RODENTICIDE INDUCED REVERSIBLE LEUKOENCEPHALPATHY

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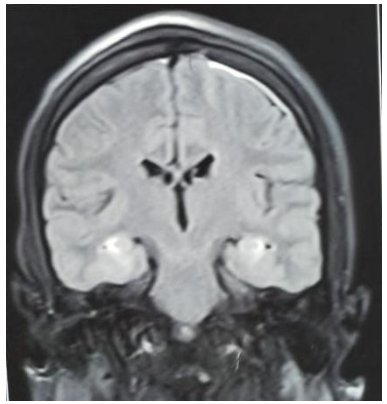
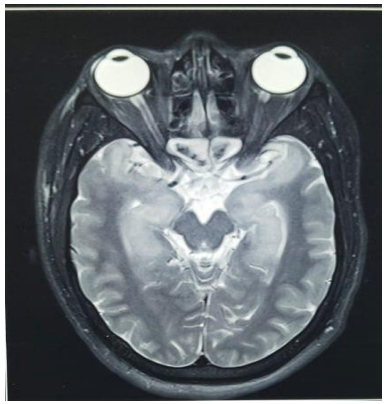
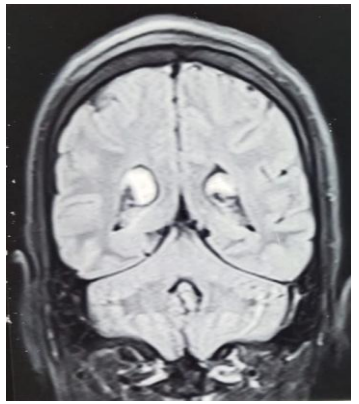
INTRODUCTION: *Rodenticide poisoning is widely known for its high mortality rate with no antidote available in market till date. It causes acute liver failure and multiorgan dysfunction in severe cases but rodenticide induced leukoencephalopathy and other potential CNS effects has not been reported yet in India.*







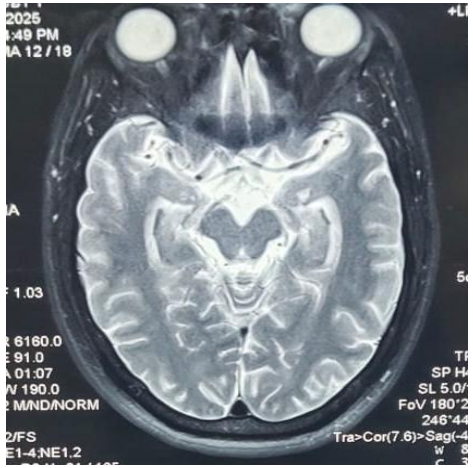
CASE DESCRIPTION: *A 30-year-old male was admitted with consumption of quarter of tube of rat killer paste. At admission, patient was stable and his baseline investigations were all within normal limits. Two days later, he developed mild icterus and had two episodes of generalized tonic clonic seizures.*

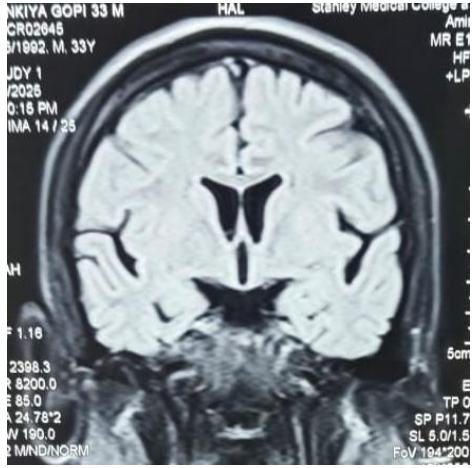
On examination he was irritable, febrile with no signs of meningeal inflammation. His total bilirubin was 3.3, SGOT-128 , SGPT-220, PT/INR-23.2/2.1. He was treated with vitamin K, NAC and antiepileptics. His fever settled in one day but he was disoriented and aggressive.

In view of new onset seizures and persisting altered sensorium, patient was suspected to have acute encephalitis. MRI brain with contrast was done which showed T2/FLAIR hyperintensities with diffusion restriction in bilateral medial temporal lobe with choroid plexus hemorrhage and left frontoparietal subdural hemorrhage.

<u>CSF analysis</u>
sugar-112 mg/dl
Protein-35 mg/dl
Total count- 0
RBC-2 cells/mm3
Culture- no growth
Viral panel- negative including HSV PCR

Patient showed persistent anger outburst at the end of ten days and possibility of Autoimmune encephalitis was considered but autoimmune panel turned out negative. Since possible etiologies like viral and autoimmune encephalitis were ruled out, possible toxin induced leukoencephalopathy was considered. Patient was discharged on antipsychotics and antiseizure medications. When he came for follow up after one month, he was completely asymptomatic with repeat imaging showing disappearance of limbic lesions





Superwarfarins, including brodifacoum, difenacoum, bromadiolone, and chlorophacinone, are anticoagulant rodenticides that are structurally similar to warfarin but contain terminal phenyl groups instead of terminal methyl groups. Substituting a terminal phenyl group makes superwarfarins 100-fold more potent compared to warfarin.

Discussion:

- *Rat killer paste contains 3% yellow phosphorus and Bromadiolone (super warfarin), which interferes with blood coagulation and can cross the BBB due to its high lipid solubility and can cause CNS toxicity.*
- *Wang et al and Li et al from China published similar cases who had bilateral symmetrical hyperintensities in internal capsule and corpus callosum and one of them had isolated CNS toxicity.*
- *Though the underlying pathophysiology is not yet well known but the presence of reversible diffusion restriction on DWI and low apparent diffusion coefficient indicates **transient intramyelinic cytotoxic edema.***
- *Vitamin K is a common cofactor for the enzyme γ-glutamyl carboxylase (GGC), which plays an important role in neuronal and glial cell physiology*
- *Deficiency of Vitamin K can decrease the carboxylation of protein in brain leading to reduced sulfatide synthesis which is critical for myelin formation.*
- *Super warfarin can have direct toxic effect in CNS by activating glial inflammation, stimulating the release of glutamate, which has an excitotoxic effect on Na-K pumps , leading to water influx into astrocytes and cytotoxic edema which might be the reason for transient white matter changes.*

Conclusion:

Rodenticide induced leukoencephalopathy is one of the reversible causes of leukoencephalopathy. Early identification and knowledge about the condition can prevent unnecessary investigations and provide reassurance for the patients

References:

1. *Wang M, Yang Y, Hou Y, Ma W, Jia R, Chen J. Effects of bromadiolone poisoning on the central nervous system. Neuropsychiatr Dis Treat. 2017 Aug 30;13:2297-2300. doi: 10.2147/NDT.S142375. PMID: 28919761; PMCID: PMC5587214.*

2. *Li, Q., Yu, W., Qu, Y. et al. Acute toxic encephalopathy following bromadiolone intoxication: a case report. BMC Neurol **21**, 8 (2021). https://doi.org/10.1186/s12883-020-02034-2*