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PSYCHIATRIC MANIFESTATIONS OF DENGUE FEVER- A CASE REPORT FROM PAKISTAN

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ABSTRACT

A 29-year-old male presented to Aga Khan University Hospital with complaints of fever, body-aches, vomiting and one episode of gum bleeding. A Dengue antigen test done prior to presentation was positive. He was admitted for medical management. During hospital stay, the patient developed manic symptoms including over-talkativeness, expansive mood, disinhibited behavior, excessive planning, paranoia and aggression. He remained oriented to time, place and person and neurological examination was unremarkable. He was managed with anti-psychotics and benzodiazepines, and his psychiatric symptoms improved with improvement in his medical condition. This case highlights the possibility of psychiatric manifestations occurring in context of a dengue infection.

Key words: Dengue fever, Psychiatric manifestations, Organic mood disorder, Mania

INTRODUCTION

Dengue fever is a disease caused by the Dengue Virus, which belongs to the Flavivirus family. Its transmission is mainly by the vectors *Aedes aegypti* and *Aedes albopictus*. Infection with the Dengue Virus can cause a variety of clinical manifestations and can have varying disease severity, ranging from mild infection to complications including dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).¹

The incidence of dengue has increased significantly over past few decades and approximately 70% global disease is in Asia.¹ In Pakistan, first dengue epidemic was reported in 1994. Since then, the country has faced multiple outbreaks of dengue infection. In 2019, more than 19,000 cases of dengue infection were reported in Pakistan.²

Common neurological symptoms encountered in dengue infection include headache, irritability, sleep disturbances and altered sensorium. Less commonly, seizures, neck stiffness and weakness may occur. Psychiatric symptoms in Dengue infection have also come into light, with cases reporting manic and psychotic symptoms in patients with dengue fever.³⁻¹⁰

To the authors' best knowledge, only a few cases of psychiatric manifestations in dengue fever have been reported from India and other countries.

CASE PRESENTATION:

A 29 year old gentleman presented to the Emergency Room at Aga Khan University Hospital with fever, body-aches, episodes of vomiting, and an episode of

bleeding from gums. A dengue antigen done prior to presentation was positive. The patient was admitted under medicine care for the management of dengue fever. On Day six of admission, a psychiatry consult was generated for complaints of agitation. The patient had disrobed and come out of his isolation room, become over-talkative with expansive mood and inappropriate laughing. He had started excessive business-related planning, and spoke about proposing marriage to a nursing staff. The patient's family did not report any previous visits to psychiatrists, and no history of substance use. There was no history of diagnosed psychiatric illnesses in the family. Initially, Tablet Olanzapine 2.5mg twice a day, along with Tablet Clonazepam 0.5mg at night were started. The next day, patient became aggressive, hitting staff and family. At that time, patient developed suspiciousness towards family and hospital staff, refused medications, demanded that they be given to everyone so that he could make sure they were safe, snatched his brother's cell phone because he believed that his brother was recording him, called the security guards as he felt unsafe and handed his brother's phone over to security. Throughout his hospital stay, patient remained awake, alert, oriented to time, place and person, with no apparent confusion. Young Mania Rating Scale was applied, and a total score of 47 out of 60 was calculated which showed severe mania.

Investigations showed thrombocytopenia which gradually improved. Malaria was ruled out and there was no growth on blood and urine culture. Detailed metabolic work-up was done and was found to be largely insignificant (Table 1).

Table 1: Results of Laboratory and Radiological investigations

Laboratory investigations	Results
Hemoglobin	14.3 g/dl
Hematocrit	41.4%
Total Leukocyte Count	$5.2 \times 10^9/L$
Platelet	$109 \times 10^9/L$
Serum Creatinine	1.3 mg/dl
Serum Sodium	126 mmol/L
Serum Potassium	3.3 mmol/L
Serum Chloride	90 mmol/L
Serum Bicarbonate	21.8 mmol/L
SGPT	27 IU/L
SGOT	51 IU/L
Prothrombin Time	13.9 seconds
Activated Partial Thromboplastin Time	29.5 seconds
Dengue Antigen	Positive
ICT Malaria Antigen	Negative
Urine Culture and Sensitivity	No growth
Blood Culture and Sensitivity	No growth
COVID 19 Qualitative PCR	Negative
Thyroid Stimulating Hormone	2.39 μ IU/ml
C-Reactive Protein	12.59 mg/L
Chest X ray	No active cardiopulmonary abnormality identified

Our differential diagnoses included delirium; however, there was no clouding of consciousness or disorientation. A diagnosis of Brief Psychotic Episode was also considered, however the patient's mood symptoms seemed to predominate the clinical presentation. Considering a possible diagnosis of viral or autoimmune encephalitis, a detailed neurological assessment and examination was done, and no significant finding was observed.

A diagnosis of Manic Episode with the background of Bipolar Affective Disorder was considered, however, there was no previous history of manic/depressive episodes, psychiatric visits or family history of psychiatric illnesses. The patient's symptoms arose in the context of Dengue infection and improved as his Dengue infection resolved.

Initially, Tablet Olanzapine 2.5mg twice a day and Tablet Clonazepam 0.5mg at night were started. This was changed to intra-muscular Haloperidol and Intra-muscular Midazolam. His symptoms improved, and he was discharged home on Tablet Haloperidol 2.5mg twice daily and Tablet Clonazepam 0.5mg at night. At the time of discharge, our patient's Young Mania Rating Scale score had come down to 9.

He was advised out-patient follow-up after discharge, where his psychiatric symptoms had improved, with

some evidence of over-spending, self-important ideas and excessive planning. His medications were continued, and he was advised follow-up in one month. However, patient was lost to follow-up.

DISCUSSION

Our case highlights symptoms of mania in a patient with Dengue Fever, who had no previous history or family history of Psychiatric illness or history of substance use. The symptoms became apparent during the first week of his admission with Dengue, with a significant improvement in symptoms as the patient's clinical and laboratory parameters improved. This, along with the lack of confusion, disorientation and absence of any abnormality on neurological examination was suggestive of psychiatric manifestations associated with dengue. The available literature reports cases of manic and psychotic symptoms in dengue, which is summarized in Table 2 below. The pathogenesis of psychiatric symptoms in dengue infection is not completely known, however the proposed mechanisms include direct invasion of the central nervous system by the virus, autoimmune-mediated reactions and metabolic changes.⁵ Early recognition and effective management is important as emergency of psychiatric symptoms can be challenging to manage in a medically ill patient. Further study in this area is required to develop guidelines for the management of such patients.

Table 2: Reported cases of manic and psychotic symptoms in dengue infection

Study	Region	Age	Sex	Confirmatory testing	Psychiatric Symptoms	Treatment
1 ⁽³⁾	India	21 years	Male	Positive serological test for Dengue IgM antibodies	Over-activity, excessive talking, argumentativeness, irritability, grandiosity, abusiveness and a decreased need for sleep	Carbamazepine 600 mg/day and Haloperidol 15 mg/ day.
2 ⁽⁴⁾	India	18 years	Male	Positive Dengue NS1 antigen, Positive dengue IgG and IgM antibodies	Auditory and visual hallucinations, persecutory delusions.	Risperidone 2 mg twice daily
3 ⁽⁵⁾	Haiti	52 years	Female	Positive serological test for IgM and IgG antibodies	Ideas of reference, delusions, acoustic and visual hallucinations, agitation and psychotic fears	Lorazepam, Risperidone and a single injection of long-acting Fluphenazine
4 ⁽⁶⁾	India	18 years	Female	Serologically confirmed	Decreased sleep, over talkativeness, irritability, over-religiosity and grandiosity	Olanzapine 15mg and Sodium Valproate 1500mg/day
	India	38 years	Male	Serologically confirmed	Decreased sleep, increased energy, over socialization, excessive talk, irritable mood, expansive ideas	Haloperidol 10mg/day
	India	48 years	Female	Serologically confirmed	Insomnia, over-talkativeness, over-religiosity, increased activity, elated mood	Olanzapine 5mg/day
5 ⁽⁷⁾	India	35 years	Male	Positive IgM antibodies	Reduced sleep, suspiciousness, fearful, agitation, poor self-care and	Olanzapine 10mg/day and Lorazepam 2mg

					emotional lability	
6 ⁽⁸⁾	India	28 years	Male	Positive IgM ELISA for dengue	Over-talkativeness, increased activity, decreased need for sleep, irritability, aggression, grandiosity	Divalproex sodium 1500 mg/day and Risperidone 6 mg/day
7 ⁽⁹⁾	Malaysia	57 years	Male	Positive IgM and IgG for Dengue virus	Visual and auditory hallucination, interrupted sleep, persecutory delusions	Quetiapine extended release (XR) 100mg at night, titrated up to 200mg at night
8 ⁽¹⁰⁾	Pakistan	51 years	Male	Positive Dengue IgG	Over-talkativeness, disinhibition, disturbed sleep, increased energy, aggression	Intra-muscular Haloperidol 10mg twice daily, Promethazine 25mg twice daily and Diazepam 10mg twice daily.

CONCLUSION

- Dengue fever may present with psychiatric manifestations and it is important that these are recognized and appropriately managed.
- There are no guidelines regarding the management of psychiatric manifestations

occurring in Dengue Fever, and further work in this context is required.

- Psychiatric symptoms such as these can be a significant cause of concern for patients and their families, and further research is needed to elucidate the cause and pathophysiology.

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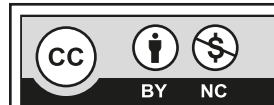
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Author's contribution:

Ifrah Hambal; concept, case management, data collection, data analysis, manuscript writing

Samrah Nasir; case management, data collection, data analysis, manuscript writing,

Tania Nadeem; case management, data analysis, manuscript revision



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