Published in final edited form as:

Schizophr Res. 2015 October ; 168(1-2): 579–580. doi:10.1016/j.schres.2015.06.029.

Undiagnosed Lyme disease in adults with schizophrenia

Maju Mathew Koola,

Clinical Research Program, Sheppard Pratt Health System, Baltimore, MD, USA

Kelli M. Sullivan,

Maryland Psychiatric Research Center, University of Maryland School of Medicine, Baltimore, MD, USA

Amber K. Earl,

Maryland Psychiatric Research Center, University of Maryland School of Medicine, Baltimore, MD, USA

Stephanie M. Feldman,

Maryland Psychiatric Research Center, University of Maryland School of Medicine, Baltimore, MD, USA

Charles Richardson,

Maryland Psychiatric Research Center, University of Maryland School of Medicine, Baltimore, MD, USA. Spring Grove Hospital Center, Baltimore, MD USA

Gopal R. Vyas,

Maryland Psychiatric Research Center, University of Maryland School of Medicine, Baltimore, MD, USA. Spring Grove Hospital Center, Baltimore, MD USA

Heidi J. Wehring, and

Maryland Psychiatric Research Center, University of Maryland School of Medicine, Baltimore, MD, USA

Deanna L. Kelly*

Maryland Psychiatric Research Center, University of Maryland School of Medicine, Baltimore, MD, USA

Keywords

Schizophrenia; Lyme disease; Lyme titer; Infection; Inflammation

*Corresponding author at: Maryland Psychiatric Research Center, University of Maryland School of Medicine, PO Box 21247, Baltimore, MD 21228, USA., dkelly@mprc.umaryland.edu (D. L. Kelly).

Contributors

Kelly designed the study and oversaw research procedures. Sullivan worked with all research participants and oversaw data collection. Koola and Kelly wrote the manuscript. Kelly, Earl, Feldman, Richardson, Sullivan, Vyas and Wehring making significant intellectual contributions in the study procedures and manuscript preparation. All authors approved the final version of the manuscript.

Conflict of interest

Kelly served on the advisory board for Lundbeck and XOMA. Other authors declare no conflict of interest.

Dear Editors

Lyme disease (LD) is the world's leading tick borne infection caused by the spirochete, *Borrelia burgdorferi* (Bb). This infection is a global health concern and is associated with numerous cardiologic, dermatologic, rheumatologic neurologic, and psychiatric manifestations (Bratton et al., 2008). Only a few epidemiologic studies have evaluated the frequency of antibodies to Bb in psychiatric patients; one study found only 1/517 (0.2%) of all adult psychiatric patients had Lyme titer seropositivity (Nadelman et al., 1997) and the other larger study found that 322/926 (35%) of psychiatric inpatients had seropositivity to antibodies to Bb (Hajek et al., 2002). While a few cases have been reported (Hess et al., 1999; Mattingley and Koola, 2015; Roelcke et al., 1992) no studies to our knowledge have examined Lyme disease prevalence in patients with psychosis or schizophrenia or from a population of those being treated in the outpatient setting where infection may be more likely. It is interesting to note that seasonal (March to April) distribution of increased LD infection risk corresponds with the birth excess for schizophrenia in the winter months (Tochigi et al., 2004). Also, areas of the world non-endemic for LD have a low prevalence of schizophrenia (Fritzsche, 2002).

We examined the presence of positive Lyme titers during routine screening in 52 potential research candidates (outpatient and inpatient) in Baltimore, MD. All were between the ages of 18 and 64 years and were on a stable dose of clozapine for at least six months. The Lyme titer was performed by Lab Corp ® by Enzyme immunoassay immuno-globulin IgG/IgM and confirmed with Lyme antibody IgM by Western blot (positivity > 1.09). Two people (3.8%) had positive titers confirmed by Western blot who were then referred for treatment and care. In both cases, it is unknown how long they had seropositivity but both were identified in the summer months. Both were treated by their general practitioner with doxycycline (100 mg twice daily) one for four weeks and the other one for eight weeks. We evaluated psychiatric symptoms, serum clozapine levels and physical symptoms at the time of the noted LD infection and at approximately 10 weeks later using clinical rating scales for symptomatology. Above we present details on both patients before and after doxycycline treatment in Table 1.

It is notable that the detection of LD may present a particular diagnostic challenge to practitioners treating individuals who are comorbidly diagnosed with schizophrenia as symptoms of LD may mimic or exacerbate psychiatric symptoms. Both these LD cases were undiagnosed, unsuspected and had never been treated previously. Psychiatric symptoms may improve following routine care; we noted improvements, as in the first case, with global psychopathology and mainly anxiety and depressive symptoms and, as in the second case, primarily negative symptoms. We also noted some improvements in somatic complaints (sedation and malaise in both and weight loss, dizziness and diarrhea in one) but no changes were seen in psychotic symptoms of the illness (data not shown). It remains unknown how long the infection was present prior to detection or if inflammatory biomarkers were abnormal. We do note that clozapine levels decreased during doxycycline treatment, despite no dose change. It is well known that clozapine levels are elevated during infection (de Leon, 2004) and this may explain why they were higher at the time of infection and before antibiotic treatment.

In conclusion, current data illustrates the important role that healthcare practitioners have in emphasizing LD as a potential health concern, as well as the opportunity to promote strategies to prevent contraction. Clinicians working in the endemic, high-risk areas should consider LD in the differential diagnosis of any atypical psychiatric presentation. Further research is warranted to investigate the differential diagnosis of LD and schizophrenia and examine the mechanisms and treatment of LD in mental illness.

Acknowledgments

Role of funding source

This study was funded by the NIMH grant R21MH091184-01A1 (Kelly, PI). Koola was supported (2010-12) by the NIMH funded T32 grant MH067533-07 (Carpenter, PI).

This data was presented at the 14th International Congress on Schizophrenia Research meeting, Orlando, FL, USA April 21–25, 2013.

References

- Bratton RL, Whiteside JW, Hovan MJ, Engle RL, Edwards FD. Diagnosis and treatment of Lyme disease. *Mayo Clin Proc.* 2008; 83(5):566–571. [PubMed: 18452688]
- de Leon J. Respiratory infections rather than antibiotics may increase clozapine levels: a critical review of the literature. *J Clin Psychiatry.* 2004; 65(8):1144–1145. [PubMed: 15323602]
- Fritzsche M. Seasonal correlation of sporadic schizophrenia to Ixodes ticks and Lyme borreliosis. *Int J Health Geogr.* 2002; 1(1):2. [PubMed: 12453316]
- Hajek T, Paskova B, Janovska D, Bahbouh R, Hajek P, Libiger J, Hoschl C. Higher prevalence of antibodies to *Borrelia burgdorferi* in psychiatric patients than in healthy subjects. *Am J Psychiatry.* 2002; 159(2):297–301. [PubMed: 11823274]
- Hess A, Buchmann J, Zettl UK, Henschel S, Schlaefke D, Grau G, Benecke R. *Borrelia burgdorferi* central nervous system infection presenting as an organic schizophrenialike disorder. *Biol Psychiatry.* 1999; 45(6):795. [PubMed: 10188012]
- Mattingley D, Koola MM. Association of Lyme disease and schizoaffective disorder, bipolar type: is it inflammation mediated? *Ind J Psychol Med.* 2015; 37(2):243–246.
- Nadelman RB, Herman E, Wormser GP. Screening for Lyme disease in hospitalized psychiatric patients: prospective serosurvey in an endemic area. *Mt Sinai J Med.* 1997; 64(6):409–412. (New York). [PubMed: 9364837]
- Roelcke U, Barnett W, Wilder-Smith E, Sigmund D, Hacke W. Untreated neuroborreliosis: Bannwarth's syndrome evolving into acute schizophrenia-like psychosis. A case report. *J Neurol.* 1992; 239(3):129–131. [PubMed: 1573415]
- Tochigi M, Okazaki Y, Kato N, Sasaki T. What causes seasonality of birth in schizophrenia? *Neurosci Res.* 2004; 48(1):1–11. [PubMed: 14687876]

Table 1

Participant characteristics diagnosed with Lyme disease (LD) and schizophrenia.

	Lyme disease case 1	Lyme disease case 2		
Age (years)	27	55		
Race	White/American Indian	White		
Sex	Male	Male		
Diagnosis	Schizophrenia	Schizoaffective disorder, bipolar type		
Clozapine dose (oral tablet)	500 mg bedtime	325 mg bedtime		
Other medications (remained unchanged during entire observation period)	Risperidone 2 mg bedtime Sertraline 100 mg morning	Valproate 1000 mg twice daily Citalopram 20 mg morning		
Medical history	Hay allergy and occasional pain on urination	Arthritis		
Presentation and symptoms	At time of LD diagnosis	10-week follow-up	At time of LD diagnosis	10-week follow-up
Lyme EIA assay	Positive	Unknown	Positive	Positive
Lyme Ab Western Blot Reflex	5.01	Unknown	6.93	5.75
Clozapine serum levels (ng/ml)				
Clozapine	1093	724	504	210
Norclozapine	691	481	152	79
Total	1724	1205	656	289
Body mass index (kg/m ²)	29.2	28.9	18.3	19.9
Complete Blood Count and Chemistry panel	Within normal limits	Within normal limits	Within normal limits	Within normal limits
Total BPRS (18 item)				
Anxiety/depression	51	36	43	45
Subscale	17	10	16	12
Total CGI	5 (Markedly ill)	4 (Moderately ill)	4	4
Total SANS	20	19	43	38
Global affective flattening	0	1	2	1
Global avolition	4	2	4	3
Global asociality	0	0	4	1
Physical symptoms	Dizziness (mild)	Dizziness (mild)	Headache (mild)	Malaise (mild)
	Sedation (mild)	Hypersalivation (mild)	Sore throat (mild)	Constipation (mild)
	Malaise (mild)		Diarrhea (mild)	Rash (mild)
			Dizziness (moderate)	
			Malaise (moderate)	
			Weight loss (moderate)	
			Mucosal ulcerations (moderate)	
			Hypersalivation (severe)	
			Sedation (severe)	

EIA = enzyme immunoassay; Ab = antibody; BPRS = Brief Psychiatric Rating Scale; SANS = Scale for the Assessment of Negative Symptoms
CGI = Clinical Global Impression, BPRS Anxiety/Depression subscale consists of four items measuring depression, anxiety, guilt and somatic concern.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript