Brucella

Human brucellosis is caused by organisms of the genus Brucella and continues to be a major public health problem worldwide. Humans are accidental hosts and acquire this zoonotic disease from direct contact with an infected animal or consumption of products of an infected animal. Although brucellosis is widely recognized as an occupational risk among adults working with livestock, much of the brucellosis in children is foodborne and is associated with consumption of unpasteurized milk products.

ETIOLOGY

Brucella are aerobic, non-spore-forming, non-motile, **gram-negative coccobacilli** that is divided into 4 types; ***Brucella abortus*** (cattle), ***B. melitensis*** (goat/sheep), ***B. suis*** (swine), and ***B. canis*** (dog).

PATHOGENESIS The major virulence factor for *Brucella* appears to be the **smooth lipopolysaccharide** (LPS) of its cell wall which makes it more resistant to killing by PMN & because these organisms are **facultative intracellular pathogens**, they can survive and replicate within the mononuclear phagocytic cells of the reticulo-endothelial system (RES) resulting in **granuloma** formation.

Routes of infection for these organisms include inoculation through cuts or abrasions in the skin, inoculation of the conjunctival sac of the eye, inhalation of infectious aerosols, or ingestion of contaminated meat or dairy products.

CLINICAL MANIFESTATIONS

The I.P. is 2-4 wk. Brucellosis is a systemic illness that can be very difficult to diagnose in children without a history of animal or food exposure.

Symptoms can be acute or insidious in nature and are usually nonspecific, beginning 2-4 wk after inoculation. The classic triad of Brucellosis ***fever, arthralgia/arthritis, and hepatosplenomegaly*** can be demonstrated in most patients.

Some present as a ***fever of unknown origin***. Other associated symptoms include abdominal pain, headache, diarrhea, rash, night sweats, weakness/fatigue, vomiting, cough, and pharyngitis.

A common constellation of symptoms in children is refusal to eat, lassitude, refusal to bear weight, and failure to thrive.

The physical findings on examination are ***Pyrexia, pallor, skin rash, arthritis (especially spine), LAP, & HSM.***

Although headache, mental inattention, and depression may be demonstrated in patients with brucellosis, invasion of the nervous system occurs in only 1% of cases. Neonatal and congenital infections with these organisms have also been described, resulting from transmission transplacentally, from breast milk, and through blood transfusions.

DIAGNOSIS

1.CBP; Pancytopenia, i.e. anemia, neutropenia, & thrombocytopenia.

2. **Culture of blood or any tissue of the RES** (e.g. liver, spleen, lymph nodes, or BM) **is the gold standard in Dx,** but remember that Brucella is a fastidious organisms, i.e. it require as long as 4 wk to be recovered from the growth media.

(A definitive diagnosis is established by recovering the organisms in the blood, bone marrow, or other tissues.)

3. **Serology**; ***Serum Agglutination Test (SAT)*** *or Brucella Agglutination Test (BAT)* can detects antibodies against *B. abortus, B. melitensis,* and *B. suis* (but **not *B. canis*** because it lacks the smooth LPS). No single titer is ever diagnostic, but most patients with acute infections have titers of ≥1:160; whereas low titers may require acute and convalescent sera to confirm the Dx.

SAT detects both IgG and IgM (IgM can remain in the serum for weeks to months after the infection has been treated), therefore the serum is treated with ***2 mercapto-ethanol*** which cancel IgM & detect IgG only. However **false-positive** results of SAT may occur due to infection with other bacteria e.g. *Yersinia, Francisella, & Vibrio cholerae*; whereas **false- negative** results may occur due to

high antibodies titers *"prozone effect"*; to avoid this effect, serum should be diluted to ≥1:320.

4. **ELISA**. **appears to be the most sensitive method for detecting *Brucella* Ab . But less specific than SAT**

5. **PCR** is very sensitive & specific.

Differential Diagnosis

Brucellosis may be confused with other infections such as tularemia, cat scratch disease, typhoid fever, histoplasmosis, blastomycosis, and coccidioidomycosis. Infections caused by *Mycobacterium tuberculosis*, atypical mycobacteria, rickettsiae, and *Yersinia* can present in a similar fashion to brucellosis.

TREATMENT

- Children < 8 yr are usually treated with TMP (10 mg/kg)- SMZ (50 mg/kg) + Rifampin (15-20 mg/kg).
- Children > 8 yr are usually treated with Doxycycline (2-4 mg/kg) + Rifampin [or Streptomycin (20-30 mg/kg) or Gentamicin (3-5 mg/kg)]. All drugs should be given for 6 wk except Aminoglycosides for 2 wk.
- Patients with Cxs e.g. osteomyelitis, endocarditis, meningitis should be treated with Doxycycline + Gentamicin +/_ Rifampin for 4-6 mo (except gentamicin for 1-2 wk).

Note: Patients should be complaint with this prolong therapy to reduce the relapse rate.

AGE AND CONDITION	ANTIMICROBIAL AGENT	DOSE	ROUTE	DURATION
≥8 yr	Doxycycline	2–4 mg/kg/day;maximum 200 mg/day	PO	4–6 wk
	+			
	Rifampin	15–20 mg/kg/day;maximum 600–900 mg/day	PO	4–6 wk
	Alternative:			
	Doxycycline	2–4 mg/kg/day;maximum 200 mg/day	PO	4–6 wk
	+			
	Streptomycin or Gentamicin	20–30 mg/kg/day;maximum 1 g/day	IM	1–2 wk
		3–5 mg/kg/day	IM/IV	1–2 wk
<8 yr	Trimethoprim-sulfamethoxazole (TMP-SMZ)	TMP (10 mg/kg/day;maximum 480 mg/day) and SMZ (50 mg/kg/day;maximum 2.4 g/day)	PO	4–6 wk
	+			
	Rifampin	15–20 mg/kg/day	PO	4–6 wk
Meningitis, osteomyelitis, endocarditis				
	Doxycycline	2–4 mg/kg/day;maximum 200 mg/day	PO	4–6 mo
	+			
	Gentamicin	3–5 mg/kg/day	IV	1–2 wk
	±			
	Rifampin	15–20 mg/kg/day;maximum 600–900 mg/day	PO	4–6 mo