Case Report

Gilles de la Tourette syndrome treated effectively with clozapine

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ABSTRACT

A report of Gilles de la Tourette syndrome in a 16-year-old male and a 20-year-old female from the Kingdom of Saudi Arabia, illustrating difficulties in diagnosis, comorbidity and management. A successful trial of clozapine therapy after failure of conventional treatments is reported over a period of more than 2 years and discussed.

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Gilles de la Tourette syndrome (TS) is a chronic neuropsychiatric childhood condition of unclear etiology.[1] Essential features of TS are multiple motor tics and one or more vocal tics with marked distress or significant impairment in social, occupational or other important areas of functioning. Other associated features are obsessions and compulsions, hyperactivity, distractibility and impulsivity.[2] Gilles de la Tourette syndrome occurs in approximately 4-5 per 10,000 and is 1.5-3 times more common in males than in females.[2-4] Gilles de la Tourette syndrome has been widely reported in different cultures,[2,4] but medline searches available showed only one case reported from the Middle East, in the Kingdom of Saudi Arabia (KSA) 15 years ago, with nothing published since then.[5] This paper reports 2 cases of TS from KSA with the role of clozapine as a possible treatment for tics.

Case Report. ***Patient One.*** A 16-year-old male who attended the clinic 2 years previously with his parents. The problems started at age 3 years with multiple motor tics of eye blinking, cheeks, neck, both shoulders and hands, then followed by vocal tics of uttering obscenities and other associated features of distractibility, obsessional slowness and impulsive behavior. His school performance was poor, he changed school twice with no improvement, and he could only pass the fifth primary grade. He had aggressive bouts and was mostly detached and socially isolated. He is the fifth of 7 siblings, 5 brothers and 2 sisters. Parents denied any family history of any neurological or psychiatric illnesses. The mother confirmed a negative pre and perinatal history. Brain computerized tomography (CT) scan, magnetic resonance imaging (MRI) and EEG (electroencephalogram) were all normal and serum copper and ceruloplasmin levels were also normal. Intelligence Quotient (IQ) was carried out using Weschler Adult Intelligence Scale (WAIS) and Jodard Board test (JBT) and both showed a 65-68 full IQ. He was diagnosed with childhood autism at age 5 years but TS diagnosis was only confirmed at the age of 11 years. This patient was treated in other clinics using haloperidol up to 10 mg daily for one year with little change and risperidone up to 4 mg daily for 6 months, also with little change. Then, clonidine was started with gradual increase up to 0.5 mg daily for 8 weeks and no improvement was noticed. A small dose of clozapine 12.5 mg at night was then introduced and gradually increased to 50 mg at night. Within 3 weeks, he showed marked improvement regarding tics, attention and impulsivity. Three months later, he showed some relapse, the tics mildly reappeared, therefore, the dose

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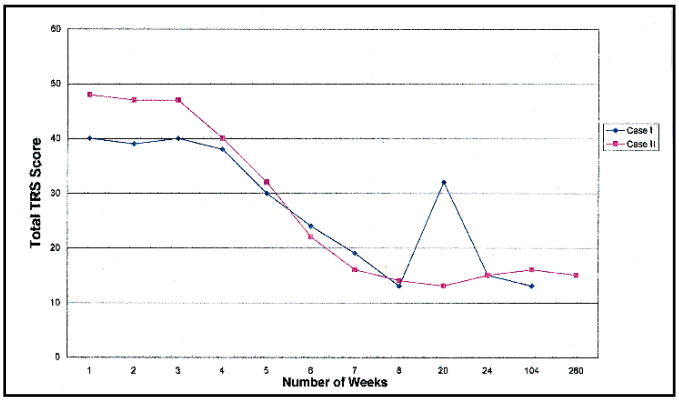

Figure 1 - Improvement of clozapine for both cases, monitored by Tic Rating Scale (TRS) scores over time of treatment.

was increased up to clozapine 125 mg daily at bedtime were he resumed his previous improvement over a period of 3 weeks and became more sociable. Four months later the dose was reduced to 100 mg at bedtime and he has maintained improvement over the past 18 months at regular follow up at the clinic. The blood maintaining safety system for clozapine was meticulously followed and the white blood cell (WBC) value was between 7.0-8.8 where the last value was 8.6. Parents were given one full session of education on the condition and how to deal with motor and socially unacceptable vocal tics. His school problem was discussed with parents and they agreed to refer him to a special education center.

Patient 2. A 20-year-old female attended the clinic 5 years ago with her parents. At the age of 5 years the illness started with multiple motor tics of eye blinking, facial grimacing, teeth clinching and other neck, trunk and hopping with left limb. Other complaints followed at the age of 10 years including vocal tics, clearing throat, grunting loudly and uttering obscene words; and other associated features of obsessional rituals of touching the sink repeatedly and washing hands excessively, distractibility and impulsivity. Her scholastic achievement deteriorated from the age of 14 and lately she refused to go to school. She is the oldest of 5 siblings and the parents denied any family history of neurological or psychiatric disorders and her pre and perinatal history was uneventful. Brain CT, EEG results and serum copper and ceruloplasmin levels were all normal. The IQ was also carried out using WAIS and was 98. The patient was treated using different medications including haloperidol up to 15 mg daily, pimozide up to 10 mg daily with no change over a period of one year. In our clinic, she was started on clonidine gradually up to 0.75 mg daily for 8 weeks with no response and then clozapine up to 100 mg daily was introduced and she showed marked improvement within 8 weeks. The patient has been followed over the past 5 years and she is still maintaining improvement.

Evaluation and monitoring. In both cases the period of treatment using clonidine and clozapine, a Tic Rating Scale (TRS) of 5 points severity from 0 = absent to 5 = extremely severe, (**Appendix 1**) was used to monitor change and improvement every week for the first 8 weeks and then was carried out at the end of 2 years for patient one and 5 years for patient 2. The improvement noticed was a marked reduction for present tics in each case from 3-5 to 0-2 on the TRS as shown in **Figure 1**. The blood monitoring safety system for clozapine was meticulously followed and the WBC value was in the range of 7.0-8.8 for patient one and 6.4-8 for patient 2.

Discussion. Gilles de la Tourette syndrome has not attracted clinicians enough in the Middle East, Arab countries, compared to other parts of the world hence, only one case has been published until now. The 2 cases reported here may explain many of the related issues. Gilles de la Tourette syndrome is easily misdiagnosed as shown in both cases. This is obvious because of the high variety of comorbid disorders. Obsessive compulsive disorders occur in 64% of cases[1,3] and were very apparent in patient 2. Attention deficit disorder is seen in 50-60% of patients[4,6] and is clear in patient one. Learning and language disability is found in a third of TS cases[6] and is prominent in both patients. Other tic and abnormal movement disorders are also easily confused with TS.[7] The diagnostic criteria of TS in the Diagnostic and Statistical Manual of Mental Disorders, 4th edition are all fulfilled in both cases, however family history was absent in both and no abnormalities of EEG, brain CT scan and MRI as reported in some TS cases,[3,4,6] were evident in either of the 2 cases.

Conventionally used drugs to treat TS such as clonidine, haloperidol and pimozide are not curative or specific, and therefore, cannot target tics, obsessive compulsive symptoms and attentional and hyperactivity problems together, let alone their poor efficacy in tic treatment specifically.[1,3,4,6] This opened room for new drugs to be tried such as Risperidone and clozapine, which inspite of their non-specificity, showed some efficacy in some cases.[6,8] Clozapine specifically has been shown to be helpful in some movement disorders especially tardive dyskinesia.[9] The peculiar mode of action of clozapine on modulation of dopamine (D)1/D2 receptors and 5-hydroxy tryptomine blockade, is another good reasons for its trial in TS.[10,11] Both cases were aged above 12 years and tried on all conventional drugs in therapeutic doses and for sufficient periods of time with little response which also added to the justification for using clozapine, taking into account the risk of its blood dyscrasias side-effect. The marked improvement documented by TRS scores and parents observation in both cases may not coincide fully with other reports where clozapine exacerbated symptoms transiently in some cases or showed no efficacy as monotherapy in other cases.[1,6] This can be explained by the lower dose used in both cases 100-150 mg/day compared to the high

dose used by other reports 150-500 mg/day. The other explanation is the longer period of treatment of more than 6 months in this report compared to 4-7 weeks in other reports and this is consistent with reports of clozapine treatment of tardive dyskinesia which showed response onset within 4 months.[10,11]

Psychosocial therapies although not well developed in many psychiatric services in KSA,[12] are very much needed for some TS patients as shown in both cases. Behavior therapy was somehow effective for obsessional symptoms and special education for attention, learning and language difficulties was also important as in patient one.[13] Parental education to ignore the tics, accommodate the socially unacceptable vocal tics and support patients at home and school cannot be emphasized more in such cases.

References

1. Bradly SP. Considerations of natural history and pathophysiology in the psychopharmacology of Tourette's Syndrome. ***J Clin Psychiatry*** 1996; 57 (Suppl 9): 24-34.
2. Diagnostic and Statistical Manual of Mental Disorders. Fourth Edition (DSM-IV), International Version with ICD-10 Codes. Washington (DC): American Psychiatric Press Inc; 1995.
3. Anzimanoglou AA. Gilles de la Tourette Syndrome. ***J Neurol*** 1998; 245: 761-765.
4. Robertson MM, Stern JS. Gilles de la Tourette Syndrome. ***Br J Hosp Med*** 1997; 58: 253-256.
5. El-Assra A. A case of Gilles de la Tourette's Syndrome in Saudi Arabia. ***Br J Psychiatry*** 1987; 151: 397-398.
6. Leung AKC, Fagan JE. Tic disorders in childhood (and beyond). ***Postgrad Med*** 1989; 86: 225-261.
7. Nemeth AH, Mills KR. Do the same genes predispose to Gilles de la Tourette Syndrome and dystonia? Report of a new family and reviews of the literature. ***Mov Disord*** 1999; 14: 826-831.
8. Shulman LM, Singer C, Weiner WJ. Risperidone in Gilles de la Tourette Syndrome. ***Neurology*** 1995; 45: 1419-1421.
9. Littrel K, Magill AM. The effect of Clozapine on pre-existing tardive dyskinesia. ***J Psychosoc Nurs Ment Health Serv*** 1993; 31: 14-18.
10. Tamminga CA, Thalou GK. Clozapine in tardive dyskinesia: Observations from human and animal model studies. ***J Clin Psychiatry*** 1994; 55: 102-106.
11. Factor S, Brown D. Clozapine: A 2-year open trial in Parkinson's disease patients with psychosis. ***Neurology*** 1994; 4: 544-546.
12. Al-Subaie A, Alhamad A. Psychiatry in Saudi Arabia, In: Al-Issa I, editor. Al-Junun: mental Illness in the Islamic World. Madison (CT): International Universities Press INC; 2000. p. 205-235.

Appendix - Tics Rating Scale (TRS).

Motor tics	**Score**	**Explanation**
Head	☐	0 Absent
Eyes	☐	1 Very mild
Mouth	☐	2 Mild
Facial muscles	☐	3 Moderate
Neck	☐	4 Severe
Right shoulder	☐	5 Extremely severe
Left shoulder	☐	
Right leg	☐	
Left leg	☐	
Trunk	☐	
Vocal tics	☐	
Sobbing	☐	
Throat clearing	☐	
Grunting	☐	
Total Score	☐	