Cukurova Medical Journal
ÇUKUROVA ÜNİVERSİTESİ TIP FAKÜLTESİ DERGİSİ

Cukurova Med J 2016;41(Suppl 1):79-81
DOI: 10.17826/cutf.254643

OLGU SUNUMU/CASE REPORT

Mania associated with cycloserine

Sikloserin ile ilişkili mani

Soner Çakmak[1], Ufuk Bal[2], Volkan Gelegen[1], Gonca Karakuş[1], Lut Tamam[1]

[1]Cukurova University Faculty of Medicine, Department of Psychiatry, Adana, Turkey
[2]Dr. Aşkım Tüfekçi State Hospital, Department of Psychiatry, Adana, Turkey

Cukurova Medical Journal 2016;41(Suppl 1):79-81.

Abstract
Cycloserine is a broad spectrum antibiotic agent commonly used as a second-line treatment for patients with multi-drug resistant pulmonary and extrapulmonary tuberculosis and associated with many neuropsychiatric adverse events. Mania is rarely reported in this context. We report a case of 38-year-old male diagnosed as Pott disease and developed manic symptoms while on second line anti-tubercular treatment for multi-drug resistant pulmonary and extrapulmonary tuberculosis. We related these manic symptoms with cycloserine. The patient remitted significantly in one week period after discontinuation of cycloserine and initiation of antipsychotic treatment. This case emphasizes that manic switch or exacerbation of psychosis can occur in early or late stage of treatment and that the necessity of periodic psychiatric evaluation before and during the treatment.

Key words: Cycloserine, tuberculosis, mania, psychosis

Öz
Sikloserin, çoklu ilaç direnci olan akciğer ve akciğer dışı tüberkülozlarda ikinci basamak tedavide sık kullanılan geniş spektrumlu bir antibiyotik ajandır. Birçok nöropsikiyatrik yan etki ile ilişkilendirilmektedir. Yan etkileri arasında nadir olmakla birlikte mani ile ilişkilendirilen olgular da bulunmaktadır. Bu olguya Pott hastalığı tanısı konulmuş ve çoklu ilaç direnci olan akciğer ve akciğer dışı tüberküloz olarak tanımlanmış, tedavisinde sikloserin kullanılmış olan 38 yaşında bir erkek hasta tartışılmıştır. Tedavi sürecinde mani gelişmiş ve sikloserin ile ilişkili olabileceği düşünülmüştür. Mani bulguları ilacın kesilmesi ve antipsikotik medikasyonla 1 haftalık süreçte gerilemiştir. Bu olgu bildirimi ile sikloserin kullanımında mani ve psikotik bulguların tedavinin erken veya geç aşamalarında ortaya çıkabileceği, tedavi öncesi ve tedavi devam etmekte iken psikiyatrik değerlendirmelerin düzenli aralıklara yapılması gerekliliği vurgulanmıştır.

Anahtar kelimeler: Sikloserin, tüberküloz, mani, psikoz

INTRODUCTION

Multi-drug resistant pulmonary and extrapulmonary tuberculosis (MDR-TB) is diagnosed by the resistance of the bacillus to both Izoniazid (H) and Rifampicin (R). These cases do not respond to the six-month standard treatment with anti-tuberculosis drugs, and it is necessary to treat them for two years with less effective but more toxic and more expensive drugs.

It is known anti-tuberculosis treatments and in particular treatments for multiple drug resistant tuberculosis can result in such psychiatric conditions as depression, anxiety and psychosis[1,2]. It has been reported that depression occurs during treatment at a rate of 13.3%, anxiety at 12% and psychosis at 12%1. Izoniazid, Cycloserine and Macrolide group drugs are anti-tuberculosis drugs which are often associated with psychogenic side effects. For Cycloserine, the rate of psychogenic side-effects (depression, psychosis, etc.) has been put at 15%.

Cycloserine is also associated with neuropsychiatric side effects such as paranoia, aggression, confusion and thoughts of self-harm in addition to depression, anxiety and psychosis. Cases of mania have occasionally been associated with Cycloserine treatment[3]. In the literature, the use of Cycloserine has been associated with cases of illusion-delusion psychotic attacks[4], epileptic fit psychosis[5,6,7], and manic switch[3].

Yazışma Adresi/Address for Correspondence: Dr. Soner Çakmak, Cukurova University Faculty of Medicine, Department of Psychiatry, Adana, Turkey E-mail: drsoncak@hotmail.com
Geliş tarihi/Received: 27.06.2016 Kabul tarihi/Accepted: 23.07.2016

Our case was a 38-year-old male diagnosed with bone tuberculosis and being treated for MDR-TB. After a treatment period of approximately 30 months, psychotic development of mania was observed which could be associated with Cycloserine. This rarely-seen condition is presented as a contribution to the literature.

CASE

A 38-year-old university educated unmarried unemployed male was admitted to the University Hospital Orthopedics clinic in January 2010 with complaints of pain in the lumbar and back areas, and swelling in the right psoas region. He was diagnosed with tuberculosis related spondilodiscitis and treatment with H, R, pyrazinamide (Z) and ethambutol (E) was started.

The patient was diagnosed with Pott disease, and was followed up by the Infection clinic. After approximately one year of continuing treatment, he was assessed as having MDR-TB because of renewed spondylodiscitis and abscesses in the paravertebral region and psoas. He was admitted to the infection clinic and treatment continued with ethambutol 1x1250 mg, pyrazanimide 1x1500 mg, PAS 2x6 gr, thioacetazone 1x120 mg and cycloserine 1x1g. From that date onwards, the patient took the medications regularly, and in January 2015, 30 months after the commencement of MDR-TB treatment, he began to show symptoms of increased self-esteem, talkativeness, sleeping little, increased sex drive, suspiciousness and irritability, accompanied by stereotypical behavior of licking and sucking his lips. He started to think that his family were trying to harm him or poison him; he saw black cats in the house and said that they were devils who were trying to turn him out of the house, and that they would hand him over to the police.

With these symptoms, he was brought to the emergency clinic by the police in January 2015. He was referred to Neurology because of his stereotypical licking behavior. As a result of the assessment he was diagnosed as having an epileptic fit, and was admitted to the Neurology clinic for evaluation between 22 and 26 January 2015.

Neurological examination was found to be normal. Biochemical serum examination showed only iron deficiency. In his physical examination, he was given a lumbar puncture (LP) despite his not having a stiff neck in order to exclude tuberculous meningitis because of his history of tuberculosis, and there were no abnormalities in biochemical analysis or culture. Cerebral MR was found to be normal, and in video EEG examination dysrhythmia was detected in observing slow activity in the temporal structure.

Because his euphoric condition and psychotic period continued, he was assessed by psychiatry; he was diagnosed with psychotic mania, and was evaluated with a score of 44 on the Young Mania Scale (YMS)[8,9]. Treatment with olanzapine 20 mg/day was started. When the patient was evaluated for infectious diseases, active tuberculosis was excluded and anti-tuberculosis medication (ethambutol, pyrazinamide, PAS, ciprofloxacin, thioacetazone and cyclocerine) was terminated. After stopping these drugs and starting olanzapine, the patient's manic symptoms had regressed appreciably at the end of seven days, and his YMS score fell to 14. Grandiosity and ideas of reference continued to a slight extent. With this clinical profile, the patient continued to be monitored in our clinic in February 2015; the infection department was again consulted and MDR-TB treatment was continued with the exception of cycloserine: ethambutol 1250 mg/day, pyrazanimide 1500 mg/day, PAS 12 gr/day, ciprofloxacin 1500 mg/day, and thioacetazone 120 mg/day. The olanzapine dose was reduced to 10 mg/day. The patient's manic symptoms showed complete remission in the second week, and his YMS score fell to 2. He was discharged from our clinic in March 2015 and later monitored as an outpatient. His remission has continued over two months of follow-up.

DISCUSSION

Although the mechanism of this effect of cycloserine is not precisely known, it has been stated that neurobiological mechanisms which can be associated with manic switch can be explained by N-methyl-D-aspartate antagonism and partial antagonism of glycin dependent NMDA receptors, or the possible antidepressant effects in the Central Nervous System (CNS) when used at 500 mg/day or more[10,11]. In cases reported in the literature, terminating cycloserine alone or together with the use of anti-manic anti-psychotic agents has caused the manic/psychotic profile to regress in a short time, and anti-manic anti-psychotic treatment for a short time has been reported to be sufficient[3,4,5,6,7].

The fact that our patient's manic episode appeared approximately 30 months after the start of cycloserine treatment at first suggested that it might be a manic episode unrelated to the drug, but there was no previous clinical or subliminal mood episode in the patient's history, the average age of onset for bipolar disorder is over 30, and there was no history of psychopathology in the patient's family, all of which suggested that the manic symptoms could be related to cycloserine. In addition, the fact that when cycloserine was discontinued and treatment was continued with the other anti-tuberculosis drugs the symptoms receded in a shorter time than the classic BPB process supports this view.

In a case reported by Bakhla AK et al., a manic episode was diagnosed seven days after cycloserine treatment was started. Three days after cycloserine treatment was stopped and antipsychotic medication was given, the patient's YMS score fell by 50%[3]. In a case of Tandon et al., psychosis developed approximately 1.5 years after cycloserine was started. After cycloserine was stopped and antipsychotic medication was started, the findings receded in ten days[6]. Sadhana et al. introduced a case in which psychosis developed two years after the start of cycloserine treatment[7]. One month after cycloserine was stopped and antipsychotics were given, it was reported that findings receded. In conformity with the literature, cycloserine treatment in our case was stopped while anti-tuberculosis treatment was continued with the use of other agents. Olanzapine 20 mg/day was prescribed, and when manic and psychotic symptoms disappeared within seven days, the olanzapine dose was quickly reduced to 10 mg/day, and it was planned to cease it altogether in a short time.

Cycloserin is a medical agent which is regularly used in the treatment of MDR-TB. Neuropsychiatric side effects can occur in the short term with use at a dose of more than 500 mg/day or with long-term use. In situations of psychosis or mania which are thought to be related to cycloserine, stopping the drug and giving antipsychotic medication creates a remission and correction of symptoms within one or two weeks. It would be useful both for tuberculosis treatment and to prevent this kind of risk to carry out regular psychiatric monitoring before, during and after cycloserine treatment, and to be alert to the potential for this kind of side effect.

REFERENCES

1. Vega P, Sweetland A, Acha J, Castillo H, Guerra D, Smith Fawzi MC et al. Psychiatric issues in the management of patients with multidrug-resistant tuberculosis. Int J Tuberc Lung Dis. 2004;8:749-59.
2. Sarkar S, Sood M. A patient of multidrug-resistant tuberculosis on category IV treatment regimen presenting with psychosis. Natl Med J India. 2011;24:244-5.
3. Bakhla AK, Gore PS, Srivastava SL. Cycloserine induced mania. Indian Psychiatry. 2013;22:69-70
4. Sharma B, Handa R, Nagpal K, Prakash S, Gupta PK, Agrawal R. Cycloseine-induced psychosis in a young female with drug-resistant tuberculasis. Gen Hosp Psychiatry. 2014;36:3-4.
5. Fujita J, Suada K, Hayashi H, Hayashihara K, Saito T. A case of multi-drug resistant tuberculosis showing psychiatric adverse effect by cycloserine. Kekkaku. 2006;83:21-5.
6. Tandon VR, Rani N, Roshi, Gupta R, Arora M, Khajuria V. Cycloserine induced psychosis with hepatic dysfunction. Indian J Pharmacol. 2015;47:230-1.
7. Sadhana N Holla, Mohan Babu Amberkar V, Rajeshkhrishna Bhandary P, Meena Kumari K, Manju Janardhanan. Cycloserine induced late onset psychosis and ethambutol induced peripheral neuropathy associated with MDR-TB treatment in an Indian patient-a rare case report. Journal of Clinical and Diagnostic Research. 2015;9:FD01-03
8. Young RC, Biggs JT, Ziegler VE, Meyer DA. A rating scale for mania: reliability, validity and sensitivity. Br J Psychiatry. 1978;133:429-35.
9. Karadağ F, Oral ET, Aran Yalçın F, Erten E. Young Mani Derecelendirme Ölçeği'nin Türkiye'de geçerlilik ve güvenilirliği. Turk Psikiyatri Derg. 2001;13:107-14.
10. Emmett MR, Mick SJ, Cler JA, Rao TS, Iyengar S, Wood PL. Actions of D-cycloserine at the N-methyl-D-aspartate-associated glycine receptor site invivo. Neuropharmacology. 1991;30:1167-71.
11. Van Berckel BN, Lipsch C, Gispen-de Wied C, Wynne HJ, Blankenstein MA, van Ree JM, et al. The partial NMDA agonist D-cycloserine stimulates LH secretion in healty volunteers. Psychopharmacology (Berl). 1998;138:190-7.