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Case report

Acute disseminated encephalomyelitis due to abrus precatorius poisoning – A case report

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ABSTRACT

Abrus precatorius, commonly known as 'Rosary pea' or 'Jequirity pea' and known as 'Shisham, Batrah-Hindi or Ain Alfreeth' in the Middle East, grows wild in the tropical and subtropical areas of the world. The seeds of the plant contain one of the most potent toxins known to man. Poisoning with abrus seeds is a rare occurrence as the harder outer coat of the seeds generally resists digestion and such reports are scarce in the literature. We present here a case of a 22 year old lady who developed severe vomiting, diarrhoea and malena at the initial stages and later seizures and acute disseminated encephalomyelitis due to deliberate chewing and swallowing of abrus seeds. She was rescued with several sessions of membrane plasmapheresis and supportive care. The neuropathological process of acute disseminated encephalomyelitis due to abrus poisoning was reversed by plasmapheresis.

1. Introduction

Abrus precatorius, an invasive plant native to India, is commonly found in the tropical and subtropical areas of the world. The bright red coloured seeds are used in bead work and jewellery making. Roots and seeds of this poisonous herb are used in Ayurveda for treatment of alopecia and arthralgia after appropriate detoxification process. The seeds when crushed and ingested are highly toxic as crushing and chewing of the seeds will release a toxin called abrin. Poisoning from rosary seeds are due to abrin, a toxalbumin that acts by inhibition of protein synthesis. Abrin, a water soluble lectin, is made of two polypeptide chains (A and B) linked by a disulfide bridge (Pillay et al., 2005). Abrus seeds (Fig. 1) are nonpoisonous when ingested as whole since digestion is resisted by the harder outer shell. But chewing of the seeds will release the toxin and the polypeptide B chain binds to the intestinal cell surface receptors while the polypeptide A chain binds to the cytoplasm. Once inside the cell, the peptide chain A acts on the 60 S ribosomal subunit, preventing the binding of elongation factor 2 and thereby causing inhibition of protein synthesis and subsequent cell death. Abrin, an immune modulator, activates the humoral response of the host and may occasionally cause immune-mediated demyelination (Sahoo et al., 2008). The abrin content of *Abrus precatorious* seeds is about 0.15% w/w. The estimated human fatal dose of abrin after oral ingestion is 0.1–1.0 mcg/kg and consumption of even one chewed jequirity seed can be lethal in either adult or child (Dickers et al., 2003).

2. Case report

A 22 year old, 65 kg lady, with alleged consumption of abrus seeds for suicidal intent, was presented with abdominal pain, vomiting and diarrhoea 24 h after ingestion. On day 2, she developed malena associated with abdominal pain and her hemoglobin level dropped to 6.5 g/dl. On day 3, there was progression of symptoms and the patient became febrile following which she had three episodes of generalised tonic clonic seizures at intervals of about 45 min. She was treated with fosphenytoin, clobazam, mannitol and antibiotics in a local hospital. Later her symptoms resolved. But on day 7 of ingestion, she had again two episodes of seizures and she was referred to our centre (Amrita Institute of Medical Sciences, Kochi) for further investigation.

Upon presentation to our centre, she had a pulse rate of 142 beats/min, respiratory rate of 24 breaths/min, blood pressure of 138/82 mm Hg (Table 1) and a Glasgow coma score (GCS) of 7 ($E_1V_2M_4$). She was maintaining 100% saturation on room air but had pallor and tachycardia (113 beats/min). There were no symptoms of active bleeding or coagulopathy. Her peripheral pulses were palpable and both pupils were 2 mm in diameter and reacted

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Fig. 1. (a): Abrus seeds. 1a: Abrus seeds. 1b: Flower, seed pods and seeds of *Abrus Precatorius.*

Table 1
Vitals of the patient during hospitalisation at our centre.

Day	Temperature (°F)	Pulse (beats/min)	Respiratory rate (breaths/min)	Blood pressure (mm/Hg)
Day 1	99.6°	142	24	138/82
Day 2	99.8°	120	22	126/84
Day 3	100.2°	112	24	115/76
Day 4	100°	106	22	106/70
Day 5	100°	100	24	118/70
Day 6	101°	98	18	120/70
Day 7	101°	100	22	100/70
Day 8	100.8°	100	22	120/70
Day 9	100.6°	100	24	100/70
Day 10	99.8°	98	20	96/60
Day 11	99.6°	100	22	118/73
Day 12	99.4°	88	22	116/60
Day 13	98.6°	88	20	128/76
Day 14	98.6°	86	22	130/80
Day 15	98.6°	84	24	120/86
Day 16	98.6°	84	24	110/70
Day 17	98.6°	82	22	100/70
Day 18	98.6°	80	22	110/80
Day 19	98.6°	82	22	100/80
Day 20	98.6°	80	22	120/70

to light. There was no papilledema. On examination, chest was clear and there were no added sounds. Initial lab investigations showed elevated C-reactive protein of 72.52 mg/L (reference range: 0.0–1.0 mg/L), neutrophilic leucocytosis, 87.6% (reference range: 60–80%), hyponatremia, 130.3 mmol/L (reference range: 136–146 mmol/L), hypokalemia, 3.1 mmol/L (reference range: 3.5–5.1 mmol/L) and elevated ammonia 63.7 mmol/L (reference range: 10–47 mmol/L).

In view of acute gastroenteritis and recurrent episodes of seizures, she was shifted to intensive care unit and treated with intravenous levetiracetam 500 mg BD, clobazam 10 mg OD and midazolam infusion. Antibiotics were administered for prevention of possible aspiration pneumonia. Later, she had an episode of desaturation and was intubated and mechanically ventilated for airway protection. Toxicological analysis of urine by thin layer chromatography tested positive for alkaloids of abrus.

Neurologic consultation was sought in view of recurrent seizures. Magnetic resonance imaging (MRI) showed hyperintense signals in bilateral thalami, right globus pallidus and right cerebral peduncle, not showing diffusion restriction or blooming on gradient sequences with mild heterogenous post contrast enhancement. Features were likely to represent acute disseminated encephalomyelitis (ADEM) and smooth pachymeningeal enhancement along the falx and bilateral cerebral convexities (Fig. 2a). The patient was treated with intravenous methyl prednisolone 1 g, followed by oral dexamethasone and antiepileptic drugs. But the steroid therapy was a failure and she continued to have seizures. After nephrology consultation, she was initiated on membrane plasmapheresis which was continued for three days along with supportive care. Plasma separators with a sieving coefficient of 0.8–0.9 were used in the hemodialysis machine instead of dialyzer. Central venous access to the patient was ensured throughout the procedure to maintain the blood flow between 100 and 150 ml/min. For prevention of clotting in the plasmapheresis circuit, 5000 IU of heparin was administered as bolus followed by 2000 IU as hourly infusion during the procedure. 150 ml of patient's blood was allowed to pass at a time into the plasma filter where plasma was removed and discarded. Safety air detector ensured that formed elements, which was pumped back into her circulation was free from air. To safeguard against hypotension, only one litre of plasma (20 ml/kg) was removed during first session of plasmapheresis followed by two litres (40 ml/kg) in the consecutive sessions. Fresh frozen plasma (FFP) and normal saline were used as replacement solutions (50:50). In order to prevent hypocalcemia caused by trisodium citrate added in FFP, 10 ml of 10% intravenous calcium gluconate was infused every hour during each session. Each plasmapheresis session was of 2 h duration.

Repeat toxicological screening of urine confirmed the previous findings of alkaloids in the urine sample. But electroencephalography (EEG) showed a complete disappearance of burst suppression pattern which was evident in the previous EEG before administration of midazolam infusion. Hence she was continued on midazolam infusion. Meanwhile, she developed fever spikes and microbiological culture of bronchoalveolar lavage isolated *Acinetobacter baumannii* and her antibiotics were escalated to meropenem 1 g TID and colistin 3 million units TID. On neurological review, midazolam was discontinued after appropriate tapering. She then showed improvement in sensorium with GCS score of 10 (E4VTM6). A follow up MRI (Fig. 2b) showed improvement in hyper

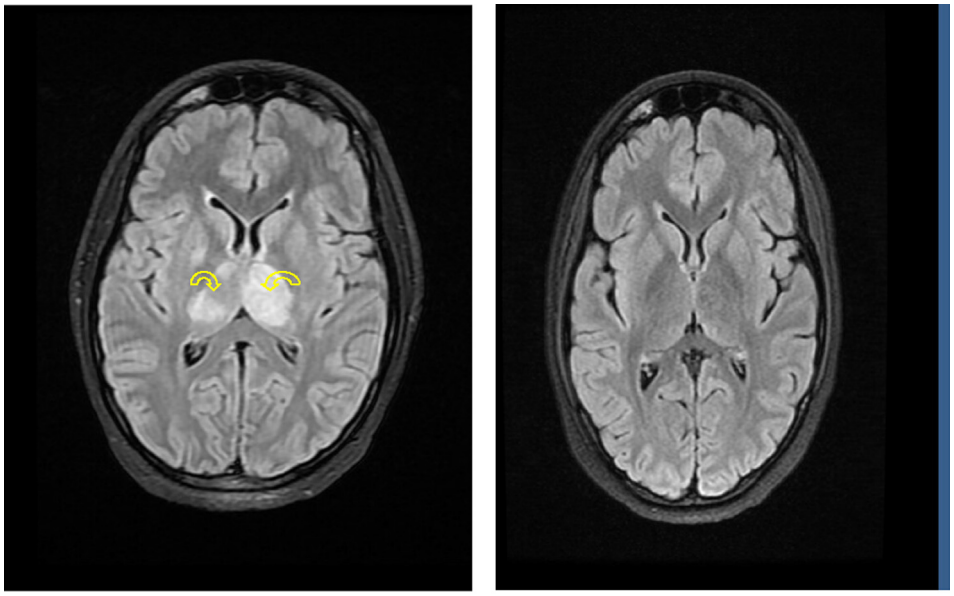

Fig. 2. (a): Magnetic resonance imaging of brain prior to plasmapheresis showing hyperintense signal in bilateral thalami (pointed arrows). (b) Resolution of ADEM after six sessions of plasmapheresis.

Table 2
Pertinent Laboratory results on various days of hospitalisation at our centre.

Parameters	Day 1	Day 3	Day 5	Day 7	Day 9	Day 11	Day 13	Day 15	Day 17	Day 18	Reference values
Hb (g/dl)	8.6	8	9.1	8.7	8.2	7.3	8.3	8.8	8.3	8.8	12.5–15.5
WBC (ku/ml)	15.44	17.84	12.19	26.6	15.8	8.9	8.56	6.18	6.93	7.61	4.0–11
N (%)	87.6	90.4	93.9	89.4	68.9	55.2	72.0.1	54.9	63.1	73	60–80
Urea (mg/dl)	18.1	41.2	56.3	42.2	31.1	–	14.9	–	–	–	17–43
S.Cr (mg/dl)	0.98	0.82	0.87	0.85	0.76	–	0.81	–	–	–	0.7–1.4
Na^+ (mEq/L)	130.3	136.2	140.0	137.5	138.9	134.7	134.7	–	–	–	136–146
K^+ (mEq/L)	3.1	3.6	3.9	3.7	3.9	4.5	4.0	–	–	–	3.5–5.1
CRP (mg/dl)	72.52	–	–	33.52	–	–	14.52	–	–	–	<1

Hb: Hemoglobin; WBC: White Blood Cell count; N: Neutrophil; L: Leucocyte; S.Cr: Serum creatinine; Na+: Serum Sodium; K+: Potassium; CRP: C-Reactive Protein.

intense flairs. Three more sessions of plasmapheresis, on alternate days, were done and subsequent lab values (Table 2) showed improvement in inflammatory markers. She was then extubated and started on incentive spirometry. Echocardiogram was normal and a repeat toxicology screen done after the sixth session of plamapheresis tested weakly positive for alkaloids in the urine sample. A repeat EEG showed no evidence of localization or epileptiform abnormalities. She had memory disturbances mainly amnesia. Anemia work up showed presence of iron deficiency (Transferrin saturation: 3.6%, reference range: 25–35%). Peripheral blood smear showed microcytic hypochromic anemia with polychromasia and thrombocytosis. She was given one dose of parenteral ferric carboxymaltose (500 mg) and switched over to oral iron supplements which she tolerated well. She remained seizure free and showed improvement in parameters of laboratory investigations (Table 2). At the time of discharge, she was conscious, hemodynamically stable, fully oriented to time, place and person but unable to recollect anything related to the primary incident.

3. Discussion

The usual fatal dose of 'rosary pea' ranges from 90 to 120 mg (1–3 seeds) though a single chewed jequirity seed may be fatal in either adult or child. The abrin content of *Abrus precatorious* seeds is about 0.15% w/w. The estimated fatal dose of abrin after oral consumption in human is 0.1–1.0 μg/kg. The minimum lethal dose in humans by intravenous injection is estimated to be 0.3 μg/kg whereas the median lethal dose (LD_{50}) in rats after abrin inhalation was 3.3 μg/kg (Dickers et al., 2003). A fatal case of abrus poisoning was reported in a two year old boy with accidental ingestion of the seeds (Patil et al., 2016). A mortality rate of 5.35% has been reported in a retrospective study of 112 patients with abrus poisoning (Karthikeyan et al., 2017).

There are only few data available on the toxicokinetics of abrin. Abrin has high molecular weight (65 kDa) which limits its gastrointestinal absorption. Experimental study done on mice showed that greatest fraction of administered intravenous dose was distributed to liver followed by blood, lungs, spleen, kidney and heart (Fodstad et al., 1979). The intact toxin is resistant to proteolytic enzymes in vitro. Inside the tissues, the toxin gets degraded after reduction of the disulfide bridge and separation of polypeptide chains. Elimination of abrin is almost completely by the renal route (Fodstad et al., 1976).

There have been cases of ingestion of large number of rosary pea seeds resulting in less severe clinical symptoms (Alhamdani et al., 2015; Fernando, 2001). This may be due to poor gastrointestinal absorption of abrin from the uncrushed seeds. The symptoms are much less likely to occur if the seeds are ingested as whole. Though there is delay in the appearance of symptoms after

ingestion of seeds, aggressive treatment is necessary in all cases. Gastric emptying methods such as induced emesis, use of activated charcoal, gastric lavage and whole bowel irrigation can be considered as useful treatment strategies at the early hours after ingestion (Pillay, 2008). Till date, there are no antidotes for abrin poisoning and the treatment is mainly supportive (Wooten et al., 2014).

As our patient was presented to the local hospital after 48 h of ingestion, gastric lavage and administration of activated charcoal were not good options. Hence she was managed conservatively. Although the cause of death was renal failure in most reported cases (Pillay et al., 2005), serum creatinine levels of our patient were normal. ADEM is one of the rare complications of 'abrus' poisoning (Sahni et al., 2007) and should be suspected in an 'abrus' poisoning case if the patient develops early central nervous system symptoms such as depression, seizures and altered sensorium. There is a report of complete resolution of ADEM with the use of corticosteroids (Sahoo et al., 2008). But our patient developed typical symptoms of abrus poisoning such as vomiting, abdominal pain, malena and seizures (Fernando, 2001) at the initial stages and her demyelination failed to respond to the administration of corticosteroids (Apak et al., 1999, Mao-Draayer et al., 2002). Hence the patient underwent plasmapheresis and her symptoms resolved after six sessions of plasmapheresis. Plasmapheresis helps in reversing the neuropathological process involved in demyelination (Shinozaki et al., 2008). It is also used in the management of autoimmune diseases like Myasthenia gravis, Guillain-Barre syndrome, Lamber-Eaton myasthenic syndrome and also in poisoning cases (Dyck et al., 1985). It removes the autoimmune antibodies that have been formed against normal tissues. The advantage of plasmapheresis over other extracorporeal techniques is the faster removal of toxins irrespective of the amount. Overdosing of drugs like carbamazepine, digoxin, phenobarbital, phenytoin, valproic acid can also be well managed by plamapheresis (Nenov et al.,2003).

Few case reports of this rare poisoning have been published till date and were managed conservatively with gastric emptying methods (Alhamdani et al., 2015, Subrahmanyan et al., 2008)). A report from China suggests a combination of continuous renal replacement therapy (CRRT) and hemoperfusion techniques for treating abrus poisoning (Huang et al., 2017). A rare case of cerebral venous sinus thrombosis due to abrus poisoning was reported (Vinod et al., 2013). Similarly, abrin induced hemorrhagic colitis and hemorrhagic gastroduodenitis were also published in the literature (Ganesan et al., 2015; Khanra et al., 2014 respectively).

4. Conclusion

Acute disseminated encephalomyelitis is one of the rare complications of *Abrus precatorius* poisoning. Although high-dose corticosteroid treatment is a widely accepted therapeutic approach in ADEM, treatment failures and relapses are still reported. Age might influence the clinical course and therapeutic response in ADEM with young patients being more prone to relapse and treatment failures. This should be taken into consideration in designing therapeutic trials in ADEM. Although there are conflicts of interests with the use of corticosteroids to manage ADEM due to abrus poisoning, this case report testifies the unequivocal role of plasmapheresis in the treatment of ADEM due to abrus poisoning.

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