

# West Coast Transplant ID Conference

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# Case History

- ■■■ yr old ■■■ with HTN, hyperlipidemia, prediabetes, HFrEF, LV thrombus presented to OSH with acute STEMI, Cardiogenic shock
- Emergent angiogram with LAD PTCA. Severe multivessel disease with poor targets for CABG
- Transferred to UW on aortic balloon pump for AHFT
- Placed on tandem heart with complex PCI attempt, complicated by LCX Perf s/p covered stent, pericardial effusion needing drain
- Converted to VA-ECMO, listed for status 1 for transplant
- RFA stent placed for IABP site bleed

## Case History Cont.

- OHT ■/23, CMV D-/R-, EBV D+/R+, Toxo D-/R-
- Standard ATG induction and started on tacrolimus/ mycophenolate/ prednisone
- Acyclovir, clotrimazole, Bactrim for prophylaxis
- Post op course complicated by:
  - Mediastinal bleed needing RTOR for reentry and suture to LA anastomosis, Blood product support
  - Provoked DVT of right arm and right leg , S/P IVC filter placement followed by anticoagulation
  - Transient AKI and post-transplant HTN treated
- Donor Blood Cultures: MSSA , treated with Cefazolin x 2 weeks and Bactrim x 2 weeks

# Social History

## Exposure Risks

- Occupation: Works as manager for Auto sales
- Has never been a smoker. No alcohol or drug use
- Sick contacts: None
- TB - No known prior testing, no known exposures
- Pets/other animals:
  - Has a 40 gal fish tank
  - Had a cat and a bird 10 years before transplant

## Travel History

- Originally from: Los Angeles. Now lives in WA
- Has lived in CA and WA
- Short trips to Las Vegas, Idaho, Massachusetts
- Spent 2 weeks in the Philippines in past
- Has taken 2-3 short vacations to Mexico, none recently

## Pertinent Serologies

- Coccidioides antibody, IgG neg (American SW)
- Strongyloides antibody, IgG neg (Philippines)

**█/24 - Admission (4 months post OHT)**

**Fever, chills and fatigue x 2 days.**

No localizing symptoms

Temp 40.4 at home, T max 38.6 at admit, VSS

Covid, Flu, RSV negative, extended RVP panel neg

CXR Non acute, CBC 10.47 ALC 0.31

CMP Na 134, cr 1.4 , Neg UA

Negative blood cultures

TTE no new changes

Empiric Antibiotics x 48 hrs – Vancomycin and cefepime

No recent travel. No sick contact

Does not handle fishtank

Remained afebrile, felt better and was discharged





### 5/■/24 – Cardiology visit

Fever and great toe pain x 1week, possible gout

? Retrospective symptoms

Monthly endomyocardial biopsy without rejection

Immunosuppression reduced – Prednisone 5 mg , Tacro goal 8-10, MMF 720 bid



### 5/■/24 – ID follow up

No fevers but severe night sweats

Aches in lower legs especially after walking (hips down)

Non focal exam

CBC/CMP: wnl, CMV/ EBV Quant PCR neg, BC neg

Pt stopped metformin and felt better, statins changed by cardio



### 6/■/24

Reports not well

CT chest, abdomen and pelvis unremarkable

TSH / testosterone: wnl



**6/■/24**

New rash in various areas of the body for the past 10 days

Painful but not itchy

Ongoing pain in the RLE, worse in upper leg/ thigh

Papule disruption with bleed- sent for studies

**Micro**

3+ PMN. Bacterial Cultures: No growth

Fungal cultures neg

AFB culture neg

Rapid HSV, VZV, CMV PCR: none detected



**7/■/24 - ED visit**

Persistent fevers, Temp 102

HR 115, RR: 20 Sat : 98% RA, BP 130/80

WBC 10.4, cr 1.7

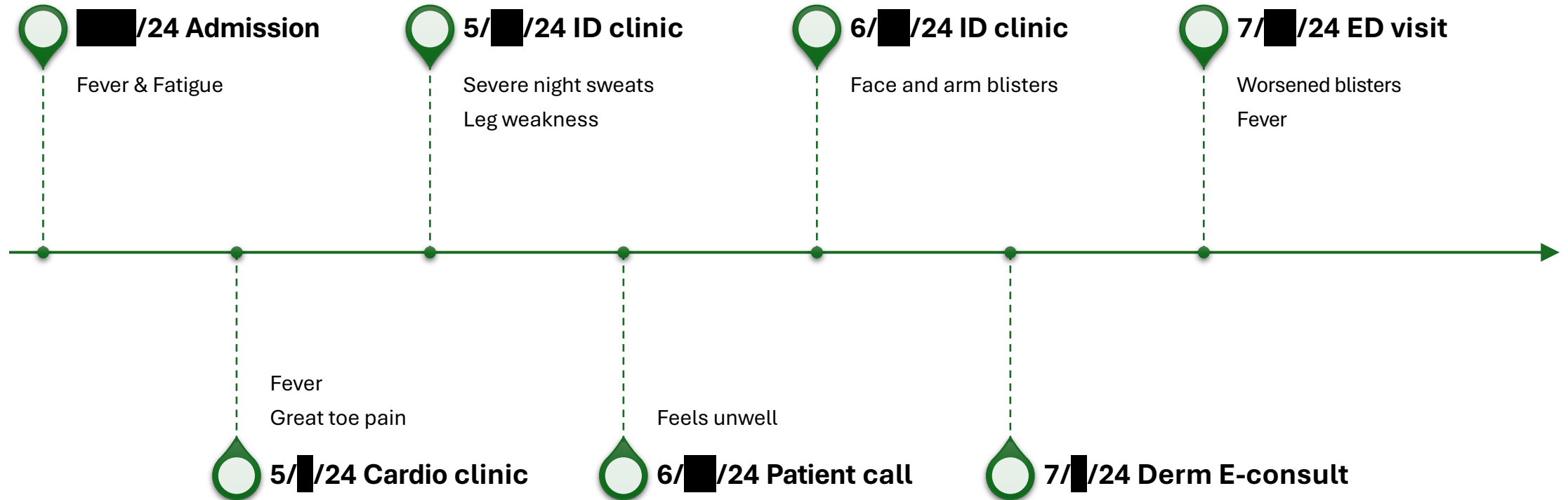
Worsening skin lesions, worse right hip and thigh pain

Small, smooth papules to purple large pedunculated nodules on scalp, face, neck, upper thorax, upper B/L extremities

No oral or mucosal lesions

Seen by dermatologist in ED who performed biopsies for H&E and tissue cultures

# Timeline





Small, smooth  
papules to purple  
large pedunculated  
nodules on scalp,  
face, neck, upper  
thorax, upper B/L  
extremities



# Diagnosis?

<input type="checkbox"/>	A) Disseminated VZV	<input type="text"/>
<input type="checkbox"/>	B) Pyogenic granuloma	<input type="text"/>
<input type="checkbox"/>	C) Kaposi Sarcoma	<input type="text"/>
<input type="checkbox"/>	D) Bacillary angiomatosis	<input type="text"/>
<input type="checkbox"/>	E) Disseminated fungal infection	<input type="text"/>
<input type="checkbox"/>	F) Molluscum contagiosum	<input type="text"/>

# Micro/Tissue pathology

Punch biopsy :

**Bacterial PCR (+) Bartonella quintana in derm biopsy**

Pathology :

Skin, left neck, punch biopsy:

Nodular dermal-based vascular proliferation with neutrophilic inflammation, see comment

Comment:

The detection of Bartonella by PCR is noted and the morphologic features in conjunction with this finding are compatible with bacillary angiomatosis. Clinical correlation is necessary.

Test	Result
Warthin-Starry	Rare bacillary structures present.
Periodic Acid Schiff (PAS) for Fungus	Negative for fungal organisms.
Gomori's Methenamine Silver	Negative for fungal organisms.
Acid Fast Bacteria	Negative for acid fast organisms.
Test	Result
HHV8 (Human Herpes Virus 8) (13B10)	Negative

Ref Range & Units	
Bartonella PCR: Detection, 16S rDNA	Detected !
NDET	
Bartonella PCR: Identification, 16S rDNA	Bartonella quintana
Bartonella PCR: Detection, ribC	Detected !
NDET	
Bartonella PCR: Identification, ribC	Bartonella quintana
Bartonella PCR: Specimen Description	Skin Biopsy

## Serologies :

### Bartonella Antibodies:

- Bartonella quintana IgG Antibody  
<1:128 titer
- Bartonella quintana Ig M Antibody  
<1:20 titer
- Bartonella henselae IgG Antibody  
1:256 titer
- Bartonella henselae IG M antibody  
<1:20 titer

## MRI Right hip w contrast :

Interfascial and intramuscular fluid signal throughout the anterior compartment of the right thigh. Findings could reflect **myositis** in the setting of suspected Bartonella infection

No findings to suggest osteomyelitis or septic arthritis

Echocardiogram with no valvular lesions

EM biopsies without rejection

# Diagnostic Challenges and Limitations

Often a combination of all used to prove diagnosis

## **Molecular tests :**

- Blood or tissue PCR has become the reliable method, speciation possible
- High specificity

## **Serological tests :**

- SOT patients have impaired immune response and delayed antibody response may lead to false negatives  
Serial titers needed
- False positives can be due to cross reactivity with other Bartonella species, Rickettsia, Coxiella, Chlamydia, Toxoplasma antibodies etc.
- Low sensitivity and specificity

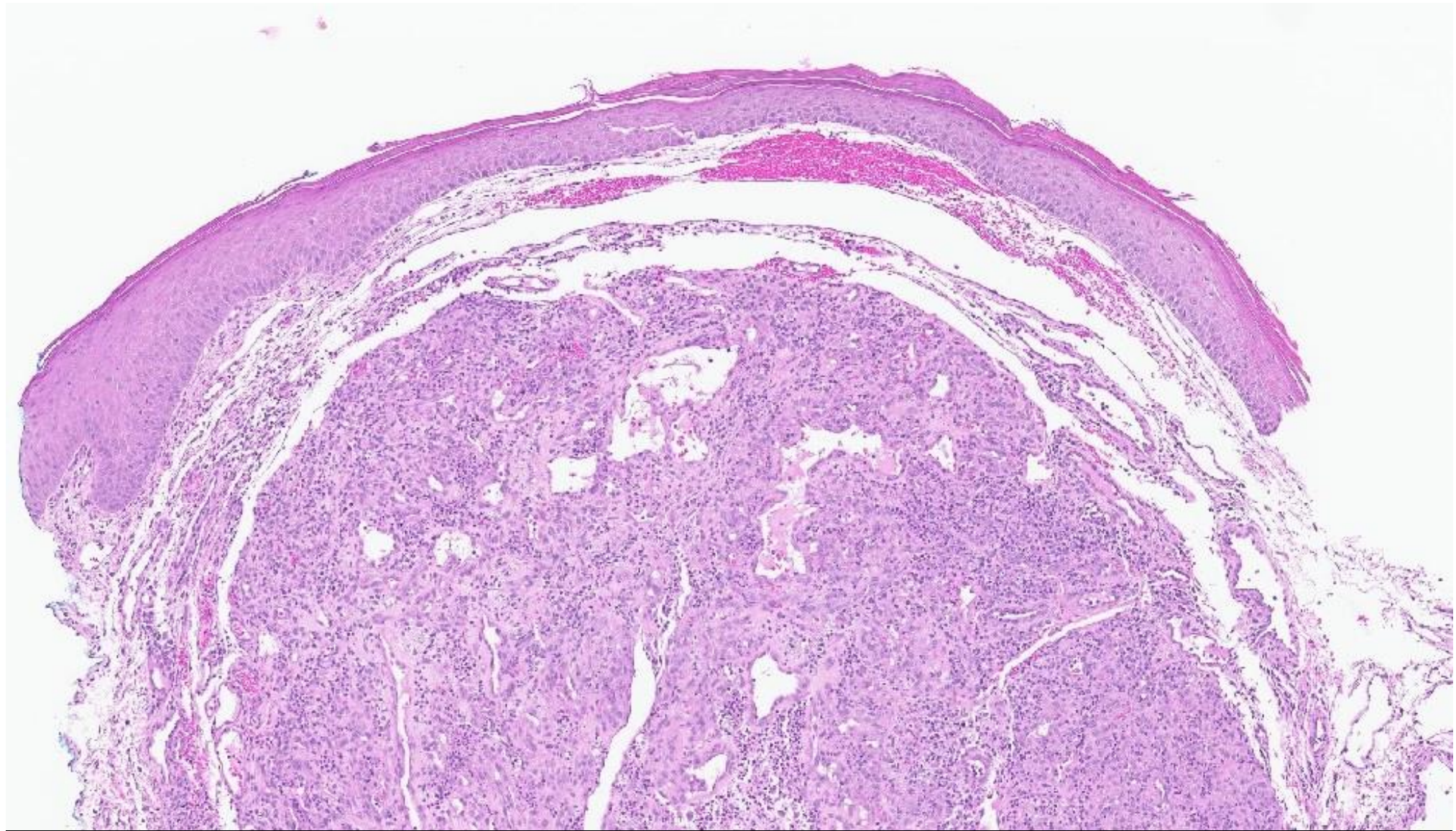
## **Blood culture :**

- Bartonella is challenging to grow as slow doubling time of 21 hours and require special conditions
- Culture should be held for a minimum of 14 days, longer often 4-6 weeks

## **Tissue pathology :**

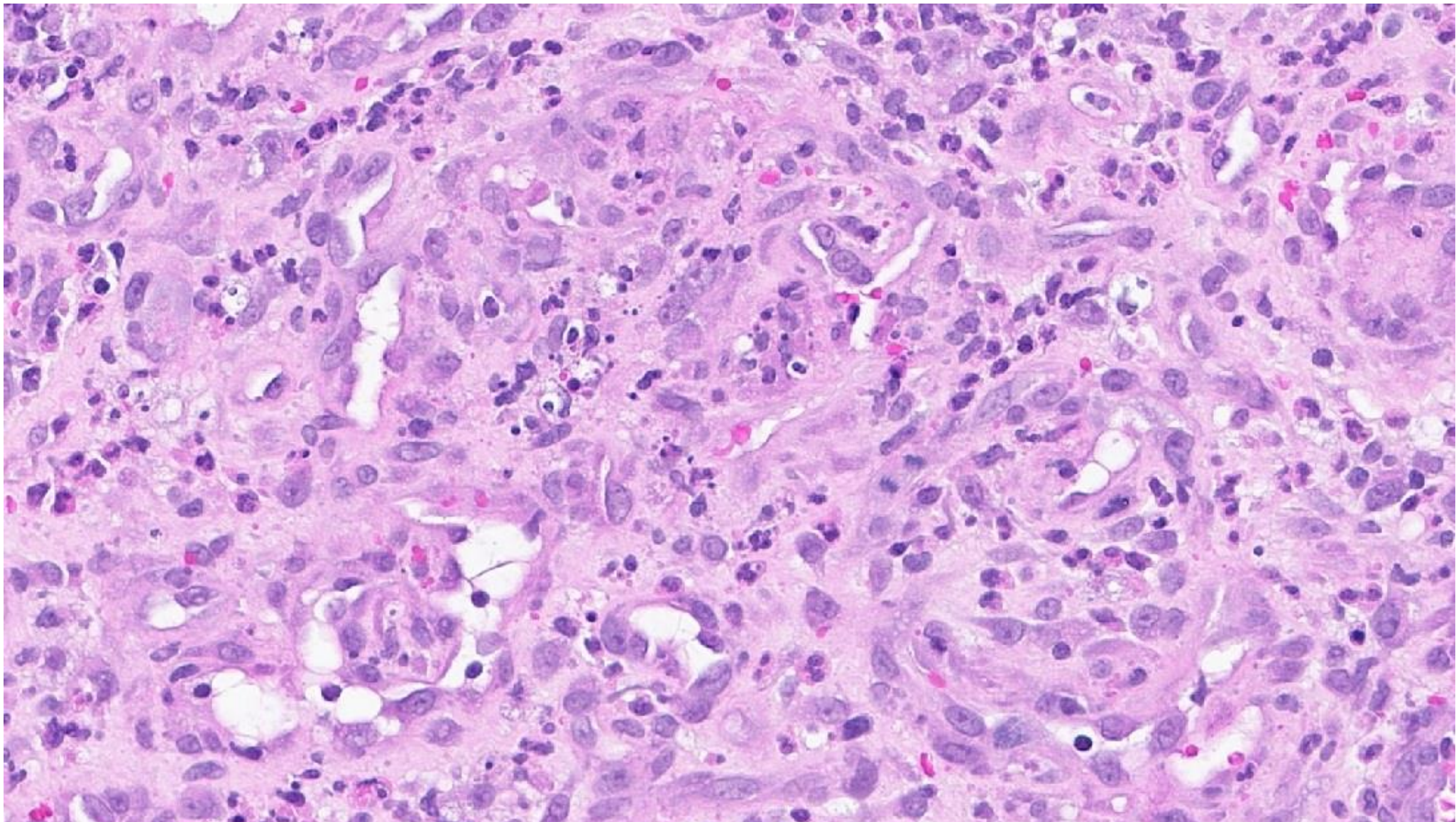
- Staining with Warthin Starry can help visualize the bacteria





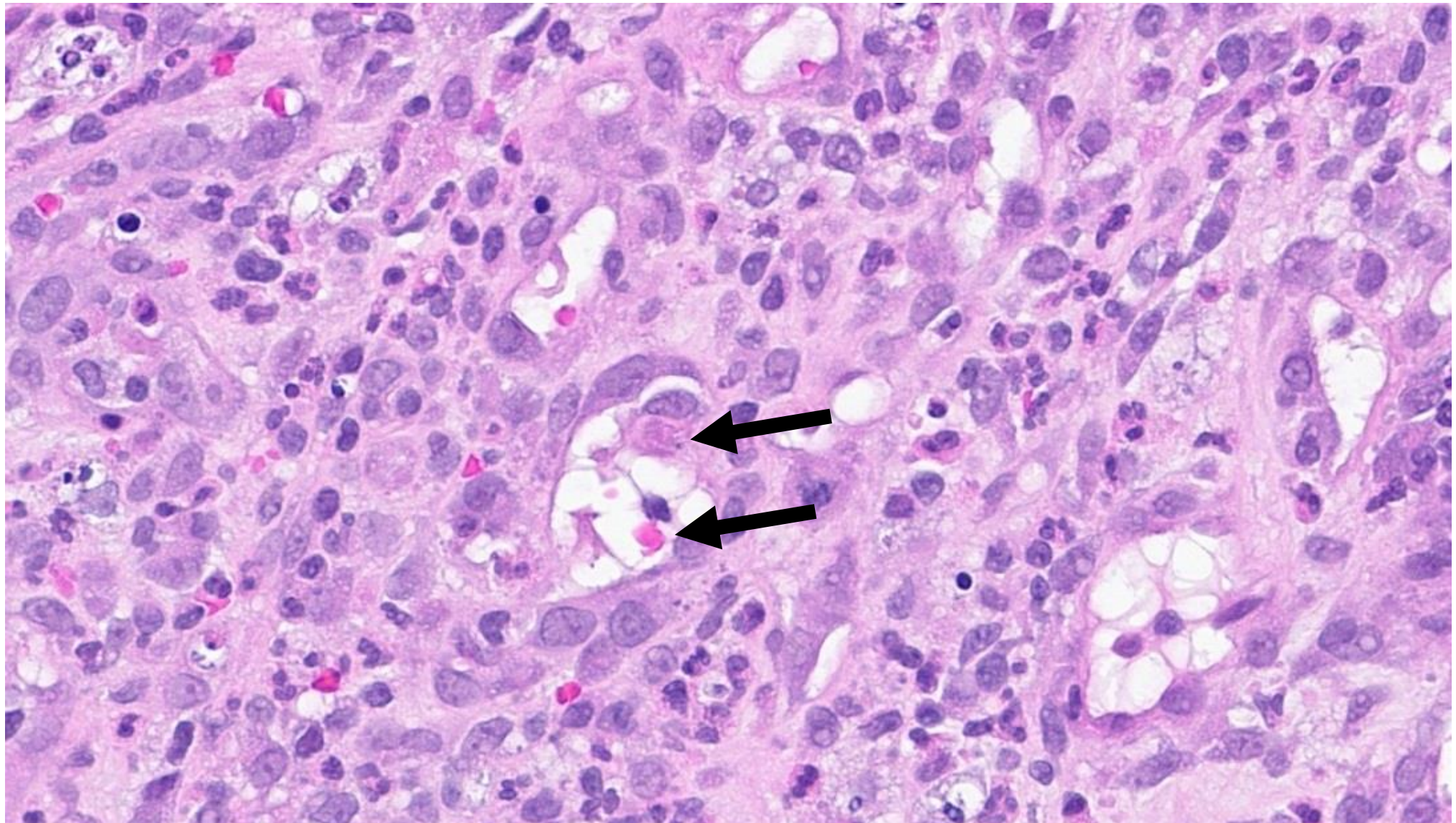
**Low power view showing a dermal nodule comprised of increased capillaries & admixed inflammation.**





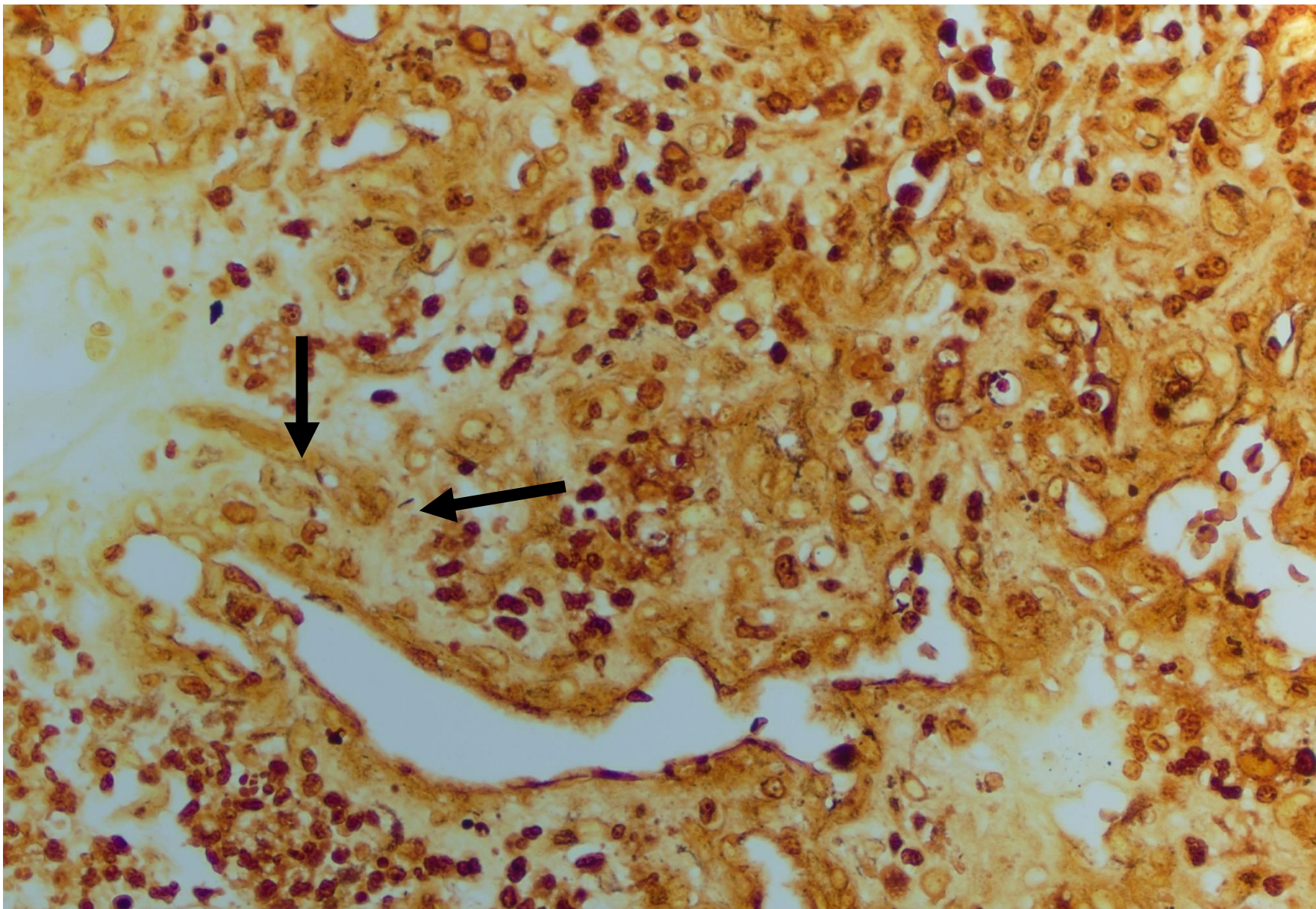
**High power view showing capillary proliferation & perivascular neutrophils**





**Arrows show clumps of amphophilic material – these may be aggregates of degenerating bacteria**





**Warthin-Starry stain highlights rare bacillary structures.**

# Bartonella

- Facultative intracellular, gram-negative bacteria belonging to Proteobacteria family
- Zoonotic infection with global implication and now with reemergence
- 45 species now identified, human infections caused by 3 common species

## **Bartonella Bacilliformis**

Carrion's disease with acute phase called "oroja fever" and a late phase "verruca peruana"

Sandfly Vector



## **Bartonella Quintana**

**Bacillary angiomatosis**, Trench fever, Bacteremia, culture negative endocarditis

Body louse Vector



## **Bartonella Henselae**

**Bacillary angiomatosis**, cat scratch disease, culture negative endocarditis, Bacillary Peliosis etc.

Cat flea Vector





# Bacillary angiomatosis

- Angio proliferative disease caused by **Bartonella quintana ( BQ)** and **Bartonella henselae (BH)**
- Commonly involves the skin, lymph node but can occur in GI/respiratory mucosa, bone, organs - spleen, liver, brain
- Bacillary peliosis of the liver or spleen is caused exclusively by B henselae
- Skin rash ranges from papules to nodules, pinpoint to 10 cm sizes, purple, violaceous, bright red color, can be single to many hundred lesions . Mucosal lesions can occur, but rare for palms and soles
- Previously BA was described mostly in HIV infected patients with very low CD4 <100
- Now associated with drug induced immunosuppression especially in organ transplant recipients, malignancies, rarely reported in immune competent hosts



# Epidemiology of B quintana

- BQ is transmitted via feces of an infected body louse (*Pediculus humanus corporis*).
- In 1990s, BQ was noted to cause various clinical diseases in PEH, who did not have HIV or immunodeficiency.
- BQ seropositivity documented in PEH in geographically diverse urban areas in US as well as in Europe, Canada, “urban trench fever”
- Studies linked BQ with alcoholism, lice infestations, homelessness
- BQ positivity rates among person experiencing homelessness (PEH) 5% to 15%
- Independent risk factors: homelessness > 1 year, age > 40 years, alcoholism, IV drug use
- 17-33% of people with *Pediculus corporis* will be affected by B quintana
- In the US *Bartonella quintana* infection occurs almost exclusively in PEH (CDC)
- Humans are the primary reservoir for this bacterium



# Bacillary angiomatosis in SOT patients

**BA is an uncommon presentation of Bartonella infection and even rare in SOT recipients**

A. Is this BA possibly from primary recipient exposure?

B. Is this donor derived infection? We hypothesize so

## **Donor Information (UNOS) for epidemiological risk factors**

- Donor was found down unresponsive in homeless camp
- Donor experienced homelessness and malnutrition for years
- Prior history of incarceration and psychiatric illness
- Unknown information about sex preferences, positive substance use history
- Prior history of heavy drinking and smoking
- No clear history of lice infestation

## Early post-transplant cutaneous bacillary angiomatosis in a kidney recipient: Case report and review of the literature

Jose A Morillas , Mohamed Hassanein, Bushra Syed , Aimen Liaqat , Wilma Bergfeld , Luis A Sardiña , Richard Fatica , Jessica Lum

- 1990-2020 14 total cases of BA/BP reported in adult SOT literature
- Eight cases were in kidney transplant recipients
- Median time to presentation was 11 months
- Many had a history of exposure to pets (mostly cats), and no cases were known to be donor derived
- Recipients presented with erythematous skin nodules that were associated with systemic symptoms. Some with splenomegaly and lymph node enlargement. Two cases with HLH
- Skin biopsy showed a pattern suggestive of BA in all patients except one, who had a lymph node biopsy with BA
- special stains (WSS), serologies and tissue PCR were used to confirm diagnosis. **Most of the cases had B henselae**
- Most patients had reduction of IS and received antibiotic treatment for a median of 3.5 months
- All patients achieved initial cure with one relapse

# Bacillary angiomatosis in the literature of adult solid organ transplant

Author	Gender/ age	Graft	Time after Tx	Source	IS	Skin lesions	Associated features
Cline <sup>10</sup>	M/24	Kidney	12 m	Cat	MMF, CyS, Prednisone	Erythematous, raised nodule Left nipple	Fever, splenomegaly
Patel <sup>2</sup>	F/26	Kidney	11 m	Cats/Dogs (Veterinarian assistant)	MMF, CyS, Prednisone. Steroid bolus 6 weeks earlier.	Erythematous, nodular lesion on distal left index finger	Fevers, sweats, myalgias, anorexia, weight loss, axillary LAD, pancytopenia
Bonatti <sup>5</sup>	M/51	Liver	5 m	Kitten	MMF, Tacro	Erythematous, nodular lesions (2) left knee	Fever, left inguinal LAD, hepatitis
Moulin <sup>7</sup>	M/58	Kidney	30 m	Trauma with branch. No cat contact	MMF, CyS, Prednisone	Scalp nodule	Fever, LAD, weight loss
Moulin <sup>7</sup>	M/60	Kidney	34 m	Cats	MMF, Tacro, Prednisone	Penile shaft nodule	Fever, night sweats, splenomegaly, LAD, HLH
Grabas <sup>11</sup>	M/56	Kidney	24 m	NA	MMF, CyS, Prednisone	Erythematous nodular lesions (3) in left hand	Fever, HLH
Orsag <sup>8</sup>	F/43	Kidney	4 m	Dog breeding. No cat contact	MMF, Tacro, Prednisone	Multiple nodules	Fever
Nadimi <sup>12</sup>	F/68	Heart	NA	NA	MMF, CyS, Prednisone	Multiple red papules	Fever
Helleberg <sup>13</sup>	M/50	Heart(9y prior)/ Kidney	7 m	No bites or scratches. Visited mother who had cat and dog	NA	Multiple red nodules (palms, arms, legs, trunk, and face)	Fatigue, splenomegaly
Brzewski <sup>14</sup>	M/65	Kidney	5 m	Several cats 1m prior to disease	MMF, Tacro, Prednisone	Numerous nodular violaceous lesions	Fever myalgias splenomegaly multiple LAD (mediastinum)
Present case	M/67	Kidney	1 m	Donor-derived?	MMF, Tacro, Prednisone	Multiple (arms, legs, abdomen, scalp, oral mucosa)	Fever, night sweats, fatigue, poor appetite, weight loss

# Bacillary angiomatosis in the literature of adult solid organ transplant

Histologic findings	PCR	Serologies	Treatment	Duration	Outcomes
Skin: BA. WSS + Lung, bone marrow: granulomas	Not done	Not done	Erythromycin. Temporary cessation of IS	6 m	Cured
No skin biopsy Lymph node: BA. WSS +	Not done	BH/BQ IgG - initially. 3 w later BH/BQ IgG >1:1024	Levofloxacin. MMF stopped	unclear	Cured
Skin: BA. WSS not performed Granulomatous hepatitis and lymphadenitis	Skin: Not done Lymph node: -	BH IgG: 1:256 BQ IgG: 1:512	Azithromycin	2 m	Cured
Skin: BA. WSS+	Skin: BH	BH IgG: 1:200 BQ IgG: 1:400	Clarithromycin	3 m	Cured
Skin: BA. WSS not done Bone marrow: HLH	Skin: BH LN: BH	BH/BQ IgG -	Ceftriaxone +steroids (HLH). MMF stopped.	6 w	Relapsed 2m later. 3 m of erythromycin
Skin: BA. WSS+ Bone marrow: HLH	Skin: BH	Not done	Ciprofloxacin IV IG MMF stopped CyS decreased	unclear	Cured
Skin: BA. WSS+	Skin: BQ	BH/BQ IgG -initially, 4 w later BH/BQ IgG 1:64	Doxycycline →Clarithromycin (because of persistent skin lesions)	6 m (3 m → 3 m)	Cured
Skin: BA. WSS-	Not done	BH IgG 1:256 BQ IgG 1:1024	Doxycycline	4 m	Cured
Skin: BA WSS not done	Skin: BH	BH IgG: 1:8000	Doxycycline	4 m	Cured
Skin: BA. WSS+ Mediastinal lymph node: inflammatory reaction. WWS not performed	Not done	Not done	Doxycycline	3 m	Cured
Skin: BA. WSS+	Skin:- Blood: + ( <i>Bartonella</i> spp.)	BH/BQ IgG - initially, 8w later BH IgG: 1:256 BQ IgG: 1:128	Doxycycline MMF decreased	1 y	Cured

Open Forum Infectious Disease – 2024

## **Donor-Derived *Bartonella quintana* Infection in Solid Organ Transplantation: An Emerging Public Health Issue With Diagnostic Challenges**

Carl Boodman, Oscar Fernandez Garcia, Dima Kabbani, Armelle Perez, Cortes Villalobos , Amy Beeson, Grace E Marx, Johan van Griensven, Karen Doucette

- In October 2023, an outbreak donor-derived *B. quintana* infection was reported in Alberta, Canada
- 5 cases of BQ infection from 3 deceased donors who experienced homelessness
- Recipients presented with BA, fever, or rash 4 to 10 months post transplantation
- Retrospective testing of archived donor serum revealed positive serologies for *B. quintana*
- In US, 2 kidney transplant recipients were infected with *B. quintana* derived from a common donor experiencing homelessness
- One recipient was diagnosed with hepatic bacillary angiomatosis and vertebral osteomyelitis; tissue PCR +ve
- Second recipient active screening identified endocarditis with positive serology and Blood PCR
- Residual tissue samples from the deceased donor tested positive for *B. quintana* by molecular methods
- Previously, only 1 confirmed case of BQ/BA disease had been reported in a transplant recipient in Czech republic

# Homelessness and Organ Donor–Derived *Bartonella quintana* Infection

Rachel Henderson, Emily Mosites, Jane E. Koehler, Carl Boodman, and Grace E. Marx

- Homelessness is increasing since 2016. PEH higher in men than women, proportion of youth higher, often marginalized, minority group
- Lack of access to basic services results in inconsistent showering, laundering, creating risk of body lice infestation & higher *B. quintana* infection
- Leading cause of death in PEH is drug overdose, PEH can become organ donors
- Increase in transplantation of organs from donors who died from drug overdose
- Availability of direct-acting antivirals for Hep-C facilitating increase in transplant of organs due to drug overdoses
- Housing status rarely included in transplantation questionnaires
- On going ethical question whether PEH should be organ donors given not considered for receipt of transplant organs



# Treatment Options?

A) Azithromycin

B) Doxycycline

C) Doxycycline + Rifampin

D) Erythromycin

E) Azithromycin + Rifampin

# Treatment

- Started on Doxycycline 100 mg bid
- Developed Jarisch Herxheimer reaction 24 hrs after the start
- Overall improving, lesions mostly resolved 11 months into treatment
- Other drugs used for BA- Macrolide/Rifampin/combo
- Duration depends on severity and immunosuppression
- No clear length of Rx, average of 3 –12 months

## Serology follow up as 10/24

### Bartonella Antibody Panel (Sendout)

Status: Final result   Dx: Heart transplant status (HCC)

Test Result Released: Yes (seen)

### 0 Result Notes

Component	7 mo ago (10/22/24)	10 mo ago (7/16/24)	10 mo ago (7/11/24)
Ref Range & Units (hover)			
Bartonella henselae IgG Antibody	1:4,096	1:1,024 <sup>CM</sup>	1:256 <sup>CM</sup>
Comment: Results suggest recent infection.			
Bartonella henselae IgM Antibody	<1:20	<1:20	<1:20
Bartonella quintana IgG Antibody	<1:128	<1:128	<1:128
Bartonella quintana IgM Antibody	<1:20	<1:20 <sup>CM</sup>	<1:20 <sup>CM</sup>
Comment: (NOTE)			



Images from 8/24

# Key Takeaways

- Keep high index of suspicion for Bartonella quintana donor derived infection in SOT recipients presenting with unexplained fever symptoms or skin rashes
- Review donor history for housing instability, high risk behaviors like substance use or alcohol use disorder and overcrowding risk
- An early diagnosis may require a combination of tests
- Retrospective testing of donor and recipient's serum should be considered to evaluate for any possible donor transmission if no clear exposures were present and if BA present early post-transplant
- Advocate for Donor Screening and monitoring of recipients
- Preventive Public Health Measures and Policy changes

Update – Bartonella PCR done a year later from donor serum by UW research lab was negative

# Thank You!