CASE REPORT

Atropine Induced Delirium in Young Female with unknown Snake Bite

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Abstract:

Venomous snakebites account for many deaths in developing countries. Administration of an Acetylcholinesterase Inhibitor (ACEI) has been recommended by WHO as a part of neurotoxic snakebite treatment. With atropine being used to reduce the undesirable muscarinic effects of ACEIs, adverse effects like delirium can occur. Delirium is characterized by acute decline in level of consciousness and cognition involving perceptual disturbances, abnormal psychomotor activity, and sleep cycle impairment. This case report describes a 17-year-old female with unknown snakebite who developed atropine induced delirium despite being under the cover of ACEIs and at a lower dose (4.5 mg) than usual for the drug to cause delirium. Though there are reports in literature about atropine induced delirium in organophosphate poisoning, to our knowledge none were reported in snakebite cases. Hence, clinicians need to be cautious while encountering such patients and should always consider the possibility of atropine induced delirium even in snakebite cases.

Keywords: *Atropine, Delirium, Snakebite*

INTRODUCTION

Venomous snake bites account for a large number of deaths in the developing countries.[1] Studies have reported that every year more than 5 million snake bites occur worldwide with an associated mortality rate of 125,000 persons per year. Mortality in India is estimated to be as high as around 30,000.[2]

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Snake venom has been shown to produce skeletal muscular paralysis causing a non-depolarizing block like action on the neuromuscular junction (NMJ).[3] Acetylcholinesterase inhibitors (ACEI) are hypothesized to reduce the neuromuscular block by increasing the amount of acetylcholine (ACh) at the NMJ. Currently WHO recommends administration of an ACEI like Neostigmine for the treatment of neurotoxic snakebite.[4] Intravenous administration of Atropine or glycopyrrolate along with ACEIs is usually done to reduce the undesirable muscarinic effects of ACEIs.[5]

Atropine causes competitive antagonism on the muscarinic acetylcholine receptors (M1-5).[6] M1 receptors are located primarily in the central nervous system and are involved in perception, attention and cognitive functioning. Hence delirium has been hypothesized to occur with antagonism of postganglionic M1 receptors.[7]

Though there are reports in the literature about atropine induced delirium in organo-phosphate poisoning, to our knowledge none were reported in cases of snake bite. With prior informed consent, we hereby report a case of 17-year-old female diagnosed with a case of unknown snake bite who developed atropine induced delirium despite being under the cover of Acetylcholinesterase inhibitors.

Case Report

Our patient, a 17-year-old unmarried female was admitted to Intensive care unit (ICU) with a history of unknown snake bite on her right leg while sleeping in her home at night. Morphology of the snake could not be described due to darkness in the room. Patient complained of headache, nausea and vomiting, burning sensation in both the eyes. On examination, the patient was conscious and oriented to time, place and person, with Glasgow Coma Score of 15/15, afebrile, pulse rate was 80 bpm, blood pressure was 96/60mm Hg, SpO2 was 99% on room air, BMI of 15.14 kg/m^2, single breath count was normal. The systemic examination was unremarkable. On local examination, two closely set puncture marks were seen on right leg, with local reactions of erythema and oedema. Clinically, no other haemorrhagic or neurological manifestations were observed. Patient was diagnosed with unknown snake bite.

In ICU, patient was given a stat dose of ten vials of Polyvalent Anti-Snake Venom (ASV) over 30 minutes, Injection Atropine 0.3mg (0.01mg/kg), Neostigmine 1.5mg, along with a short acting corticosteroid, an anti-histaminic and fluid therapy.

Her blood investigations showed pH - 7.37, PCO2 - 37.1, PO2 - 75.6, HCO3 - 21.6mmol/L. Creatine kinase was 95 U/L, Coagulation profile revealed Prothrombin time (PT)- 12.8 s (Control - 12.5), Activated Partial Thromboplastin Time (APTT) - 30.5 s (Control - 30.0) and International Normalized Ratio (INR) - 1.02. Liver function tests, renal function tests and complete blood count were within normal limits. Her Electrocardiogram and chest X-Ray did not reveal any abnormality.

Patient was then given 20 vials of ASV in 500ml of 5% Dextrose (5D) over 1 hour followed by 10 vials of ASV in 500ml of 5D over next 6 hours, Injection Neostigmine 1.5 mg half hourly for 5 cycles followed by 1.5mg 2 hourly with a total of 10.5mg over 7 hours. Injection Atropine was started at a dose of 0.6mg half hourly for 5 cycles followed by 0.6mg 2 hourly with a total of 4.2mg over 7 hours along with an antihistaminic, a short acting corticosteroid, antacid and fluids.

On Day 2 morning, she was afebrile, pulse rate was 140 bpm, pupils were dilated, and non-reactive, systemic examination was unremarkable. Patient was seen talking to self, speaking as if she was at home, telling her mother "To replace the emptied gas cylinder", "I'm going to take bath, put my clothes in the bathroom", she would talk as if she was interacting with her friend regarding studies (who was not present in the ward) and said she could see her friend. Mental status examination revealed that she was not oriented to time and place but was oriented to person, had auditory hallucinations and visual hallucinations.

Patient was given 10 vials of ASV in 500ml of 5D over 6 hours. Injection Neostigmine 1.5 mg 2 hourly with a total of 15 mg over 20 hours. Injection Atropine was given at a dose of 0.6mg 2 hourly with a total of 6mg over 20 hours along with supportive treatment. Her pupils were dilated and non-reactive, and heart rate was 130 bpm. Patient continued to be disoriented throughout the day, she was suspicious that her parents were talking about her (when they were not), she was also suspicious that someone may harm her and would ask her mother to be close to her revealing delusions of reference and persecution along with hallucinations on mental status examination.

On Day 3 early morning, a call for psychiatric consultation was noted. Blood investigations were repeated which were within normal limits. There was no past or family history of any psychiatric disorders. Patient's treatment chart and investigations were reviewed, and atropine induced delirium was suspected. Hence, it was advised to

stop Injection Atropine. The patient scored 9 on Naranjo Adverse Drug Reaction Probability Scale8 which suggests definite chance of adverse drug reaction. The patient was later continued on Injection Neostigmine 1.5mg, 8 hourly with supportive care.

After 3-4 hours of stopping atropine, patient's general condition was stable, she was oriented to place and person but not oriented to time, denied delusions but had fleeting auditory hallucinations. Towards evening, she was oriented to time, place and person, denied delusions or hallucinations. The patient was later discharged after 2 days with symptomatic improvement.

Discussion

We described a case of young female with a history of unknown snake bite who developed delirium after a day of atropine administration. Atropine toxicity can occur as a manifestation of an unusual sensitivity to a therapeutic dose (idiosyncrasy) or after an over-exuberant use in the treatment. Over-dosage of atropine may lead to manifestations such as dryness of mouth, flushing, dilated and non-reactive pupils, tachycardia and marked CNS disturbances which can range from disorientation to an active delirium.[9]

According to current FDA, the usual dose of parenteral atropine is 0.4 - 0.6mg (range: 0.3-1.2mg). Initial adult dose in muscarinic toxicity is 1-2 mg. Additional 2mg doses may be administered every 5-60 minutes until muscarinic symptoms and signs subside. Severe adverse effects such as ataxia, excitement, disorientation, hallucinations, delirium and coma can occur at dose of 10mg or more in an adult.[9] But our patient first developed symptoms and signs of delirium after a cumulative dose of 4.5mg of atropine over 8 hours. Gradually symptoms worsened when she was given an additional 6mg of atropine over next 20 hours.

Considering the presentation, the possibility of neurotoxicity due to snake bite can also be considered. But the patient received anti-snake venom and ACEI within 2 hours of snake bite, making this possibility remote. As the patient had temporal onset of symptoms following administration of atropine and subsequent resolution of symptoms occurred within 3-4 hours of stopping atropine, it suggests a remarkable association between the drug and the induced delirium. And these symptoms have occurred despite the patient receiving antimuscarinic agents in combination and at a lower dose (4.5 mg) than usual for the drug to cause these symptoms. Furthermore, other possible causes of delirium were ruled out with investigations.

Hence, clinicians need to be cautious while encountering such patients and should always consider the possibility of atropine induced delirium even in a case of snake bite. Limited research poses significant challenges in the management. There is a need for more research about proper guidelines for addressing such adverse events and atropine therapy in general.

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CONFLICT OF INTEREST

Nil.

Competing interests

Authors have declared that no competing interests exist.

Authors' contributions

This work was carried out in collaboration among all authors. All authors have read and approved the final manuscript.

Consent

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

Ethical approval

As per international standard written ethical approval has been collected and preserved by the author(s)

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