

The Connection between Strep Infections, Obsessive-Compulsive Disorder, and Tourette's Syndrome

I would like to tell you a story about a patient who I'll call Mr. I. Dr. Carol Brebion and I first saw Mr. I. in July 1996, while covering for the consultation-liaison psychiatrist who had been following him, during that psychiatrist's vacation.

Mr. I. is a 43 year old single man, living alone but with sitters 16 hours each day, seven days a week. He pays for the sitters mostly himself, as he gets a disability pension from the National Film Board because of his severe osteoporosis. One of these sitters had described Mr. I. as having a "Howard Hughes syndrome"; that is, Mr. I. had not gone out of his house for the previous 3 years, and during that time had refused to bathe, or even to have the windows opened.

Mr. I. had presented to the ER in May 1996 with a painful and swollen knee. As he refused to have diagnostic tests done, and was also refusing to eat or drink, he was referred to psychiatry. The psychiatrist found him to be competent to refuse, and accordingly Mr. I. was sent home.

Two days later, Mr. I. returned to the ER, this time with a fever. He talked about killing himself, and was again sent to see psychiatry. This time, he was admitted to 4 East, where he stayed for 2 days before being transferred to 7NW for treatment of a pneumonia. After 3 weeks, he was discharged to a private nursing home, Chateau Westmount.

He only lasted 9 days there. Chateau Westmount sent him back to the ER as he was complaining of severe pain, and wasn't eating because he insisted he couldn't swallow. He was again admitted to 7NW to treat dehydration and pneumonia.

I would like to summarize his medical problems at this point:

First, Mr. I. had severe wasting. Although 6 feet tall, he only weighed 87 pounds. This BMI of 13 is felt to be "incompatible with life".

Second, he had severe osteoporosis, thought to be due to malabsorption, but there was no satisfactory explanation.

Third, he had had very high prolactin levels since 1993, over 1500, when the range of normal is from 5 to 15. Again, no good explanation.

Fourth, he had been known to have a total absence of IgA for a number of years, also unexplained.

And finally, he had low testosterone levels, as well as low LH and FSH levels.

On the ward, Mr. I. was a difficult patient, frequently refusing treatments and medications. He had his own sitters in to look after him, would order food to be delivered, and refused to go for imaging studies.

The ward staff also found him peculiar: he looked bizarre with his extremely skinny frame, long hair, and long, matted, and drool-flecked beard. Constantly drooling and spitting up saliva, he would go through 6 boxes of Kleenex per day. He ate with his fingers, and talked in a peculiar, high-pitched voice. His speech was interspersed with a variety of strange sounds: grunts, squeaks, and muffled barks. He also had tics involving his head and eyebrows.

It seemed to Dr. Brebion and I that medicine had given up on him. They felt he had a personality disorder, as well as an eating disorder, and talked about sending him to the Eating Disorders Unit at Douglas Hospital, or just finding a nursing home for him.

In reviewing his chart, Dr. Brebion and I found that Mr. I. had already been seen by 4 different psychiatrists during the previous two months, who had documented many signs and symptoms of both Obsessive-Compulsive Disorder and of Tourette's Syndrome.

The patient was quite aware that he had both: Tourette's had been diagnosed in January 1996 by Dr. Schondorf. Mr. I. had himself figured out that he must have OCD when he developed a handwashing compulsion at the beginning of 1995. He read widely about his various symptoms, and took an extreme interest in trying to understand his medical conditions.

These overhead slides show Mr. I.'s scores and the symptoms he checked off on the Yale-Brown Obsessive-Compulsive Scale.

Dr. Brebion and I took quite an interest in Mr. I. We found that if you took time to sit down and listen carefully to him, you would discover that behind all the disgusting mannerisms and drooling there was an intelligent, articulate person who was genuinely in pain, frightened, and suffering.

He couldn't understand why he wasn't being adequately worked up for his medical problems. His refusal to go for imaging tests was based on fear: fear of the excruciating pain he knew he would suffer from lying on a hard CT scanner table. A well-founded fear, as his near-total absence of body fat meant that his bones, muscles, and skin had no protective padding.

He was also very worried that the movements required to get on and off the table would result in broken bones. Again, a valid concern; he'd had a number of spontaneous fractures, including broken ribs just from coughing, due to his severe osteoporosis.

Our interest was also piqued by medicine's readiness to ascribe Mr. I.'s problems to "supra-tentorial factors", medicalese meaning, "it's all in his head". It was clear to us that he suffered from at least one clearly neurological condition, the

Tourette's, and the documented severity of his various medical conditions made it unlikely that they were psychological in origin.

A prolactin level of over 200 is almost certain to be a prolactin-secreting tumour of the pituitary gland. The fact that an MRI the previous year at the Montreal General Hospital had been read as negative for such a tumour, we felt, was insufficient reason to not investigate further. We thought also that his low testosterone might equally be caused by a pituitary tumour compressing normal pituitary tissue; the low testosterone might help to explain some of the muscle wasting and the osteoporosis.

We felt that we had to advocate for the patient, to have these issues adequately investigated.

We were also fascinated by the co-occurrence of OCD and Tourette's in this man, and the possibility that we had come across an adult form of PANDAS. I'll get back to PANDAS shortly.

In our role as advocates, we convinced Mr. I. to have a CT scan, to which he agreed if the table were well-padded. We also talked medicine into ordering a stat CT scan, before the patient changed his mind. He had the scan done the same day, and it showed a large mass eroding the floor of the sella turcica and protruding into the nasopharynx.

Briefly, Mr. I. had neurosurgery, a partial removal of the mass which proved to be a prolactin-secreting adenoma of the pituitary. Unfortunately, it had invaded normal tissue to such an extent that it could not be entirely removed. Mr. I. continued to take clomipramine and risperidone for the OCD and Tourette's, with some symptomatic improvement. He also accepted injections of testosterone, and was able to gain a little weight before his discharge near the end of October 1996. Dr. Brebion arranged followup for him at the OCD/Tourette's clinic at the Royal Victoria Hospital.

As I promised, let's now look at PANDAS. PANDAS are cute furry bears that live in China. No, seriously, PANDAS is an acronym that stands for Pediatric Auto-immune Neuropsychiatric Disorders Associated with Streptococcus infection. Whew! Took me a week to get that down!

We know that strep infections can have neurological consequences. For example, an untreated strep throat can turn into rheumatic fever, with arthritis involving multiple joints as well as destruction of heart valves. In 10 to 20% of cases of rheumatic fever, a condition called Sydenham's Chorea manifests, usually between 1 to 6 months after the original strep infection.

Sydenham's Chorea patients have muscular weakness, choreiform movements, as well as psychological symptoms which frequently appear before the motor symptoms. The psychological manifestations are obsessive and compulsive symptoms in three quarters of Chorea patients, while one-third will have full-blown OCD.

Moreover, many Chorea patients have movements which strongly resemble tics.

Dr. Susan Swedo and her colleagues at the National Institute of Health were seeing children who presented with sudden onset OCD and/or Tourette's. They were struck by the similarities to some cases of Sydenham's Chorea, especially those children who had had strep throats or other strep infections prior to the onset of OCD or Tourette's.

They studied this phenomenon and have published a number of papers which document the relationship between OCD, Tourette's, and strep, and coined the term PANDAS. They showed that in these children, the severity of OCD and Tourette symptoms increased during times of active strep infection, while antibiotics, or immune modulating treatments such as plasmapheresis or corticosteroids led to symptomatic improvement in both OCD and Tourette symptoms.

They went on to formulate the hypothesis that in certain individuals with a genetic predisposition, the antibodies produced in response to a strep infection cross-react with cells in the basal ganglia structures of the brain. The genetic predisposition is thought to cause these brain cells to have high concentrations of certain molecules on their surfaces. These molecules look similar enough to a streptococcal antigen protein so that the antibodies normally produced during a strep infection, attach themselves to basal ganglia cells using these molecules as hooks. Once attached, they cause local inflammation, which impairs the functioning of these brain regions and thereby cause symptoms of OCD and Tourette's.

In support of this hypothesis are a couple of case studies in which serial MRI scans showing increases and decreases in the volume of basal ganglia structures in patients whose symptoms waxed with acute infection and waned with plasmapheresis treatment.

Other studies show that an antigen found on B lymphocytes, called D18/7, which is structurally similar to one of the strep antigenic proteins, occurs at a very high frequency in PANDAS and Sydenham's Chorea patients, but at very low frequencies in normal controls. D18/7 is thought to be a trait marker for rheumatic fever. These studies suggest that it may also help identify individuals at risk for PANDAS.

I consider the discovery of PANDAS by Dr. Swedo and her colleagues, which has now been replicated by at least one other group, to be a true revolution in psychiatry.

OCD is a relatively common psychiatric illness; it develops in 1 out of every 200 children. That at least some cases of childhood OCD have an infectious etiology is a paradigm shift of the same magnitude as the discovery that Helicobacter Pylori infection causes peptic ulcers.

I'm not a child psychiatrist, so PANDAS might not affect me directly.

To return to Mr. I., he had told us that his OCD and Tourette symptoms had begun rather suddenly in early 1995. During that year, he had had several severe throat infections. He couldn't tell us what the infections were caused by, however. He had also gone to the ER in early 1993 for a sore throat. Recall that his refusal to bathe or to leave the house seems to have started around that time.

This information is tantalizing, but it only suggests the possibility of an adult version of PANDAS.

However, it seems that OCD symptoms begin in childhood in 1/3 to 1/2 of adult OCD cases. So it may be worthwhile to look at our adult patients.

I also work in the Psychogeriatrics Clinic. I have only two patients with OCD in my caseload. In reviewing with them the onset of their symptoms, I found links to strep infections in both cases.

Mrs. L. is a 70 year old married woman, who initially presented to psychogeriatrics with depression and obsessional symptoms. Her depression resolved with sertraline, but her obsessions of having contracted an HIV infection from a toilet seat previously used by an HIV-positive patient remained disabling. Mrs. L. has an artificial heart valve.

On reviewing her case with PANDAS in mind, she first contracted scarlet fever and rheumatic fever at age 10, and again at age 15, being out of school for a year each time. It wasn't until she became a teenager that she became aware that her excessive worrying, her tendency to attach excessive significance to certain events, as "omens", were unusual.

Mr. B., a 68 year old businessman, has had OCD since age 5 or 6. He also has chronic tics. He says that he had a "mild" case of rheumatic fever at age 7 or 8. He was in bed for 3 months, and was convinced that he would never get to age 35. He also recalls scarlet fever in his pre-teen years.

These cases suggest that at least some of our adult OCD cases may be related to strep infection.

Why is this important? Well, we might be able to identify children at risk of developing OCD by looking for the D18/7 marker. Prophylactic penicillin might prevent the occurrence of strep infections, and thereby prevent OCD.

For individuals who are identified as having OCD or Tourette's associated with strep, there are at least four potential treatments: antibiotics, plasmapheresis, corticosteroids, and intravenous immune globulin.

If you have cases of OCD in your practices which seem to be related to strep, is there any interest in getting together to organize a trial of immune modulating therapy? I'd like to hear from you.

Thank you very much.