

## Short reports

### Apnoea and seizures

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**SUMMARY** We report two infants with near miss sudden infant death syndrome events exhibiting seizure disorders after caffeine treatment, suggesting there is an infant subgroup diagnosed as near miss sudden infant death syndrome who have apnoea possibly with seizures whose seizure threshold may be lowered by central nervous system stimulants like caffeine.

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The infant presenting with an episode of apnoea probably represents a heterogenous group of clinical disorders. A diagnosis of 'Near miss sudden infant death syndrome' is usually made after a thorough evaluation fails to reveal the cause of an apnoeic episode. Infants considered to be at risk for further episodes may be placed on apnoea monitors or may be treated pharmacologically with caffeine or theophylline.<sup>1</sup> These drugs are potent central nervous system (CNS) stimulants and when used in high doses may produce convulsions in infants.<sup>2</sup> Therapeutic doses of methylxanthines may also precipitate convulsions in infants with latent seizure disorders not detected by routine electroencephalogram (EEG). This possibility was documented in two infants who presented with episodes of apnoea and forms the basis of this report.

Experience in these infants suggests that there is a subgroup of infants diagnosed as near miss sudden infant death syndrome who have apnoea associated with seizures. Seizure threshold may be lowered by CNS stimulants like the methylxanthines and result in clinical seizures.

#### Case reports

**Case 1.** A 2.5 month old boy was admitted to our hospital after an apnoeic episode. The infant was well until the mother noted an apnoeic episode lasting roughly 20 seconds. This occurred during quiet sleep and was not associated with colour changes or any abnormal movements.

Physical examination and further diagnostic evaluations, including EEG, yielded normal results (Figure (a)). A polygraphic recording performed simultaneously with the EEG showed one episode of central apnoea lasting 14 seconds, without associated abnormalities in the EEG, during a 20 minute testing period. A diagnosis of near miss sudden infant death syndrome was made, and the patient was started on treatment with caffeine. Two hours after an intravenous loading dose of caffeine citrate (20 mg/kg) a 15 minute generalised tonic-clonic seizure occurred. Repeat tests yielded normal results and a plasma caffeine concentration was 13.7 mg/l (therapeutic 8–20 mg/l). A repeat EEG, two days later, revealed epileptiform foci over the left temporal region (Figure (b)). A diagnosis of seizure disorder was made and the patient was started on treatment with phenobarbitone. No further episode of apnoea was noted.

On follow up, two years later, the child was off all drugs, had a normal neurological examination, and a normal EEG.

**Case 2.** A 4 month old girl was evaluated after three episodes of apnoea and cyanosis. The patient was well and had been developing normally until 10 days before admission when the mother noted that the infant was limp, apnoeic, and cyanotic while lying in the crib. This lasted 10–15 seconds. On the day of admission two more episodes occurred lasting 30 and 45 seconds.

Physical examination and further diagnostic evaluations yielded normal results. An EEG showed underlying delta wave disturbances and amplitude depression over both frontal poles. No epileptiform foci were observed.

A diagnosis of near miss sudden infant death syndrome was made and the patient was placed on treatment with caffeine. Twenty minutes after an oral loading dose of caffeine citrate (20 mg/kg), massive myoclonic jerks of all extremities were noted. This lasted 10 minutes. Repeat tests produced normal results. A diagnosis of infantile

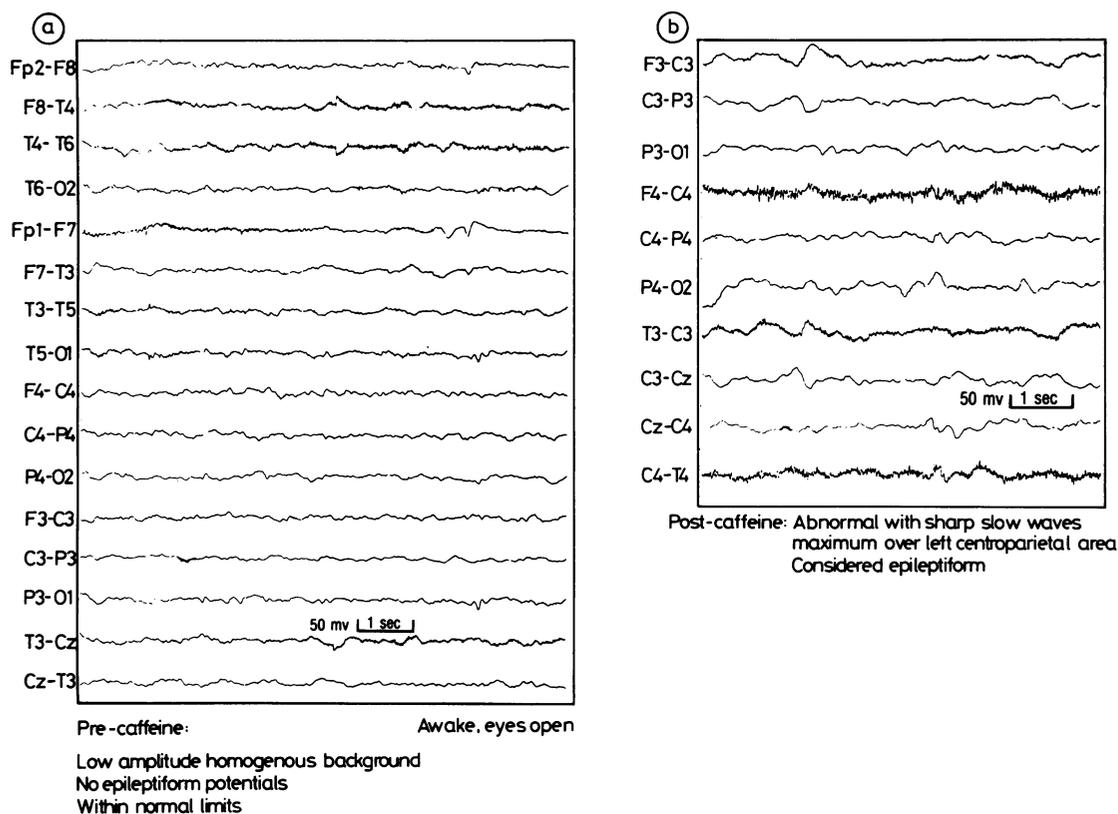


Figure (a) Electroencephalogram record of case 1 before caffeine administration. (b) EEG record of case 1 after caffeine administration and seizure episode. Note abnormal sharp slow waves, especially over the left centroparietal area.

myoclonic seizure disorder was made and the patient was started on treatment with clonazepam and prednisone. The EEG continued to show depression over both frontal poles. No epileptiform foci were observed.

The seizures were controlled with anticonvulsants and no further episode of apnoea has been observed. During the next two years, however, the patient showed developmental delay and neurological deficits.

## Discussion

When an infant presents with an apnoeic episode investigations are performed to detect abnormalities associated with apnoea. Only when a definitive aetiology cannot be established can a diagnosis of near miss sudden infant death syndrome be made.<sup>3</sup>

Kelly *et al* have observed that 50% of infants with near miss sudden infant death syndrome will experience another serious event and that 10% will die despite current monitoring techniques.<sup>4</sup> Recent

studies have recommended treating these infants with pharmacological agents that increase central respiratory drive, such as caffeine or theophylline.<sup>5,6</sup> Resolution of apnoea and normalisation of breathing patterns have been observed. It is still unclear, however, whether treatment with these drugs will prevent the syndrome.

Besides increasing central inspiratory drive, caffeine exhibits a variety of other actions, including CNS stimulation, smooth muscle relaxation, skeletal muscle stimulation, cerebral vessel constriction, and cardiac stimulation.<sup>2</sup> Caffeine possibly provokes or unmasks a seizure in infants with an underlying seizure disorder not shown by routine EEG. It is unlikely that caffeine given in therapeutic doses could directly cause seizures. A group of premature infants with neonatal apnoea treated with much greater dosages of caffeine showed only transient jitteriness with plasma caffeine concentrations as high as 84 mg/l.<sup>7</sup>

We also have treated 20 babies over the past two years for near miss sudden infant death syndrome

with caffeine and have had no other complications. All 20 infants had EEGs performed before treatment with caffeine and 13 of these infants had EEGs performed while being treated with caffeine. No abnormalities have been observed. The mechanisms involved in the 'unmasking' may be due to the stimulatory effect of caffeine on the CNS with lowering of the seizure threshold.

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## Neuroleptic malignant syndrome

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**SUMMARY** A case of the neuroleptic malignant syndrome, an idiosyncratic response to neuroleptic drugs, is described. Symptoms persisted for eight weeks. The stopping of neuroleptics and general supportive measures are the mainstay of treatment. Failure to recognise this syndrome can lead to morbidity and death.

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The neuroleptic malignant syndrome is the most serious yet least known complication of neuroleptic therapy, characterised by muscular rigidity, hyperthermia, altered consciousness, and autonomic dysfunction. It was first described in 1960<sup>1</sup> and up to 1984 over 80 cases had been reported, mainly in adult, medical, and psychiatric spheres. We report a case of the neuroleptic malignant syndrome occurring in childhood.

#### Case report

The case was an 8 year old boy, who had presented at the age of 10 months with microcephaly and mental handicap considered to be due to maternal treatment with phenytoin during pregnancy. He had attended a special school and was not being treated with drugs but had been given thioridazine in 1979 for nine days. There was no family history of anaesthetic problems. He had had a febrile illness

before admission and had been prescribed 5 mg prochlorperazine six hourly because of vomiting. After three days of treatment he had sudden onset of extreme agitation, opisthotonos, and episodic dystonic movements. This persisted and he was admitted to hospital.

On admission he had a fever of 38°C and was dehydrated. His remarkable posture and involuntary movements were unabated (Figure), yet he was able to recognise his parents. Except for transient benefit from sedation he remained in this state for the following eight weeks, also showing widespread evidence of autonomic dysfunction—that is, periodic rises of temperature to 40°C, profuse diaphoresis, apex rate 100 to 140 per minute, respiratory rate 45 to 50 beats per minute, and blood pressure 90/50 to 120/70. Investigations showed a white blood cell count of 13 000 and normal result of blood count, tests on cerebrospinal fluid, viral studies, electroencephalography, and computed tomography. He had raised liver and muscle enzymes: aspartate aminotransferase 662 (normal 8-40) iu/l, alanine aminotransferase 226 (normal 5-35) iu/l, and creatine phosphokinase 5243 (normal 0-130) iu/l. Initially, this was thought to be a prolonged drug induced dystonia, but the condition was unresponsive to the usual therapeutic regimens. It was noteworthy that the only drug that seemed to be of benefit in sedating the patient was thioridazine, itself a phenothiazine. After an interval of