Uttar Pradesh Journal of Zoology

Volume 45, Issue 18, Page 652-657, 2024; Article no.UPJOZ.4112
ISSN: 0256-971X (P)

Recovery of Accidental Traumatic Brain Injury (TBI) in an Infant Bonnet Macaque (*Macaca radiata*) by Progesterone Therapy

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Authors' contributions

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

Article Information

DOI: https://doi.org/10.56557/upjoz/2024/v45i184482

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://prh.mbimph.com/review-history/4112

Case Study

Received: 14/07/2024
Accepted: 18/09/2024
Published: 23/09/2024

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Cite as: *Premalatha, N., P.K. Ramkumar, S. Sathishkumar, E. Tamileniyan, M. Saravanan, M. Veeraselvam, and S. Senthilkumar. 2024. "Recovery of Accidental Traumatic Brain Injury (TBI) in an Infant Bonnet Macaque (Macaca Radiata) by Progesterone Therapy". UTTAR PRADESH JOURNAL OF ZOOLOGY 45 (18):652-57. https://doi.org/10.56557/upjoz/2024/v45i184482.*

ABSTRACT

An infant male bonnet macaque with a history of accident and lateral recumbency presented to the Veterinary Clinical Complex, VCRI, Orathanadu. On examination he scored a 10 on the modified Glasgow Coma Scale (GCS), and the animal had racoon eyes. Immediately skull X-ray was taken and it revealed two radiating temporal bone fracture. These characteristics strongly pointed to a tentative diagnosis of Traumatic Brain Injury. In addition to supportive care, Progesterone, a neuroprotective steroid, was continuously administered to the animal at a dose rate of 0.2 mg per kg SID P.O. In order to manage and monitor the animal health, it was admitted to the critical care unit. On the tenth day, the animal showed slight improvement and had hemiparesis on the contralateral side of the cranial lesion. The animal's limb reflexes were fully restored by day 20. However cerebral and vestibular lesions persisted with signs of blindness, nystagmus, and circling. After 60 days of continuous treatment animal recovered uneventfully.

Keywords: Bonnet macaque; brain injury; progesterone; neurology; TBI; temporal fracture.

1. INTRODUCTION

Among India's 22 known primate species, the bonnet macaque (*Macaca radiata*), rhesus macaque (*Macaca mulatta*), long-tailed macaque (*Macaca fascicularis*) and Hanuman langur (*Semnopithicus* sp.) are the most common commensal primates in India due to their adaptation to a human-dominated environment. *Macaca radiata* is the most commonly seen monkey in South India, found in both villages and forests of Tamil Nadu [1]. Traumatic brain injury (TBI) poses a significant threat to the survival and well-being of wildlife populations, with particular concern for species inhabiting regions where human activities intersect with natural habitats. Among these species, the bonnet macaque in Tamil Nadu, India, emerges as a focal point of study due to the escalating instances of road accidents resulting in severe brain injuries, damages, and fatalities. As urbanization expands and road networks crisscross through their habitats, the bonnet macaque faces a heightened risk of collision with vehicles [2], leading to detrimental consequences for individual primates and potentially impacting the overall population dynamics. The vestibular system was a complex network of structures within the inner ear and brain that was responsible for maintaining balance and spatial orientation. This paper highlights the successful therapeutic management of accidental traumatic brain injury (TBI) in a bonnet macaque. The creation of novel translational models of traumatic brain injury (TBI) that concentrate on a range of injury-related comorbidities is advancing efforts to enhance the daily lives of these patients.

2. CASE HISTORY AND TREATMENT

An infant male bonnet macaque was presented to the Exotic and Special Species Medicine Referral Clinic, Veterinary Clinical Complex, VCRI, Orathanadu, TANUVAS with a history of accident and lateral recumbency by the forest department, Pattukottai division. Clinical examination of the monkey on the day of presentation revealed the presence of racoon eyes (Fig. 1) which is a characteristic feature of basillar skull fracture, with the temperature of 31.8^{o}C and pale mucous membrane. Based on the Modified Glasgow Coma Scale, the monkey was assigned a score of 10 (Table. 1) and treated as an emergency. The bonnet macaque was immediately subjected to the warmer with a temperature of 40^{o}C and with fluids Ringer's lactate @1ml/kg. Once the temperature returned to normal, the monkey was subjected to radiographic examination which revealed the radiating temporal, parietal and occipital bone fracture (Fig. 2). Initially the animal was treated with Chloramphenicol @25 mg/kg and multivitamin supplementation for 2 days. Observation on Day 3, showed signs of recumbency, partial blindness, nystagmus and circling. Pupillary light reflex and pain reflex were sluggish, which was highly suggestive of traumatic brain injury (Figs. 3, 4). The condition was diagnosed as accidental Traumatic brain Injury. The treatment regimen was re-scheduled accordingly and the animal was treated with Hydroxyprogesterone @0.2 mg/kg B.W. PO [3] from the Day 1 and continued for 20 days, Ceftriaxone @15 mg/kg B.W. I/V, and Cholecalciferol @0.1 mg/kg B.W. S/C for 5 days. The animal was supplemented with methylcobalamine, nicotinamide syrup, liver tonics and haematinics.

Table 1. Treatment regimen

Component	Description	Obtained score
Eye Opening	Eyes open in response to verbal stimuli	3
Verbal Response	Sound produced was sluggish	3
Motor Response	Withdraws from painful stimuli	4
Total	Comatose	10

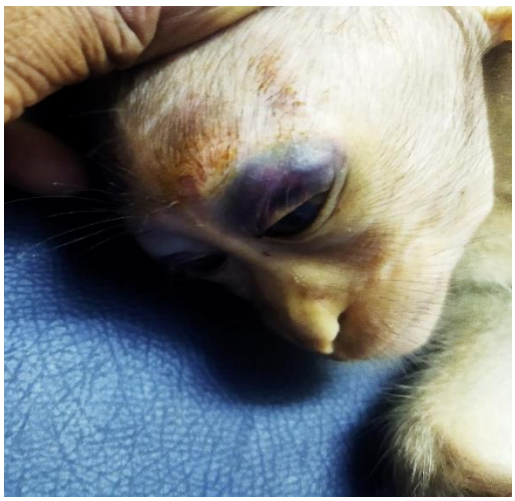

Fig. 1. Infant bonnet macaque presented with racoon eye appearance

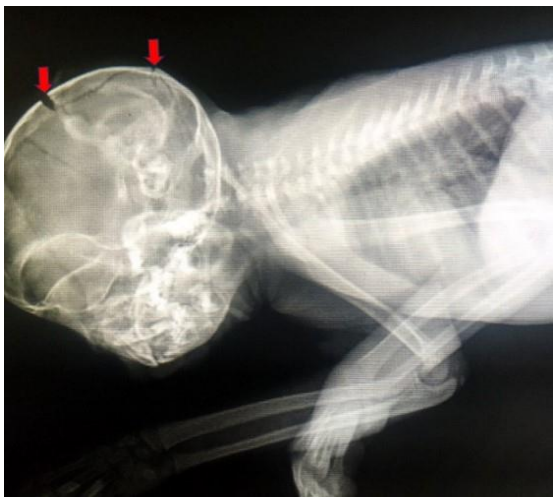

Fig. 2. Radiograph showing multiple skull fracture (Arrow)

Fig. 3. Day – 3 of presentation with recumbency, partial blindness and nystagmus

Fig. 4. Day – 3 of presentation with absence of placing reflex

3. DISCUSSION

Clinical examination on Day 20 showed Positive for Pupillary Light Reflex with sluggish menace, still partial blindness was noticed (Fig. 5). The examination on Day 60 revealed normal vital parameters (Figs. 6, 7), with the fracture almost healed and all internal organs appearing normal in the sonogram.

TBI is physical injury to brain, in which our present case was TBI with Basilar skull fractures leading to possible subdural hematoma. Basilar skull fractures, usually caused by substantial

blunt force trauma, involve at least one of the bones that compress the base of the skull which tends to influence vestibular and cerebellar function. Cerebellar disorders cause loss of fine motor control in the head and body, which manifests clinically as cerebellar ataxia, intention tremor and hypermetria [4]. The most common sign of vestibular dysfunction is the loss of balance. In some instances, the symptoms were usually limited to the affected side of the vestibular system [5]. Animals with damaged vestibular systems exhibited symptoms such as head tilt, ataxia, nystagmus and circling in which our case exhibited the signs of circling and ataxia. In traumatic brain injuries (TBI) involving cranial fractures, specific cranial nerve deficits can occur depending on the location of the fracture. A temporal bone fracture often leads to deficits in cranial nerves 7 (facial nerve) or 8 (vestibulocochlear nerve), resulting in facial paralysis or vestibular dysfunction. Vestibular signs, such as balance issues or vertigo, commonly indicate damage to cranial nerve 8. In contrast, a parietal bone fracture may affect cranial nerves 3 (oculomotor), 4 (trochlear), 5 (trigeminal), or 6 (abducens), causing issues with eye movement, sensation, or mastication. Hemiparesis on the contralateral side of the lesion is often seen due to motor pathway disruption.

Diagnosis and treatment in traumatic brain injury (TBI) in animals was highly difficult due to the multi-variant signs exhibited. To prevent deterioration or death, moderate to severe TBI needs to be identified and treated immediately. In contrast to humans, there has been no agreement regarding ways to deal with animal TBI. Although many diagnostic and therapeutic targets had been identified,

Fig. 5. Day 20 with circling and partial blindness

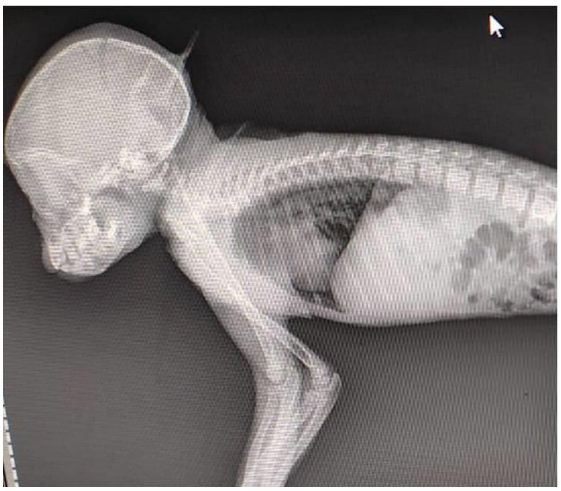

Fig. 6. Day 60 – Healed fracture in skull

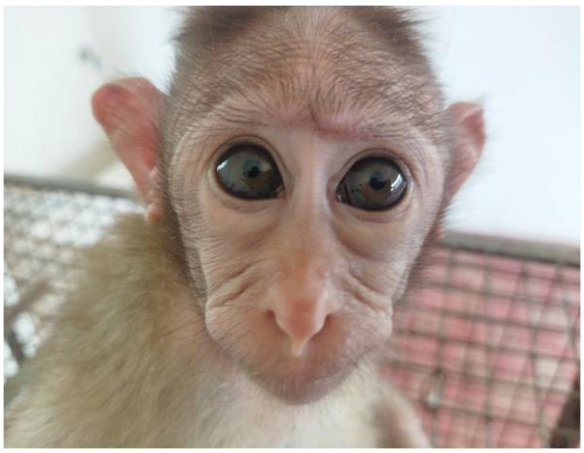

Fig. 7. Day 60 of presentation – Monkey with all normal reflexes

their use and efficacy remain uncertain. Advanced imaging techniques, like as MRI, have been demonstrated to have predictive utility in canine head trauma, although their high cost and risks have to be addressed. There was also debate about conventional and novel TBI treatments, such as hypertonic saline or mannitol for intracranial hypertension. While human and canine head trauma patients were more likely to experience post-traumatic seizures, it was unclear whether prophylactic anticonvulsant medication was useful [6]. In the case of Meningoencephalomyelitis of Unknown Origin (MUA), the exact cause and pathophysiology remain unknown. In studies involving animal models of traumatic brain injury, progesterone has demonstrated neuroprotective effects, including the reduction of oedema and infarct/lesion volume, the regulation of the inflammatory response, and the promotion of neurological recovery, as highlighted in research by Stein [7] and Jiang et al. [8].

Progesterone also demonstrated neuroprotective properties in models of traumatic brain injury, as shown in studies by Cutler et al. [9]. The pharmacokinetics of progesterone are well known, as the drug has been safely used for a long time. At the preclinical level, there is increasing evidence that progesterone could produce beneficial effects in brain and spinal cord injuries [10], stroke, brain hemorrhage, and neurodegenerative diseases [11]. Cerebral edema is responsible for much of the secondary injury seen after TBI. Thus, cerebral edema is an important target for reducing morbidity and mortality. Furthermore, progesterone was shown to significantly reduce cerebral oedema and aid in cognitive recovery following acute global cerebral ischemia [12]. Progesterone played a crucial role in providing neuroprotection and promoting the growth and survival of vulnerable neuronal populations, particularly those susceptible to excitotoxic and ischemic damage. These included pyramidal cells in the hippocampus and cortex, Purkinje cells, and mesencephalic dopaminergic cells [13]. At both the central and systemic levels, progesterone suppresses synthesis of proinflammatory cytokines such as TNF-α, IL-1, and IL-6,9–11 [8] limiting inflammation, microglial activation, and further neuronal injury. There is also evidence that progesterone reduces lipid peroxidation and free radical formation and enhances scavenger mechanisms to eliminate reactive oxygen species. Progesterone also helps to stabilize the blood-brain barrier by mediating fluid and ion exchange through membrane aquaporins. Vitamin D3 (cholecalciferol) plays a neuroprotective role in traumatic brain injury (TBI). It enhances antioxidant defense mechanisms, reduces inflammation, and modulates neuronal calcium homeostasis, thus preventing excitotoxicity. Additionally, Vitamin D3 promotes neuronal survival and brain repair by influencing neurotrophins release and regulating immune responses. Supplementation of Vitamin D3 may reduce the severity of TBI outcomes and improve cognitive recovery [14]. Finally, the bonnet macaque was released into a non-human area with the help of forest officials.

4. CONCLUSION

This case report describes the successful management of an infant male bonnet macaque with accidental traumatic brain injury, emphasizing the significant role of progesterone therapy in the treatment. This case highlights the promising outcomes associated with progesterone therapy in the context of traumatic brain injuries in non-human primates. The successful rehabilitation of the bonnet macaque offers valuable insights into the potential benefits of incorporating progesterone into the treatment protocols for similar cases, contributing to the evolving field of exotic and special species medicine.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

ACKNOWLEDGEMENT

The authors express their sincere gratitude to The Dean, Veterinary College and Research Institute, Orathanadu, TANUVAS, for the invaluable support and the provision of research facilities. Furthermore, we would like to extend our thanks to the Pattukottai Forest officials, Pattukottai, for offering the support. The authors are thankful to The Professor and Head, Veterinary surgery and radiology, VCRI, Orathanadu for supporting and provision of radiographic facilities. We wish to express our deep gratitude to The Professor and Head, Veterinary Clinical Complex, VCRI, Orathanadu, for the unwavering support.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
https://prh.mbimph.com/review-history/4112