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FINDING NEEDLE IN A HAYSTACK; NEUROLEPTIC MALIGNANT SYNDROME DISGUISED AS MENINGITIS IN A 2-YEAR-OLD GIRL

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ABSTRACT:

Fever with CNS symptoms in children is almost, always considered to be a CNS infection and treated as Meningitis. Central causes of fever are not usually taken into account in such cases. We present a case of a 2-year-old girl who developed fever and CNS symptoms after she was given anti-emetic medications for her initial presentation of acute gastroenteritis. She developed high grade fever and spasticity and was treated on lines of meningitis empirically without any evidence of infection. She did not improve and once she fulfilled clinical criteria of Neuroleptic malignant syndrome, her condition improved, fever and spasticity settled. The case report highlights the importance of central causes of fever in children to be considered in differential diagnosis while managing patients with fever and CNS symptoms.

KEYWORDS: Central fever, Neuroleptic malignant syndrome, Meningitis

INTRODUCTION:

Fever is a common symptom in a paediatric outpatient or emergency department. Most of these febrile episodes are caused by infections. In one of the studies it was found that 23% (87/387) of patients in Neurology intensive care had fever, 52% of cases with fever had infection (predominantly pneumonia or bronchitis), and 28% were unexplained despite a complete diagnostic evaluation.⁽¹⁾ One of the causes of unexplained fever is central fever resulting from complex disturbances of central mechanisms of thermoregulation.⁽²⁾ One such example is the use of dopamine receptor blocking agents, such as metoclopramide, a commonly used off-label agent for vomiting in children. The off-label use is often justified as vomiting is not only unpleasant for children and families, but can lead to frequent hospital admission.⁽³⁾ The D2 receptor blockade results in Neuroleptic malignant syndrome (NMS) which is a rare but potentially lethal complication of treatment with antipsychotic medication and also some non-neuroleptic agents that block central dopamine pathways, such as metoclopramide, amoxapine and lithium.⁽⁴⁾ This results in an unexplained fever along with neurological signs, resembling meningitis. In the developing world, the issues of frequently used off-label medications and infections such as meningitis being the leading cause of morbidity and mortality in children

presenting with fever and neurologic signs, a knowledge about rare conditions such as neuroleptic malignant syndrome can be life saving.

CASE PRESENTATION:

A 2-year-old girl presented in paediatric emergency department with the complaints of fever, fits and stiffening of the whole body for 15 days. Patient had history of loose stools and vomiting, two weeks back for which she was taken to a nearby clinic where an unknown injection for vomiting was given after which she developed high grade fever and stiffness of whole body within 24 hours of the administration of the injection. She continued to have fever, documented as 104F and it was not relieved by antipyretics. She was admitted in the hospital and treated for meningitis with broad spectrum antibiotics despite CSF analysis being normal. During the course of admission, she continued to have fever despite the broad spectrum antibiotics and antipyretics in appropriate doses, she became drowsy gradually and also had episodes of Generalised tonic clonic fits. Her stiffness increased and she started to arch her body. She did not have any history of trauma or needle prick suggestive of tetanus. Due to the deterioration of the condition she was shifted to the tertiary care hospital and admitted under the paediatric neurology services.

She had an unremarkable birth history with normal development and had completed her immunization schedule. Examination revealed an extremely irritable girl in an opisthotonos posture, running a fever of 103 F She had generalised body stiffness. Her tone was increased exhibiting lead pipe-rigidity. Reflexes were brisk and Pupils bilaterally equally reactive to light and other accessible cranial nerves were intact. Lab workup for showed normal CSF and no electrolyte imbalances. Magnetic resonance imaging (MRI) showed hypoxic changes in the left post parietal and parasagittal area. Electroencephalogram (EEG) was done which showed marked slowing of background rhythm and no epileptiform discharges. Work up for infectious causes was extended and no definitive infectious aetiology could be identified. Dengue IgM, IgG and malaria parasite were negative. Urine analysis was also normal and inflamaotory markers, procalcitonin were also within normal range. The clinical picture was suggestive of Neuroleptic malignant syndrome so CPK & LDH was sent that turned out to be high. The Lactate Dehydrogenase was 804units/L (Normal range in children 60-170 units/L) and creatine phosphokinase 1370 mcg/L (Normal range 10-120 mcg/L) were raised. Considering diagnosis of Neuroleptic Malignant Syndrome, shewe started on Bromocriptene 0.5mg once daily. Patient showedimprovement in spasticity and there was no documented fever spike with bromocriptine. He was kept on bromocriptine for 7 days and discharged home afebrile and with markedly reduced spasticity. However she had residual CNS symptoms secondary to hypoxic insult due to the delay in diagnosing the condition.

DISCUSSION:

Due to high fever, rigidity all over the body, a change in the level of consciousness and a high level of creatinine phosphor kinase, our patient fulfilled the criteria for NMS and that was due to metoclopramide injection. NMS is a rarely observed side effect ofmetoclopramide. Neuroleptic malignant syndrome (NMS) is less common but potentially lethal complication of the use of certain medications. Paediatric population is more vulnerable to this condition because of the increasing use of both typical and atypical antipsychotics in children and also the off-label use of various antiemetic medications which may disrupt the thermoregulation. Dopamine neurotransmission plays a central role in regulating body temperature, mediated in the thermoregulatorycentre of the hypothalamus, particularly the anterior pre-optic nucleus. Antipsychotics have antagonistic effect on

dopamine receptor-mediated signalling in neurons in the thermoregulatory centre and can potentially lead to a disturbance in thermoregulation .dopamine receptor blockade is found in the central nervous system even with low doses of neuroleptics. Blockade of striatal dopamine receptors contributes to muscle rigidity and tremor. There are different criteria for the diagnosis of NMS.The most well-known is from the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-V) which is based on the history and clinical examination. It include severe muscle rigidity and elevated temperature associated with the use of a neuroleptic medication as well as at least 2 of a list of additional multiple criteria including diaphoresis, dysphagia, tremor, incontinence, altered mental status, mutism, elevated or labile blood pressure, tachycardia, leucocytosis, or laboratory evidence of muscle injury. ⁽⁵⁾ The pharmacotherapy of NMS has not been well established, as there is lack of head-to-head studies to compare treatments. The current recommendations are based on case reports and expert opinion, and are sometimes conflicting.Pharmacotherapies that have been used with success are dantrolene, bromocriptine, amantadine, and benzodiazepines. Bromocriptine and amantadine are both dopamine agonists that displace antipsychotic dopamine antagonists. Both bromocriptine and amantadine are only available as oral formulations. That's why we usedbromocriptine in our patient. Aggressive supportive management is the basis of treatment of NMS, and a reasonable pharmacotherapeutic approach based on drug efficacy, availability, and experience would be to start drug therapy with a benzodiazepine and bromocriptine, and escalate to the addition of dantrolene in severe cases.⁽⁶⁾ Much of the work in literature is reflective of the NMS being studied as a complication of typical and atypical antipsychotic medications .Not much is known, regarding the use of non-antipsychotic medications such as Metoclopramide which has a huge tendency to cause NMS due to its dopamine antagonist effects.This case report highlights this important aspect of NMS. This rare complication is an important consideration in the developing countries where the off-label use of antiemetic medications in children is frequent and also because fever in children is almost always, thought of as a symptom of underlying infection. Fever with CNS symptoms is always taken as a CNS infection therefore, having NMS in differentials of the physician can be lifesaving.

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Raman kumar; data collection, data analysis, manuscript writing, manuscript review

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