



# Seronegative Relapse of Brucellosis in the Central Nervous System

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## Background and Aims

- Brucellosis: the most common zoonotic infection in the world
- High risk areas: Mediterranean Basin, Eastern Europe, Middle East
- Clinical presentation: heterogenous
- CNS involvement: *Neurobrucellosis*, 0,5 to 25%<sup>1</sup>
  - a high prevalence in endemic areas
  - lack of established criteria for a diagnosis<sup>1</sup>

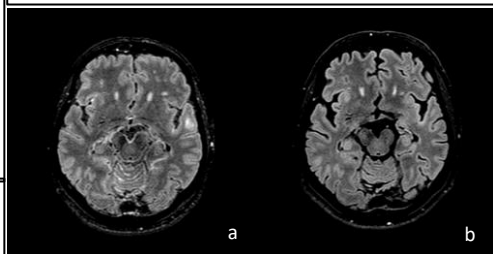
We present a patient with a seronegative relapse of brucellosis, confined in the CNS, as revealed by Brucella IgG ELISA and 16S rRNA sequencing

## Case presentation

- 60-year-old man, farmer, history of systematic brucellosis
- High fever, headache and agitation
- Serum agglutination test, anti-Brucella IgG ELISA: negative
- CSF lymphocytosis, low glucose. Culture negative
- Ceftriaxone, ampicillin, acyclovir: initial remission
- Relapse: ceftriaxone and acyclovir reinitiated → improvement
- Lymphocytic meningitis persisted

## Results I

- Brain MRI severe meningitis and non specific subcortical lesions
- CSF oligoclonal bands positive
- CSF agglutination tests, CSF IgG ELISA positive for Brucella.
- CSF PCR for *Brucella* negative
- 16S rRNA sequencing *Brucella spp* positive



**Figure.** Contrast-enhanced 3D Flair sequence showing the robust enhancement of the meninges and non specific lesions at presentation (a), compared to a remarkable improvement in the one year follow up (b).

## Results II

- Treatment: Ceftriaxone, Doxycycline, Rifampicin and Dexamethasone
  - initial worsening: tremor, loss of balance, hearing loss and diplopia
  - clinical remission after 1 month
- Return home: per os regimen: cotrimoxazole 2880mg/day + rifampicin 900mg/day
  - relapse of lymphocytosis in the CSF (5<sup>th</sup> – 9<sup>th</sup> month of treatment)
- Readmission, ceftriaxone 4gr/day
  - Laboratory remission after ten months of treatment

CSF Parameters (normal range)	WBC/mm <sup>3</sup> (0-8/mm <sup>3</sup> )	Protein (mg/dl) (15-60 mg/dl)	Glucose (mg/dl) (40-70mg/dl)	Oligoclonal bands	Brucella IgG ELISA index (<1,09)
Initial puncture	315	187	39	T2	CSF: 5,06 Serum: <1,09
1st month	180	197	27	T4	CSF: 4,7 Serum: 4,4
2nd month	297	73	71	T2	
4th month	23	114	42	T2	
5th month	82	132	43	T2	CSF: 4,0 Serum: 3,3
9th month	58	184	40	T2	CSF: 5,1 Serum: 4,2
9½ month	18	173	43	T2	
10th month	9	145	47	T2	
13th month	9	81	48	T2	CSF: 4,4 Serum: 3,6

**Table.** CSF parameters during treatment

## Summary

- Relapse of systematic brucellosis, confined in the CNS
  - Severe progression with marked disability
- Surprisingly<sup>2</sup>, *ceftriaxone* was the most effective component in our therapeutic regimen

## Conclusions

- Neurobrucellosis: variety of clinical syndromes
  - Should be considered in highly endemic areas<sup>1</sup>
- Establishing a diagnosis is challenging
- CSF oligoclonal bands, agglutination test in the CSF
  - possible role in the diagnostic criteria
- Though under debate, corticosteroids and prolonged use of ceftriaxone seem to be crucial<sup>2</sup>

## References

1. Dreshaj S et al. Clinical Manifestations in 82 Neurobrucellosis Patients from Kosovo. Mater Sociomed 2016
2. Pappas G et al. Treatment of neurobrucellosis: what is known and what remains to be answered. Expert Rev Anti Infect Ther 2007