

MULTI-DRUG THERAPY INDUCED PSYCHIATRIC MANIFESTATIONS

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INTRODUCTION

Leprosy is successfully treated with multi-drug therapy (MDT). ENL (Erythema Nodosum Leprosum) commonly seen in Lepromatous leprosy (LL) is treated with corticosteroids, thalidomide or clofazimine (Walker et al.2015). Psychiatric comorbidities seen with leprosy are depression, anxiety, and rarely psychosis (Filaković et al. 2009, Colle et al.2019). Apart from disease itself, behavioral associations can also be seen with antileprotic drugs. This case report presents behavioral symptoms resulting from MDT in a case of LL with ENL, and how different specialities liaised for management.

CASE DESCRIPTION

Brief History

A 20-year-old male diagnosed with LL and ENL was prescribed MDT (daily Dapsone and Clofazimine with monthly Rifampicin, Clofazimine, Dapsone), prednisolone (10-40 mg) and Thalidomide 300mg. During the sixth, fifth and third month respectively of initiation of these drugs, he had first manic episode which remitted with olanzapine and valproate. He completed the MDT course and psychotropics were successfully tapered off. After 2 months, he developed recurrent lepromatous lesions leading to admission in dermatology ward. Examination revealed steroid induced hypertension and diabetes mellitus managed appropriately. Furthermore, he exhibited Cushing's syndrome with adrenal insufficiency necessitating intravenous hydrocortisone 150mg tapered over 2weeks followed by oral prednisolone 15mg.

Following the stabilization of his medical condition, he was reinitiated on MDT. On third day, he exhibited confusion and disorientation prompting psychiatry consultation. Within a day, he progressed to a catatonic state characterized by mutism, staring, posturing, poor oral intake, and self-neglect. Hemogram, liver, kidney, thyroid

function tests, and vitamin levels were within normal limits. A positive Lorazepam challenge test indicated catatonia, which subsequently resolved with low-dose oral Lorazepam. However, euphoria, pressured speech, grandiosity, overfamiliarity, and decreased need for sleep became apparent. A diagnosis of organic bipolar affective disorder was made.

Management approach

Decision was taken to stop the possible offending drug in liaison with dermatology and endocrinology. Due to persisting symptoms of adrenal insufficiency, Prednisolone 15mg was continued. Despite discontinuing Thalidomide for a month, no changes in symptomatology occurred. Improvement commenced with Risperidone (up to 6mg), and the patient was discharged with expectations of further recovery post-MDT completion.

Follow Up

On subsequent monthly follow up, family members disclosed that patient had stopped MDT due to logistical reasons and had shown drastic improvement in mood shortly thereafter. Notably, the remission of symptoms following MDT cessation, without any alteration in Prednisolone dosage, established a clear cause-effect relationship. The patient consistently maintained well during monthly follow-ups, remaining free of further episodes.

DISCUSSION

There is abundance of literature on steroid induced psychiatric manifestations. Symptoms in our patient started after complete withdrawal of steroids which puts a question to this association. Since symptoms showed no change even after stopping thalidomide for a month, its association also seems less likely.

Table 1 Case reports on behavioral symptoms induced by Dapsone

Author, date	Subject	Dose (mg)	Symptoms
Sahu 1972	Leprosy	50	Irrelevant speech, insomnia, irritability
Krishna Murthy & Raja Babu 1980	Accidental ingestion	NM	Delirious Psychosis
Fine et al. 1983	Dermatitis Herpetiformis	50	Psychosis
Bhatia et al. 1988	Tuberculoid Leprosy	50	Psychosis
Carmichael & Paul 1989	Erythema Multiforme	100	Bipolar Disorder
Gawkrodger 1989	Dermatitis Herpetiformis	50	Depression, anger and argumentative
Sheela et al.1993	Accidental ingestion	NM	Acute Psychosis
Panda et al., 2017	Tuberous Sclerosis misdiagnosed as leprosy	100	Psychosis
Colle et al. 2019	Immune thrombocytopenic purpura	100	Mania

NM: Not mentioned in the article

There are reports of various behavioral symptoms induced by Dapsone (Table 1). The onset of symptoms within three days of initiating MDT aligns more closely with Dapsone than the other mentioned drugs. Existing literature suggests that dapsone could induce mania by enhancing oxidative stress (Colle et al.2019). Proposed to be a dose-independent side effect, it occurs rapidly on rechallenges (Fine et al.1983).

In our case, the first episode occurred after six months of Dapsone use, while the second episode emerged on the third day. Despite the absence of definitive treatment guidelines, researchers have explored strategies such as drug discontinuation and the use of antipsychotics (Sahu 1972, Fine et al.1983). Successful remission in our patient was achieved through the timely cessation of MDT, coupled with concurrent antipsychotic administration.

IMPLICATIONS

This study underscores the importance of vigilant monitoring for psychiatric manifestations in patients undergoing MDT for leprosy, particularly considering the potential neuropsychiatric effects of Dapsone. Healthcare professionals across various disciplines should be aware of the diverse range of symptoms associated with Dapsone use. The study highlights the need of further research into the underlying mechanisms of these symptoms, the dose-dependent relationship, and effective management strategies. In upcoming research endeavors, the exploration of innovative methodologies like Online Photovoice also holds promise which enables patients

to directly express their experiences, fostering a deeper understanding of the lived experiences of individuals and enhancing the development of more personalized interventions tailored to individual needs (Tanhan and Strack, 2020).

CONCLUSION

In conclusion, the symptoms, potentially linked to Dapsone, exhibited a spectrum ranging from delirium to catatonia and mania. The presence of comorbidities added complexity to the clinical picture. Effective management necessitates close collaboration between different medical specialties. Key measures for improvement involve prevention, timely diagnosis, and appropriate treatment. Future research should focus on elucidating the underlying mechanisms, guiding a more rational and targeted approach to drug usage in such cases.

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