

Pediatric Cervical Lymphadenopathy and Head and Neck Masses

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Epidemiology

- 38-45% of normal children will have palpable cervical lymphadenopathy
- 90% of children aged 4-8 years old will present with cervical lymphadenopathy
- These masses can be mistaken for other local and systemic processes
 - Congenital Masses
 - Malignancies
 - Local presentation of systemic disease
- Found by parents and caregivers and demand workup...

Outline and Objectives

1. Cervical lymphadenopathy in children

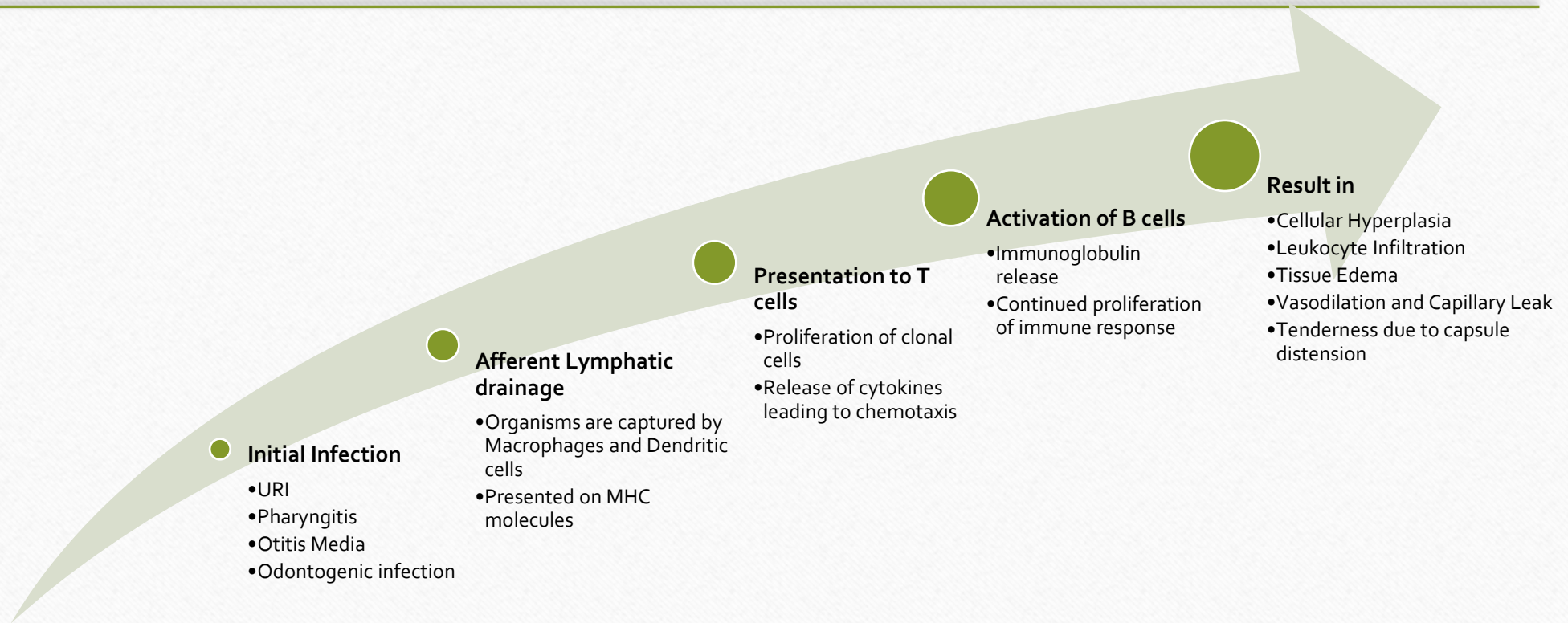
- Describe important History and Physical findings including workup of cervical lymphadenopathy
- Discuss pathogens responsible for acute vs subacute/chronic lymphadenitis
- Review literature on the common causes and management of lymphadenopathy
- Review literature on the use of ultrasound and biopsy to aid in diagnosis
- Summarize a plan for diagnosis and treatment

2. Pediatric Head and Neck Masses

Definitions

- Pathologic Lymph Node
 - >2cm in children is considered abnormal
- Acute Lymphadenopathy
 - < 2 weeks duration
- Subacute Lymphadenopathy
 - 2-6 weeks duration
- Chronic Lymphadenopathy
 - > 6 weeks duration

Pathophysiology



History

- “OLD CARTS” - onset, location, duration, character, aggravating and relieving factors, timing and situation in which the problem is occurring
- Fever, malaise, anorexia, myalgia
- Pain or tenderness of node
- Sore Throat
- URI
- Toothache
- Ear pain
- Insect Bites
- Exposure to animals
- History of travel or exposure to TB
- Immunizations
- Medications

Drug Induced Lymphadenopathy

- Medications
 - Phenytoin
 - Pyrimethamine
 - Allopurinol
 - Phenylbutazone
 - Isoniazide
- Immunizations
 - Smallpox (historically)
 - Live attenuated MMR
 - DPT
 - Poliomyelitis
 - Typhoid fever

**Usually self limited and resolves with cessation of medication or with time in the case of immunization induced LAD

Physical exam

- **General**

- Febrile or toxic appearing

- **Skin**

- Cellulitis, impetigo, rash

- **ENT**

- Otitis, pharyngitis, teeth, and nasal cavity

- **Neck**

- Size
- Unilateral vs Bilateral
- Tender vs Nontender
- Mobile vs Fixed
- Hard vs Soft

- **Lungs**

- Consolidations suggesting TB

- **Abdomen**

- Hepatosplenomegaly

- **Extremities**

- Inguinal and Axillary adenopathy

Differential diagnosis

- **Thyroglossal duct cyst**
 - Moves with tongue protrusion and is midline
- **Dermoid Cyst**
 - Midline and often has calcifications on plain films
- **Branchial Cleft Cyst**
 - Smooth and fluctuant along SCM border
- **Laryngocele**
 - Enlarges with valsalva

Differential diagnosis

- **Hemangioma**

- Mass is presents after birth, rapidly grows, plateaus, and is red or bluish in color

- **Cystic Hygroma**

- Transilluminates and is compressible

- **Sternocleidomastoid Tumor**

- Lymphadenopathy does not present with torticollis

- **Mumps**

- Mass palpated superior to jaw line

Laboratory workup

- CBC with Differential
- ESR, CRP
- Rapid Streptococcal screen
- Urine VMA
- LDH

Laboratory workup

- Serology
 - EBV
 - CMV
 - Bartonella
 - Toxoplasmosis
 - Syphilis
 - HIV
- PPD placement

Imaging workup

- CXR
 - To look for mediastinal lymphadenopathy
- Ultrasound
 - To evaluate for or follow progress of an abscess
 - To differentiate benign from malignant
- CT/MRI
 - To evaluate for abscess
- EKG/ECHO
 - If suspect Kawasaki Disease
- Biopsy
 - FNA or Excisional

Etiology of lymphadenopathy

- Acute Infectious
- Subacute/Chronic Infectious
- Malignancy
- Systemic disease/Non-infectious

Infectious Lymphadenopathy

Viral Lymphadenitis

- Most common form of reactive lymphadenopathy
- Common viruses involved:
 1. Adenovirus
 2. Rhinovirus
 3. Coxsackie virus A and B
 4. EBV

Viral Lymphadenitis

- Lymphadenopathy often bilateral, diffuse, non-tender
- Other Signs/Symptoms are consistent with URI
- Management is expectant but they are often biopsied due to slow regression
- Nodal architecture and hilar vascularity are normal on pathologic examination

Suppurative bacterial lymphadenitis

- Staphylococcus aureus and Group A Streptococcus
- Brodsky et al. showed aerobes 67% vs anaerobes 19%
- Common history reveals recent
 - URI
 - Earache
 - Sore Throat/Toothache
 - Skin Lesions
- Management is initially with oral or IV antibiotics depending on severity of infection



Suppurative bacterial lymphadenitis

- If not resolving or getting worse
 - CT with contrast and/or Ultrasound to evaluate for phlegmon/abscess/infiltrate
- FNA vs Surgical I&D vs Surgical Excision if abscess is identified



Subacute Lymphadenitis

- 2-6 weeks duration
 - Usually seen and treated with antibiotics without improvement
- Parents start to worry and want to know "What is it?"
- Margalith et al. 1995
 - Atypical Mycobacteria
 - Cat Scratch disease
 - Toxoplasmosis
 - EBV and CMV less common

Choi et al 2009 -Archives Otolaryngology-HNS

- Retrospective review of 60 patients <18 y/o with persistent LAD and negative cultures at 48 hours.
- Performed general and specific PCR amplification of surgically excised tissue or abscess contents
- Surgically removed lymph nodes were also sent for permanent staining of specific organisms
- Diagnostic characteristics
 - Mean age of 4.7 years with slight female predominance at 53%
 - Average lymph node size was 3.2 cm
 - Superior cervical chain and submandibular nodes most involved

Choi et al 2009 -Archives Otolaryngology-HNS

- Most common Pathogens
 - Mycobacteria 61.7% of cases and 73% of these were MAI
 - Legionella represented 10% of cases
 - Bartonella represented 10% of cases
 - Unidentified etiology in 18.3% of cases

Choi et al 2009 -Archives Otolaryngology-HNS

- Method of identification
 - Mycobacteria
 - Stain (70%), Culture (86.5%), PCR (81%)
 - Bartonella and Legionella
 - PCR (100%), Culture and Gram stain (0%)

Choi et al 2009 -Archives Otolaryngology-HNS

- Results of surgical therapy
 - 90 surgical procedures performed on 60 patients
 - Cure rate was as follows
 - 95% for excisional lymphadenectomy
 - 58% for curettage
 - 23% for incision and drainage

Choi et al 2009 -Archives Otolaryngology-HNS

- Conclusions

1. Nontuberculous mycobacterial infections

- PCR is a rapid way to diagnose causative organisms of LAD as culture can take over 2 weeks for result
- Surgical excision results in the highest cure rate and is therefore preferred unless the facial nerve or cosmetics are at risk.
- Simple observation also works if nodes are not suppurative but this leads to protracted course

2. Cat Scratch Disease

- PCR again is a rapid way to make the diagnosis since serologic studies have low sensitivity and specificity
- Too small of sample size to determine if surgical vs antibiotics vs observation is superior treatment
- Surgical treatment is necessary if abscess is identified as reported in 10-20% of cases difference.

Choi et al 2009 -Archives Otolaryngology-HNS

- Conclusions

- 3. Legionella lymphadenitis

- PCR provides rapid diagnostic benefits as legionella grows on special media
 - Levofloxacin/Moxifloxacin/Azithromycin +/- Rifampin
 - Incision and drainage plus antibiotics showed recurrence in 6/7 patients
 - Surgical excision is recommended but larger sample needed to detect significant difference.

Atypical Mycobacteria

- #1 cause of subacute disease
- Species involved:
 - *Mycobacterium avium-intracellulare*
 - *Mycobacterium scrofulaceum*
- Develops over weeks to months

Atypical Mycobacteria

- Lymph nodes are tender, rubbery, and may have violaceous discolored skin over the node
- Diagnosis by acid fast stain and culture of material from lymph node (FNA) which can take weeks
- Untreated disease may lead to sinus tract and cutaneous drainage for up to 12 months
- Treatment historically has been surgical excision of involved lymph nodes

**Different from Tuberculous LAD where lymphadenopathy is a more ominous sign of disseminated disease if found in lymph nodes

Zeharia et al 2008

Pediatric Infectious Disease

- Retrospective review of 92 children with chronic non-TB mycobacterial cervical lymphadenitis
- Parents opted for conservative treatment
- Patients followed for at least 2 years.
- Cultures and PCR used to verify mycobacteria

Zeharia et al 2008

Pediatric Infectious Disease

- Diagnostic Characteristics
 - <4 yrs old and nodal size > 3 cm in 80% of cases
 - Unifocal lymphadenopathy in 90% of cases
 - Submandibular (50%) > Cervical (25%) > Preauricular (10%)
 - Positive PPD >10mm in 85% of cases
 - *MAI* and *M. haemophilum* isolated in 90% of cases

Zeharia et al 2008

Pediatric Infectious Disease

- Outcomes
 - Dominant nodes showed purulent drainage in 97% of patients for 3-8 weeks
 - Total Resolution
 - 6 months in 71%
 - 9 months in 98%
 - 12 months in 100%
 - No complications other than a skin colored flat scar in the area of drainage at 2 year follow up

Zeharia et al 2008

Pediatric Infectious Disease

- Conclusions
 - Previous randomized controlled trials have shown increased benefit of Surgery over Clarithromycin plus Rifabutin
 - Surgical Therapy Complication rates of 10-28%
 - Large incision with poor cosmetic result
 - Fistula formation and prolonged wound drainage
 - Repeat surgical procedures for recurrence
 - Secondary *S. aureus* wound infections
 - Transient or permanent facial nerve paralysis
 - Therefore expectant management is recommended ,however a randomized study comparing surgery and observation is needed

Cat scratch disease

- Species involved:
 - *Bartonella Henselae*
- Age <20, M>F,
- 90% have had exposure to cat bite or scratch
- Can take up to 2 weeks to develop



Cat scratch disease



- Tender LAD are usually present however, fever and malaise are mild and present in <50% of patients (Twist)
- Diagnosis with serology for antibodies or PCR
- Historically management has been expectant with antibiotics reserved for rare cases with complicated courses (Windsor 2001)
- Antibiotics always given to immunocompromised patients to prevent disseminated disease

**Other less common zoonotic causes are tularemia, brucellosis, and anthracosis.



Bass et al. 1998-Pediatric Infectious Disease

- Prospective Randomized Double Blinded Placebo controlled trial
- 29 patients randomized to Azithromycin x 5days vs Placebo (14 and 15 respectively)
- Lymph node volume calculated until total lymph node volume was less than 20% original value

Bass et al. 1998-Pediatric Infectious Disease

- Results
 - Azithromycin group showed 50% success rate at 30 days
 - placebo group showed only 7% success ($p < 0.02$)
- After 30 days however the rate or degree of resolution was not significantly different between groups

Bass et al. 1998-Pediatric Infectious Disease

- Conclusions
 - Antibiotic therapy is indicated to rapidly decrease node size within the first 30 days
- Antibiotic therapy should be considered in all patients, especially those who are immunocompromised and at increased risk for disseminated disease.
- Suppurative lymphadenitis occurs in 10% of patients from previous reports, but surgical drainage is rarely necessary.

Toxoplasma gondii

- Mechanism
 - Consumption of undercooked meat
 - Ingestion of oocytes from cat feces
- Symptoms
 - Malaise, fever, sore throat, myalgias
 - 90% have cervical lymphadenitis
- Diagnosis by serologic testing
- Complications include
 - myocarditis
 - pneumonitis
- Risk of TORCH infection to fetus
- Treatment with pyrimethamine or sulfonamides

Infectious mononucleosis - EBV

- Epidemiology
 - 50% seropositive by age 5
 - 90% seropositive by age 25
- Signs/Symptoms
 - Fever
 - Exudative pharyngitis
 - Painless generalized lymphadenopathy
 - Axillary LAD and Splenic enlargement increase likelihood50% lymphocytosis with >10% Atypical lymphocytes on peripheral smear is suggestive Diagnosis

Infectious mononucleosis - EBV

- Positive monospot test
- Serum heterophile Antibody definitive
 - 60% positive at 2 weeks while 90% are positive at 1 month
- Treatment is expectant and supportive
- Tonsillar hypertrophy can become bad enough to produce airway obstruction and you may need to place nasopharyngeal tube and start high dose steroids
- Do not give amoxicillin as patients will develop an iatrogenic rash in 80% of patients.
- No sports for 8 weeks to prevent splenic injury and rupture

Chronic lymphadenopathy

- >6 weeks
- Subacute pathogens frequently implicated
- Risk of Malignancy increased
 1. Neuroblastoma
 2. Rhabdomyosarcoma
 3. Leukemia/Lymphoma
 4. Nasopharyngeal carcinoma metastasis.

Chronic lymphadenopathy

- Supraclavicular (Ellison 1999) and posterior triangle adenopathy (Putney 1970) are at increased risk for malignancy.
- Almost all patients receive biopsy at this point
- Excisional biopsy often needed to obtain enough tissue for diagnosis
- Management is usually a referral a medical oncologist given the age group and most common cancers identified

Non-Infectious Lymphadenopathy

Kawasaki Disease

- Lymphomucocutaneous Disease
- Five Characteristics of Disease (4/5 for diagnosis)
 - Fever >5 days
 - Cervical lymphadenopathy (usually unilateral)
 - Erythema and edema of palms and soles with desquamation of skin
 - Nonpurulent Bilateral Conjunctivitis
 - Strawberry Tongue

Kawasaki Disease

- Complications
 - Coronary artery aneurysms
 - Coronary artery thromboses
 - Myocardial infarction
- Treatment
 - IVIG and Aspirin
- **Be sure to get Echo and EKG if Kawasaki disease is suspected

Rosai - Dorfman

- Massive, painless, bilateral cervical adenopathy
- Benign condition
- Generalized proliferation of sinusoidal histiocytes
- First decade of life with 2M:1F



Rosai - Dorfman

- Associated signs and symptoms
 - Fever
 - Neutrophilic leukocytosis
 - Polyclonal hypergammaglobulinemia
 - Most patients will get a biopsy given the large adenopathy
- Characteristic biopsy showing sinus expansion with histiocytes and phagocytosed lymphocytes (Foucar 1990)
- Treatment is supportive and most patients have spontaneous regression



Langerhans Cell Histiocytosis

- Eosinophilic Granuloma
 - Solitary bone, skin, lung, or stomach lesions
- Hands-Schuller-Christian Disease
 - Diabetes Insipidus, Exophthalmos, Lytic bone lesions
- Letterer-Siwe disease
 - Life threatening multisystem disorder
 - 50% 5 year survival

Langerhans Cell Histiocytosis

- 1/3 of patients will have background LAD
- Histopathology shows normal lymph node architecture but increase sinusoidal Langerhan's cells, macrophages, and eosinophils
- Treatment with topical steroids, oral steroids, and even chemoradiation therapy

Role of Ultrasound (Ahuja et al. 2005)

- No radiation exposure
- Good for following the progress of an abscess
- Differentiate Reactive vs Malignant nodes
- **Reactive**
 - <1 cm
 - Oval (S/L ratio <0.5cm)
 - Normal hilar vascularity
 - Low resistive index with high blood flow

Role of Ultrasound (Ahuja et al. 2005)

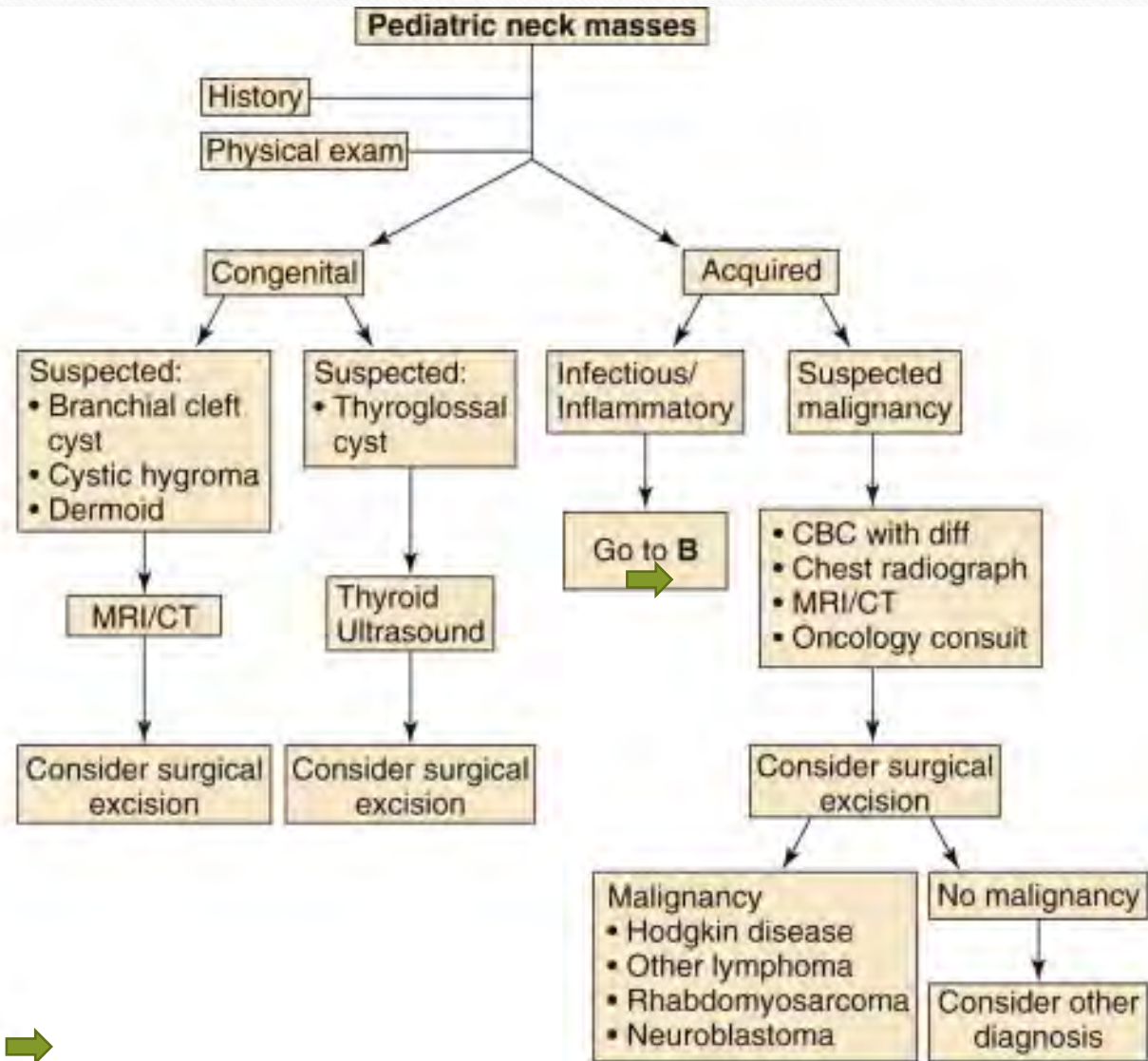
- **Malignant**
 - >1 cm
 - Round (S/L ratio >0.5cm)
 - No echogenic hilus
 - Coagulative necrosis present
 - High resistive index with low blood flow
 - Extracapsular spread
- Sensitivity 95% and Specificity 83% for differentiating reactive vs metastatic lymph nodes

FNA – Fine Needle Aspirate

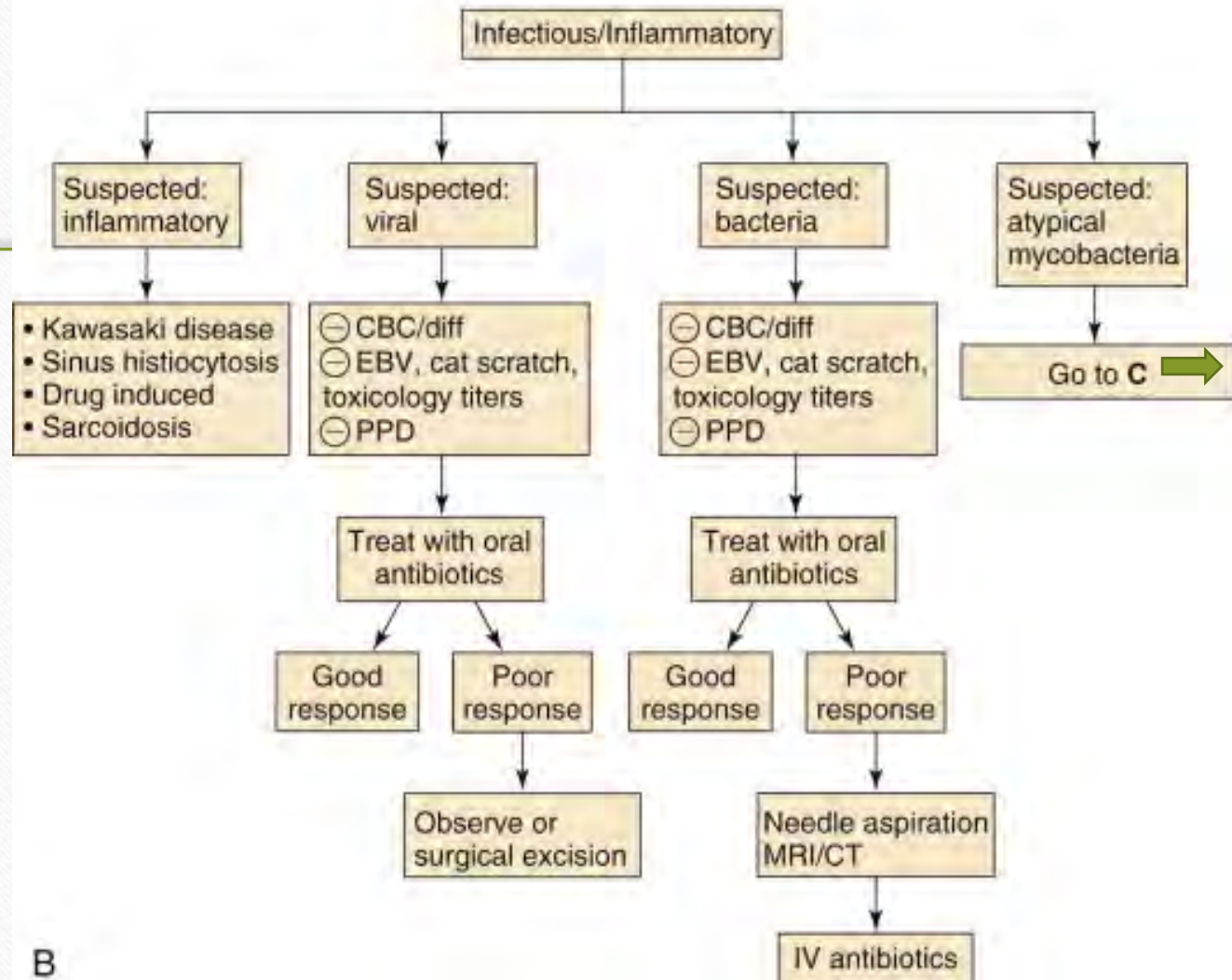
- Minimally invasive
- Low morbidity
- Not as reliable in children as in adults so you can only trust FNA if it is positive (Twist 2000)
- Chau et al. 2003
 - Evaluated FNA of 289/550 patients referred with LAD
 - Sensitivity 49% and Specificity of 97%
 - False negative rate of 45%
 - 83% of false negatives were lymphomas

Excisional Biopsy

- Gold standard for diagnosis
- Consider if FNA is inconclusive or if FNA is negative but your suspicion for malignancy is high
- You must excise the largest and firmest node that is palpable and must remove the node with the capsule intact (Twist 2000)



A →



B

Suspected atypical mycobacteria

PPD

Treat with anti-Tbc chemotherapy

Trial of oral antibiotics/
anti-Tbc chemotherapy

Good response

Poor response

Surgical excision

← C

Thank you for listening
