

Case Report

Complication of Brain Disease During a Radiological Intervention-an Alleged Case of Medical Negligence

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ABSTRACT

Infections are the most common predisposing factor both in neonates and children, followed by hematological states, dehydration and various other conditions. Cerebral sino-venous thrombosis (CSVT) encompasses a spectrum of disorders involving thrombosis of the cerebral venous system. Timely diagnosis and treatment are critically important for optimizing outcome. Twenty three months old male child with complaints of vomiting and abnormal eye movements (more on left side) was admitted in a hospital. To rule out intracranial pathology for asymmetrical movements, the child was advised Contrast MRI of Brain. At 08:00 pm, he was given Inj. Gadodiamide (Omniscan) 0.5 mmol/ ml solution for contrast imaging. The child developed sudden cardiac arrest immediately after MRI scan was completed, at 08:50 pm and declared as dead at 09:40 pm. MR Venogram showed thrombus in superior sagittal sinus, proximal part of transverse sinuses & part of straight sinus. Non-Visualization of cerebral cortical veins on both sides was suggestive of thrombosis. Autopsy was performed by board of doctors after a complaint of medical negligence was made by the parents of the deceased. After perusal of clinical record, post-mortem report and FSL report, the board was of the considered opinion that findings were suggestive of thrombus in superior sagittal sinus and proximal part of transverse sinus and in cortical veins of both cerebral hemispheres and was a sudden natural death.

Keywords: Thrombosis, MRI, Medical Negligence, Autopsy

CASE SUMMARY

A 23 months old male child with complaints of vomiting, since 02 days, and abnormal eye movements, since 1 day, was admitted in a hospital. There was no respiratory distress and no neurological deficit but asymmetrical eye movements were present on left side more than the right side. Routine tests came within normal ranges. To rule out intracranial pathology for asymmetrical movements,

the child was advised Contrast MRI of Brain. On the set date at 07:30 pm, he was given Inj. Midazoam 2 ml slow iv and Inj. Emset 2 ml slow iv. After 30 min i.e. 08:00 pm, he was given Inj. Gadodiamide (Omniscan) 0.5 mmol/ ml solution for contrast imaging. The child developed sudden cardiac arrest immediately after MRI scan was completed, at 08:50 pm. Standard resuscitative measures were followed but he could not be revived and declared as dead at 09:40 pm.

MRI Report

Blooming seen from cortical vein, transverse sinuses and superior sagittal sinus on gradient images. MR Venogram showed thrombus in superior sagittal sinus, proximal part of transverse sinuses & part of straight sinus. Non-Visualization of cerebral cortical veins on both sides were suggestive of thrombosis.

The body was shifted to mortuary after a complaint of medical negligence was made by the parents of the deceased. A board of doctors was constituted to perform an autopsy on the body of the deceased to investigate medical negligence.

On post mortem examination no significant findings were noticed on external examination apart from the documented injection prick marks. On internal examination, all the organs were congested and edematous. Brain was edematous with flattening of Gyri and obliteration of Sulci, with weight of 1050 gm. Lungs were congested and edematous with weights of 100 gm and 80 gm for right and left lungs respectively. Pericardium and heart were unremarkable, with weight of heart 75 gm. The alimentary tract was unremarkable. Both the kidneys were congested, edematous and with distinct cortico-medullary differentiation. Other findings were unremarkable.

Histopathology examination

On Gross examination, multiple dilated blood filled spaces seen throughout the lung parenchyma and on microscopy lungs showed presence of mucus and RBCs in bronchioles, denudation of lining epithelium, marked vascular congestion, interstitial edema with thickened

alveolar septa and focal lymphocytic aggregates were also seen. Brain on gross examination showed multiple pinpoint area of congestion in white matter and on microscopy show vascular congestion.

SUBSEQUENT OPINION

After perusal of clinical record, post-mortem report and FSL report, the board was of the considered opinion that

1. The concentrations of midazolam and Gadodiamide (omniscan) in post-mortem blood are within normal administered doses.
2. The cause of death in this case was cerebral edema which could be possible in a patient suffering from neurological condition findings suggestive of thrombus in superior sagittal sinus and proximal part of transverse sinus and cortical veins of both cerebral hemispheres and was a sudden natural death.

DISCUSSION

Causes of Thrombosis in Pediatric Patient

Infections are the most common predisposing factor both in neonates and children, followed by hematological states, dehydration and various other conditions. In most of cases, it results from combination of prothrombotic risk factors with or without underlying clinical condition^[1].

Cerebral sino-venous thrombosis (CSVT) encompasses a spectrum of disorders involving thrombosis of the cerebral venous system. There is a male predominance (60–70%), and neonates accounting for 30–50% of cases^[3,4].

Table 1: Chemical Analysis Report of Viscera

Concentration	Concentration of Midazolam, Diazepam and Gadodiamide in Exhibits		
	Blood	Bile	Urine
Midazolam	0.0106 µgm/ml	0.645 µgm/ml	0.0438 µgm/ml
Diazepam	0.0108 µgm/ml	1.948 µgm/ml	0.355 µgm/ml
Gadodiamide (Omniscan)	250 µgm/ml	98 µgm/ml	24 µgm/ml

No other poison was detected in the viscera analysis.

The cerebral venous system is composed of a network of cortical, medullary, and deep veins which drain into dural venous sinuses. These comprise the superficial dural sinuses (sagittal, transverse, and sigmoid) and the deep venous system (straight sinus, vein of Galen). Thrombosis of cerebral venous system impedes venous outflow, resulting in increased central venous pressure, which in turn causes intracranial hypertension. In some cases, this leads to cerebral ischemia, which may evolve to infarction, often hemorrhagic. In the most severe cases, diffuse cerebral edema and widespread infarction and hemorrhage may result in permanent neurologic disability, or herniation and death.

Timely diagnosis and treatment are critically important for optimizing outcome. As in arterial ischemic stroke, “time is brain” should be the guiding principle in managing CSVT. This begins with raising awareness of the clinical signs and symptoms, particularly among front line providers, for children who are at greatest risk—neonates, children with acute head/neck infections, and children with those chronic diseases carrying an increased risk of thrombo-embolism. The triad of symptoms—progressive unremitting headache, altered mental status, and vomiting—should prompt consideration of a diagnosis of CSVT, and neuro-imaging evaluation specifically targeting this condition.

Presentation of child with thrombosis

Thrombosis often occurs within the posterior fossa and may occur in association with dural malformations such as dural arteriovenous shunts. The foetal venous drainage system may be less susceptible to thrombosis compared with the neonate, as foetal anastomosis may result in the foetus being able to redirect venous blood flow^[6].

The common signs and symptoms would be seizures focal or generalised, depressed level of consciousness, coma, Lethargy, vomiting, Nausea, headache, visual disturbances or blindness, papilledema, hemiparesis, hemisensory loss, ataxia, speech impairment, dysarthria, VI nerve palsy, acute psychiatric symptoms, respiratory failure in neonates, jittery movements in neonates^[7].

On CT scans there are three direct signs of CSVT in the CT-scan, the “string sign, the “dense triangle sign,” and the “empty delta sign. “The “string sign” is found in 25% of CSVT patients, it appears when there is cortical vein thrombosis in the non-contrast enhancing CT. It looks like an elongated hyperdense image relating to the brain parenchyma.

The “dense triangle sign” can be seen during the first 2 weeks in up to 60% of and represents spontaneous SSS opacification from fresh coagulated blood. Mimicking occurs in patients with increased haematocrit or dehydrated. Overall, this sign has been reported in only 2% of CSVT cases; and the “empty delta (or empty triangle) sign,” seen after the contrast medium is administered, has been reported in between 10% and 35% of cases;^[9] it is produced due to an intraluminal filling defect surrounded by contrast in the posterior portion of the SSS;^[8] there is enhancement in the wall of this sinus that is outlining the hypodense clot within the lumen^[10]. Usually is associated with poor prognosis.

An MRI can even be normal in up to 30% of patients^[10]. The presence of thalamic oedema is highly suggestive of deep venous occlusion; this is an alarming finding, because the patient may deteriorate quickly to coma. Parenchymal haemorrhage can be seen in up to 30% of the CSVT cases. In patients with SSS thrombosis, typically is the finding of flame-shaped, irregular zones of lobar haemorrhage in the parasagittal frontal and parietal lobes. This should prompt additional imaging evaluation with MRV or CTV. The transverse sinus thrombosis can be seen as haemorrhage lesions in temporal or occipital lobes. MRI with T2 sequences is sensitive in the depiction of zones of parenchymal haemorrhage. MRV and CTV have equivalent sensitivity and specificity for demonstration of the thrombosed segment.

Midazolam

A medication used for anesthesia, procedural sedation, trouble sleeping, and severe agitation and seizures.^[10,11] Side effects can include a decrease in

efforts to breathe, low blood pressure, and sleepiness^[11]. Paradoxical effects, such as increased activity, can occur especially in children and older people^[12].

Midazolam is known to cause respiratory depression. In healthy humans, 0.15 mg/kg of midazolam may cause respiratory depression.¹³ Concentrations of midazolam or its major metabolite, 1-hydroxymidazolam glucuronide, may be measured in blood, to confirm a diagnosis of poisoning in hospitalized patients, or to assist in a forensic investigation of a case of fatal overdose.

Diazepam

Diazepam, typically produces a calming effect^[14]. It is used as a premedication for inducing sedation, anxiolysis, or amnesia before certain medical procedures^[15]. Benzodiazepines have a relatively low toxicity in overdose^[12]. Too much diazepam typically displays one or more of these (Drowsiness, Mental confusion, Hypotension, Impaired motor functions, Impaired reflexes/coordination/balance, Dizziness, Coma) symptoms in a period of approximately four hours immediately following a suspected overdose^[16].

Diazepam may be analyzed in blood to confirm a diagnosis of poisoning in hospitalized patients, or in a medico-legal death investigation. Blood or plasma diazepam concentrations are usually in a range of 0.1–1.0 mg/l in persons receiving the drug therapeutically and 2–20 mg/l in victims of acute overdose.

Gadodiamide

Gadolinium-based contrast agents (GBCAs) are intravenously administered drugs that help radiologists interpret magnetic resonance imaging (MRI) examinations by enhancing contrast in body tissues where the GBCA is located. OMNISCAN™^[17] (gadodiamide) is a linear, non-ionic, non-protein binding GBCA.

Serious side-effects are less common but are occasionally fatal despite local acute care. Previously, a large number of independent clinical studies have shown concordant results, and demonstrate that non-ionic, linear

GBCAs such as Omniscan have measurably lower acute hypersensitivity reaction rates than other agents.

Sudden onset of thrombosis of cerebral sinus coinciding with radiological intervention i.e. MRI contrast may trigger suspicion of medical negligence in the mind of patients relative.

As the patient care is in line with the commonly followed protocol and the treatment was provided by qualified doctors at the imaging center, which was an authorized imaging center, as per the facts provided by the police, the possibility of medical negligence in this case can be ruled out.

CONCLUSION

A child who is already suffering from cerebral sinus thrombosis may be perceived as a case of medical negligence by the relatives of the patient especially when the child's condition gets worsened in natural course of the disease during the radiological intervention/investigation which are usually advised in such cases.

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