

Obsessive Compulsive Disorder Associated Autoimmune Conditions *Self-Study Answer Kev*

Contributors

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Pre-Assessment Learning

- Mataix-Cols D, Frans E, Pérez-Vigil A, Kuja-Halkola R, Gromark C, Isomura K, Fernández de la Cruz L, Serlachius E, Leckman JF, Crowley JJ, Rück C, Almqvist C, Lichtenstein P, Larsson H. A total-population multigenerational family clustering study of autoimmune diseases in obsessive-compulsive disorder and Tourette's/chronic tic disorders. Molecular Psychiatry (2017) 00, 1–7.
- Gray SM, Bloch MH. Systematic Review of Proinflammatory Cytokines in Obsessive-Compulsive Disorder. Curr Psychiatry Rep. 2012 Jun 1;14(3):220–8.

Clinical Vignette

Marcia H. is a 27-year-old partnered G1P1 of Eastern European Jewish heritage. She has a strong family history of autoimmune disease, with a mother and brother with ulcerative colitis. Marcia was diagnosed with Crohn's disease at age 12 and has had a moderate disease course. Since childhood, she has also exhibited numerous fears and anxieties, with a childhood ritual that involved counting and turning all the objects on her bureau before bed out of fear that her family would come to harm if she did not. Her parents did not seek mental health treatment for her, and over time she was able to pare down the ritual so that by the time she left for college she was merely tapping two objects. In college she considered herself to be a "high-anxiety" person but found that this trait meant she was always prepared for her classes, and she does not feel that it interfered with her functioning. Since giving birth to her first daughter 6 weeks ago, she has been consumed by fear that her husband will come to harm during his commute to work. She frequently follows him in her car to ensure that he arrives safely, although this means she must strap the baby into her car seat and sometimes endure her crying for some time. She always calls her husband to make sure he has arrived at work, and will often call him multiple times (up to 3 or 4) during his forty-minute evening commute to ensure that he is okay. She understands that these fears are not rational. She presents for a psychiatric evaluation at the urging of her husband and of her gastroenterologist, both of whom have reported that her intrusive thoughts and rituals are consuming a considerable portion of her time each day. She is also undergoing a flare of her Crohn's disease in the postpartum, though it was in relative remission during pregnancy.

Use the above vignette and the pre-reading material (additional sources at end) to answer the following questions:

1) Based on the information given here, what is Marcia's most likely psychiatric diagnosis?

Marcia is likely suffering from OCD. Her childhood symptoms may have been OCD as well, so it is unclear whether her OCD is perinatal onset or not. But she has intrusive thoughts (harm to her husband) and compulsions (following him, calling him for reassurance) that interfere with her daily functioning (take up too much time each day).

2) Is the fact that she has Crohn's disease relevant here? Why or why not?

Yes! Autoimmune diseases are more common in those with OCD. One recent study found that individuals with OCD were 43% more likely to have any autoimmune disease (Mataix-Cols et al., 2017). The strongest associations were for:

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- Sjogren's
- Celiac
- Guillan-Barré
- Crohn's
- Hashimoto's
- DM1
- scarlet fever
- ITP
- UC
- MS
- psoriasis

3) Why does the vignette bother to point out that Marcia's mother and brother also have autoimmune diseases?

First-degree relatives of people with OCD are at significantly increased risk of having an autoimmune disease (Mataix-Cols et al., 2017). It may therefore be clinically appropriate to screen for autoimmune disease in patients with OCD and their relatives. See Figure 1 below, from Mataix-Cols et al., 2017.



Figure 1. Sensitivity analyses. Risk (ORs and 95% Cls) of any AD in probands and relatives of probands with OCD (**a**) and TD/CTD (**b**). Analyses exclude any AD among probands as well as OCD or TD/CTD in the relatives (full data available in Supplementary Table 5). Gray shapes indicate probands, red shapes first-degree relatives, green shapes second-degree relatives, and yellow shapes third-degree relatives. AD, autoimmune diseases; Cl, confidence interval; CTD, chronic tic disorder; OCD, obsessive-compulsive disorder; OR, odds ratio; TD, Tourette's disorder.

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4) Marcia's Crohn's was in remission during pregnancy, but has flared in the postpartum. What is the usual pattern for autoimmune diseases during pregnancy?

Most autoimmune diseases (those characterized by Th1 cells) will go into remission during pregnancy. This includes Crohn's as well as rheumatoid arthritis and multiple sclerosis. Some autoimmune diseases, such as lupus, work through different mechanisms and will NOT go into remission in pregnancy. Normal postpartum women experience a rebound of Th1 cells; for women with autoimmune disease, that means a flare of the disease in the postpartum period.

5) Does Marcia's Crohn's flare have anything to do with her OCD symptoms?

Maybe. Previous studies have found associations between obsessive compulsive symptoms and peripheral cytokines including TNF- α (90),IL-6 (89), CCL3, CXCL8, sTNFR1, and sTNFR2 (91), IL-1B (94,96) (Pacheco et al., 2007; Fluitman et al, 2010; Fontenelle et al., 2012; Gray et al., 2012; da Rocha et al., 2008) The pro-inflammatory surge that characterizes the postpartum, and is involved with her Crohn's flare, may also be related to OC symptoms – but the evidence in this area is limited. We don't know whether treating her autoimmune disease will influence the course of her OCD.

6) Can anti-inflammatory treatments help OCD?

Maybe. There is some evidence that supports NSAIDs as an adjunctive antidepressant treatment (Akhonzadeh et al., 2009; Sayyah et al., 2011). We don't yet know much about supplements or alternative anti-inflammatory treatments. Curcumin has been studied (LoPresti et al. 2017), but there is not yet enough evidence to draw conclusions. Omega-3s have been studied in one small trial that did not find an effect (Mischoulon & Freeman, 2013).

7) What about pediatric OCD? How should we think about PANDAS?

Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection (PANDAS) is a controversial hypothesis positing that antibodies directed toward streptococcal bacteria can cross-react with the basal ganglia, causing symptoms of OCD. Some studies have found such autoantibodies and/or brain inflammation in children with PANDAS compared to healthy controls, and some studies have found that immunotherapy has been helpful for OCD symptoms – but other studies have had opposite findings, and most studies have been small with numerous methodological shortcomings. A recent Danish registry study found an increased incidence of any mental disorder, and particularly OCD, after streptococcal infection – but also found significantly increased risks after non-streptococcal infection. The available evidence thus suggests a role for immune activation in the onset of OCD and other mental disorders, but does not specifically support the PANDAS hypothesis (Orlovska et al., 2017).



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