccidioides

Blastomyces

Pneumocystis

Aspergillus
Using the tissue reaction as a clue

Necrotizing granuloma in mycobacteria, histoplasma and coccidioides.

Neutrophils in granuloma should suggest blastomyces.

Eosinophils in granuloma indicates coccidioides.
Examining special stains for organisms

The search for organisms must always begin with hematoxylin- eosin stained sections. Many pathologists incorrectly assume that organisms are not visible on H&E and skip directly to special stains.
The histochemical stains mostly used for identification of organisms are Ziehle-Neelson (ZN) stain (acid fast stain) for mycobacteria and silver stain for fungi. Fluorescence techniques have been shown to be equivalent to culture and superior to acid fast stain.
When H&E stained sections are examined, it is recommended to examine silver stained sections before the time consuming ZN stained sections. The most important point to remember in most cases that mycobacteria are few and difficult to find because of use of xyline in routine processing, and organisms are by far more common in the center of necrosis than at the periphery.
Necrotizing granuloma of T.B (H&E)
Mycobacteria are demonstrated using ZN stained sections
Necrotizing granuloma of histoplasma infection identical to that of T.B.

Histoplasma is a small non budding yeast identified using silver stain.
Non necrotizing granuloma of cryptococcus infection, note the round small yeast within histiocyte with halo
Cryptococcus is a small rounded shaped yeast with marked variation in size demonstrated with silver stain.
Granuloma of coccidioides: spherules filled with endospore are detected in pulmonary granuloma using both H&E and silver stains
Blastomyces: single thick walled yeast within the giant cell and neutrophilic reaction. The single broad based bud of blastomyces is detected with silver stain.
Allergic bronchopulmonary Aspergillosis with necrotizing granuloma destroying a bronchiole. With abundant eosinophils in necrotic material (arrow)
Allergic bronchopulmonary Aspergillosis with dilated bronchus filled with mucoid material, the branching hyphae are present within the mucus with abundant eosinophils.
Step 2: look for histological features of non infectious granulomatous inflammation
The main role of pathologist is to identify features not consistent with sarcoidosis and to exclude presence of organisms
Sarcoidosis
prominent small well formed discrete non necrotizing granuloma in pleura, interlobular septa and walls of bronchioles with normal lung away from granuloma is seen in sarcoidosis
Pink spider-like structures (Asteroid body) in sarcoidosis
Hypersensitivity pneumonitis
Prominent interstitial chronic inflammation with scattered *small poorly formed granulomas* or only multinucleated giant cells in interstitium is seen in hypersensitivity pneumonitis.
Needle shaped crystalline inclusion (endogenous) in hypersensitivity pneumonitis
Cholesterol cleft (endogenous) in hypersensitivity pneumonitis
Aspiration pneumonia
Vegetable particles in aspiration pneumonia
wegener
granulomatosis
Wegener granulomatosis: necrotizing granuloma with dirty suppurative necrosis
Vasculitis is an additional differentiating feature of Wegener granulomatosis, the predominant cellular infiltrate is neutrophil.
While the main inflammatory infiltrate that accompany the vasculitis of mycobacterial infection are lymphocytes
Thank you