

GRANULOMATOUS LYMPHADENITIS

Granulomatous lymphadenitis is a reactive phenomenon of lymph nodes that displays a distinctive pattern of chronic inflammation and histiocytes. It is caused by a heterogeneous collection of diseases, including reactive, infectious and malignant etiologies.

Histologically, granulomatous lymphadenitis (i.e. granulomas) can be divided into three distinct categories based on the type of inflammation present (acute versus chronic), and whether or not necrosis accompanies the inflammation (see table below).

Fine needle aspiration biopsy (FNA) can be extremely useful for patients with adenopathy. FNA samples can be cultured, sent for flow cytometry, or molecular testing. FNA should be the first test chosen when no underlying cause for the adenopathy is readily apparent, or for adenopathy in which antibiotics do not shrink the mass. FNA is quick, easy to perform, and patients tolerate it well.

Clinical History

Patients with granulomatous lymphadenitis typically present clinically with one or more enlarged lymph nodes. How should you approach these patients?

As always, history is extremely important, and can, in fact, offer critical diagnostic clues. On physical exam, some

granulomatous diseases have a particular predilection for affecting certain body sites.

- Eosinophilic Granuloma – Bone
- Wegener's Granulomatosis – Face
 - Giant Cell Granuloma – Oral Cavity
 - Granuloma Annulare – Skin
- Various Infectious Agents – CNS

History of travel or animal exposure is a particularly helpful clue. Has the patient traveled and possibly been exposed to infectious agents? Mycoses (fungal infections) are endemic in many parts of the country. In particular, the Midwest harbors *Blastomycosis dermatitidis*, while the Ohio River Valley has *Histoplasma capsulatum* and the Southwest/California sees *Coccidioides immitis*.

Spring and fall are the peak times for cat scratch fever (*Bartonella henselae*). Eliciting a history of owning/working with a cat or getting scratched is important. *Rhodococcus equi* should be considered if the patient had contact with horses or soil contaminated with horse manure; this is most commonly seen in the Southeast. Does the patient hunt and skin animals, especially rabbits? *Francisella tularensis* can occur when humans come in contact with an infected rabbit or gets a bite from a tick or deer fly.

GRANULOMATOUS INFLAMMATION

CASEATING
(chronic with necrosis)

Tuberculosis
Histoplasmosis
Cryptococcosis
Blastomycosis
Syphilis
Eosinophilic Granuloma
Hodgkin's Disease
T-Cell Lymphoma

NON-CASEATING
(chronic without necrosis)

Sarcoidosis
Toxoplasmosis
Crohn's Disease
Infectious Mononucleosis
Whipple's Disease
Leprosy
Syphilis
Leishmaniasis
Drug Reaction

SUPPURATIVE
(acute with necrosis)

Squamous Cell Carcinoma
Seminoma
Thymoma
Hodgkin's Disease
T-Cell Lymphoma
Metals
(Berylliosis And Silicosis)
Silicone
Foreign Body

Atypical Mycobacteria
(especially in children)
Cat-Scratch Disease
Lymphogranuloma Venereum
(*Chlamydia*)
Yersinia Infection

Laboratory Tests

Usually, routine laboratory tests are nondiagnostic; cultures of blood, skin lesions or lymph nodes are frequently negative. Fortunately, if there is suspicion of an infectious agent, there are specific serologic studies that can confirm the diagnosis. Polymerase chain reaction (PCR) and antibody titers also are very helpful. Direct and indirect fluorescence antibody tests are also available and have good sensitivities.

Mycobacterium is re-emerging, and numerous cases have been seen in Washington County and in Sevierville. Construction workers, gardeners, and farmers are exposed to the dirt and can inhale spores. It is still prudent to perform TB skin tests and culture blood, sputum or urine. Some universities are performing PCR for TB. If there is an abscess associated with the granulomatous disease, and the patient has not been on antibiotics, then cultures can be obtained.

Blastomycosis is found in the Southeast and the spores can be inhaled or enter through a small cut in the body. Again, blood tests and PCR are helpful.

Cultures and antibody titers for **Cat Scratch Disease** are performed at the CDC, but it takes 4-6 weeks to obtain serologic results. Routine cultures are usually negative. Many physicians will empirically treat this entity.

If **Sarcoidosis** is a consideration, work-up would include a chest x-ray with specific findings for sarcoid (bilateral hilar adenopathy), an elevated serum angiotensin converting enzyme (ACE) and lysozyme, which is seen in two-thirds of patients. Some people will have an elevated 24-hour calcium level. Diagnostic tissue is usually obtained via a transbronchial lung biopsy.

Hodgkin's Disease frequently will have granulomas. FNA is useful in florid cases where there are many Reed-Sternberg cells present. It is also helpful in diagnosing recurrent disease. Immunoperoxidase markers can now be utilized on FNA specimens to render a definitive diagnosis. Subclassification of Hodgkin's lymphoma is no longer important for treatment, as was historically thought.

Granulomatous disease can be seen with **T-Cell lymphomas**. These peripheral lymphomas encompass a variety of lymphomas such as mycosis fungoides, HIV-associated lymphomas, angiocentric T-Cell lymphoma, Lennert's lymphoma and intestinal lymphomas. Patients will have painless adenopathy that may be generalized and is often associated with autoimmune disease. FNA can obtain material for flow cytometry for these entities.

Testing for **infectious mononucleosis** has changed. The monospot test has replaced the older heterophile antibody test. It's easier and more sensitive. If the monospot test is negative and infectious mononucleosis is still suspected, antibodies to viral capsid antigens (VCA) can be obtained. Initially, IgM antibodies appear, and later, IgG.

Granulomatous disease caused by **silicone** is seen with contamination of a wound with particles from soil or glass that contains silicone dioxide. Contamination of a surgical wound with talcum powder that contains magnesium silicate is another method. Rupture of silicone breast implants can also give a widespread granulomatous pattern embedded with silicone crystals.

If **toxoplasmosis** is suspected, the best tests are IgG and IgM toxoplasma antibody titers or an enzyme linked immunosorbent assay (ELISA).

COMPANY PROFILE

OUTPATIENT CYTOPATHOLOGY CENTER (OCC) is an independent pathology practice, accredited by the College of American Pathologists, that specializes in performing and interpreting fine needle aspiration biopsy specimens. The practice was established in 1991 in Johnson City, Tennessee. Patients may be referred for aspiration biopsy of most palpable masses as well as for aspiration of non-palpable breast and thyroid masses that can be visualized by ultrasound. OCC is a participating provider with most insurance plans. Our primary referral area includes Tennessee, Virginia, West Virginia, North and South Carolina, and Georgia.

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