Second Impact Syndrome or Cerebral Swelling after Sporting Head Injury

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Abstract

Second impact syndrome is believed to be the catastrophic consequence of repeated head injury in sport. The scientific evidence to support this concept is nonexistent, and belief in the syndrome is based upon the interpretation of anecdotal cases more often than not, lacking sufficient clinical detail to make definitive statements. The fear of this condition has driven many of the current return-to-play guidelines following concussion. Diffuse cerebral swelling (DCS) following a head injury is a well-recognized condition, more common in children than in adults, and usually has a poor outcome.

Introduction

The phenomenon of the second impact syndrome (SIS) continues to appear in the medical literature in spite of the lack of systemic evidence for its existence. Over a decade ago, the existence of this syndrome was brought into question, and since that time, other authors have begun to raise similar concerns as to the underlying entity (1,3,15,19).

SIS has been defined as occurring when "an athlete who has sustained an initial head injury, most often a concussion, sustains a second head injury before symptoms associated with the first have fully cleared" (4,15,22). This second injury, it is believed, results in catastrophic brain swelling and a usually fatal outcome. The key question that remains controversial is whether a repeated head injury or blow is required to cause this entity or whether the brain swelling is the result of a single blow to the head, which is a well-recognized sequela of head injury.

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The fear of the existence of SIS continues to drive anecdotal sports concussion guidelines and to be cited by many clinicians as the basis for the use of computerized neuropsychological tests in determining return to play for concussed athletes. The premise that neurocognitive testing prevents the likelihood of complications such as diffuse brain swelling remains firmly opinion-based.

What Is the Evidence for SIS?

The concept of SIS largely rests on the interpretation of anecdotal case reports. The majority of reported cases, including the index case, of this entity actually have not involved a "second" impact (22). In the only systematic review of this topic, a total of 17 cases of reported SIS were identified in the world literature (12,15). Of these, only five cases actually involved a repeated injury, and all these occurred within 7 d of the initial injury. Even in these cases, it was not clear that the initial injury played a contributory role insofar as providing evidence that the athlete had objective evidence of ongoing symptoms and/or injury prior to the putative second impact. Of the 14 cases in this series that went to autopsy, 11 had evidence of other structural brain injuries such as intracranial bleeding (typically an acute subdural hematoma) in addition to the cerebral swelling. A more recent literature review of the pathophysiology of the "thin subdural hematoma + brain swelling" syndrome, involving a total of 18 cases, confirmed the presence of thin subdural hematomas on all cases in which computed tomographic (CT) scanning had been obtained (17). This finding of subdural hematomas also has been noted in athletes (5). While it may be understandable that a structural injury, such as a subdural hematoma, may cause brain swelling, the traditional view of SIS is that this entity occurs in the absence of structural injury.

How Common Is SIS?

If SIS actually exists, then its occurrence vanishingly is rare. The only anecdotal reports of SIS are from the North American literature. As mentioned previously, a recent report from Japan noted 18 cases of brain swelling associated with CT-diagnosed subdural hematomas (17). It is

surprising that there are no reports of SIS in the European or Australian literature, in particular, from sports such as Australian football, which has both a high participation rate and a high concussive injury rate (approximately 15 times that of American football (16)). An Australian study examining all sports-related deaths over a 35-year period did not find a single case of SIS (16).

The 2010 report from the U.S. National Center for Catastrophic Sport Injury Research (based at the University of North Carolina) cited 145 cases of catastrophic cerebral injury during the period of 1984 to 2010 with only a single case of a "possible" SIS noted in a case that actually presented an acute subdural hematoma (18). Based upon an annual participation rate of 1.8 million subjects in U.S. high school and collegiate sports, Randolph and Kirkwood (20) have estimated that this corresponds to one instance of "possible" SIS for every 205,000 player seasons. For a squad size of 50 players, this would translate to one such injury every 4,100 seasons (19,20). Given that virtually all of these injuries occur as the result of the immediate consequences of a single traumatic brain injury that typically results in an intracranial hematoma, the support for SIS from the recent data available from this source is limited.

What Is the Underlying Pathophysiology?

It is known that a single brain impact can result in increased cerebral blood volume that, in turn, is secondary to a failure of cerebral vascular autoregulatory mechanisms. The increased cerebral blood volume results in cerebral swelling (2,21). Death from raised intracranial pressure usually follows rapidly because of transtentorial brainstem herniation. Animal models, as well as evidence from human cases, demonstrate the extreme rapidity by which these vascular changes can occur (8,28). One human case report demonstrated catastrophic brain swelling within 20 min of a single head impact (28).

While there is no doubt that brain swelling may occur in response to a head injury, the issue of whether recurrent concussive injury is a risk factor for this condition is disputed. In the SIS literature, McCrory and Berkovic (15) found 12 reports that clearly describe sport-related catastrophic brain injury associated with unexplained cerebral swelling. In these cases, the players did not have a second impact; rather, they either collapsed during sport participation or walked off and collapsed without any further injury occurring (15).

Who Is at Risk of SIS or Brain Swelling?

Based on the published case studies, there are two groups of athletes proposed to be at a higher risk of SIS: boxers and children. As described previously, the concept of SIS in these situations largely rests on the interpretation of anecdotal case reports.

Particular note of the cases of cerebral swelling reported in boxers should be made. With the likelihood of numerous head impacts during a single bout, it makes it almost impossible to determine what is, in fact, a "first" or "second" impact. If SIS is a real entity, the repetitive head impacts in boxing should make boxers much more likely to suffer from this entity. It is well understood that boxers suffer more frequently from other forms of catastrophic brain injury, such as subdural hematoma, than athletes in other sports (14,29,30). Given that significant head impact episodes occur in virtually every bout fought, why then is SIS not more frequently seen in boxing?

In a published case series of boxers aged 17 to 24 years described as having SIS, there was a variety of diagnostic issues (4). In one case, there was no CT or postmortem performed, so it is uncertain whether death was secondary to intracranial hemorrhage or edema. In two of the cases, the boxers sustained multiple significant blows to the head, resulting in multiple eight counts, before the onset of cerebral edema and death. It is highly probable that any of the blows that triggered an eight count was of sufficient force to induce acute malignant cerebral edema, without needing to invoke the concept of a second impact. Finally, the other two cases both demonstrated brain swelling and subdural hematoma on CT.

Outside of boxing, only two cases of "probable" SIS exist, one in a 16-year-old ice hockey player and the other in a 17-year-old gridiron football player (15). In the pediatric literature, this same phenomenon has been labeled "malignant brain edema" (2). Additional case series of diffuse cerebral swelling in children following a single minor brain trauma have been reported by Snoek *et al.* (23) and Mandera *et al.* (10,11). This phenomenon may be related to a calcium channel subunit receptor gene mutation (9).

Similarly, Cantu and Gean (5) have described 10 cases of teenagers playing American football (aged 13 to 19 years) who developed a small subdural hematoma and cerebral edema. In nearly every case, a significant impact to the head preceded the injury, and the outcome was universally poor, with five dead and the other five left with severe neurological deficit. While brain swelling was noted, it is more likely that the magnitude of force required to produce the subdural hematoma was sufficient to induce cerebral edema, independent of any earlier concussive injury (7).

Can Cerebral Swelling Be Prevented?

The risk factors for posttraumatic acute brain swelling are not understood at present. Our current limited knowledge suggests that children and adolescents are at a higher risk, and increased clinical vigilance and perhaps more aggressive investigational strategies may be necessary after all head injuries in this age group. Certainly, the presence of postconcussive symptoms should be an important factor prompting further medical assessment.

The presence of postconcussive symptoms should be seen as a significant risk factor for further injury to occur, and any symptoms should mandate restriction from further sports participation until the symptoms fully resolve. There is a large body of research on the neuropsychological effects of sport-related concussions indicating that the principal cognitive deficits in the postinjury period relate to reduced reaction times and impaired speed of information processing (6). Premature return of a concussed athlete presumably would lead to an increase in injury rates, consequent on the fact that the athlete's ability to respond appropriately to the demands and threats of the sport would be slowed — not an increase in mortality due to the putative SIS.

It also has been proposed that concussive head injury opens a temporary window of brain vulnerability because

of the impairment of cellular energetic metabolism. Evidence from animal and human proton magnetic resonance spectroscopy suggests that metabolic change persists up to 15 d following concussive injury (24–27). While not directly addressing SIS *per se*, it does raise indirect evidence that the possibility of a further concussive injury during this period may result in a more severe injury due to impaired cerebral metabolism.

Arbitrary exclusion periods based on a fear of a nonexistent entity are not the answer in this era of evidence-based medicine. We need to assess return-to-play strategies prospectively on the basis of symptom resolution and cognitive recovery, and determine that the outcomes of this approach are safe for the player concerned and appropriate for the sport played (13). Until such studies are performed, the management of concussion should follow the experience of most team physicians who safely treat concussed athletes with a combination of good common sense and clinical judgment.

Conclusions

The critical questions are how can we prevent the onset of cerebral swelling and can we predict which children or athletes are at risk of developing this condition and treat them aggressively to reduce the morbidity and mortality? To date, we do not have the answers to these questions. The rarity of this condition of DCS suggests that it is more likely to be due to an underlying genetic susceptibility than simply a response to impact alone. The rarity of this condition also creates a significant barrier to effective research to identify the exact cause. In the interim, it is inherent upon all those involved in the treatment of children following head injury to be aware of the potential for delayed deterioration and to have at their disposal the appropriate facilities and personnel to manage this condition in a timely fashion.

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References

1. Bey T, Ostick B. Second impact syndrome. *West. J. Emerg. Med.* 2009; 10:6–10.
2. Bruce DA, Alavi A, Bilaniuk L, *et al*. Diffuse cerebral swelling following head injuries in children: the syndrome of "malignant brain edema". *J. Neurosurg.* 1981; 54:170–8.
3. Byard RW, Vink R. The second impact syndrome. *Forensic Sci. Med. Pathol.* 2009; 5:36–8.
4. Cantu RC. Second-impact syndrome. *Clin. Sports Med.* 1998; 17:37–44.
5. Cantu RC, Gean AD. Second-impact syndrome and a small subdural hematoma: an uncommon catastrophic result of repetitive head injury with a characteristic imaging appearance. *J. Neurotrauma.* 2010; 27:1557–64.
6. Collie A, Maruff P, Makdissi M, *et al*. CogSport: reliability and correlation with conventional cognitive tests used in postconcussion medical evaluations. *Clin. J. Sport Med.* 2003; 13:28–32.
7. Davis GA. Neurological outcomes. In: Kirkwood M, Yeates K, editors. *Pediatric Mild Traumatic Brain Injury: From Basic Science to Clinical Management*. Guilford Press; 2011.
8. Kobrine AI, Timmins E, Rajjoub RK, *et al*. Demonstration of massive traumatic brain swelling within 20 minutes after injury. Case report. *J. Neurosurg.* 1977; 46:256–8.
9. Kors EE, Terwindt GM, Vermeulen FL, *et al*. Delayed cerebral edema and fatal coma after minor head trauma: role of the *CACNA1A* calcium channel subunit gene and relationship with familial hemiplegic migraine. *Ann. Neurol.* 2001; 49:753–60.
10. Mandera M, Wencel T, Bazowski P, Krauze J. How should we manage children after mild head injury? *Childs Nerv. Syst.* 2000; 16:156–60.
11. Mandera M, Zralek C, Krawczyk I, *et al*. Surgery or conservative treatment in children with traumatic intracerebral haematoma. *Childs Nerv. Syst.* 1999; 15:267–9; discussion 270.
12. McCrory P. Does second impact syndrome exist? *Clin. J. Sport Med.* 2001; 11:144–9.
13. McCrory P, Meeuwisse W, Johnston K, *et al*. Consensus Statement on Concussion in Sport: the 3rd International Conference on Concussion in Sport held in Zurich, November 2008. *Br. J. Sports Med.* 2009; 43(Suppl. 1): i76–90.
14. McCrory P, Zazryn T, Cameron P. The evidence for chronic traumatic encephalopathy in boxing. *Sports Med.* 2007; 37:467–76.
15. McCrory PR, Berkovic SF. Second impact syndrome. *Neurology.* 1998; 50:677–83.
16. McCrory PR, Berkovic SF, Cordner SM. Deaths due to brain injury among footballers in Victoria, 1968–1999. *Med. J. Aust.* 2000; 172:217–9.
17. Mori T, Katayama Y, Kawamata T. Acute hemispheric swelling associated with thin subdural hematomas: pathophysiology of repetitive head injury in sports. *Acta Neurochir. Suppl.* 2006; 96:40–3.
18. Mueller F, Cantu R. *Annual Survey of Catastrophic Football Injuries 1977–2010*. Chapel Hill (NC): National Centre for Catastrophic Sports Injury Research; 2011. Available at: http://www.unc.edu/depts/nccsi/2010FBCatReport.pdf.
19. Randolph C. Baseline neuropsychological testing in managing sport-related concussion: does it modify risk? *Curr. Sports Med. Rep.* 2011; 10:21–6.
20. Randolph C, Kirkwood MW. What are the real risks of sport-related concussion, and are they modifiable? *J. Int. Neuropsychol. Soc.* 2009; 15: 512–20.
21. Reilly PL. Brain injury: the pathophysiology of the first hours. "Talk and Die revisited." *J. Clin. Neurosci.* 2001; 8:398–403.
22. Saunders RL, Harbaugh RE. The second impact in catastrophic contact-sports head trauma. *JAMA.* 1984; 252:538–9.
23. Snoek JW, Minderhoud JM, Wilmink JT. Delayed deterioration following mild head injury in children. *Brain.* 1984; 107(Pt 1):15–36.
24. Tavazzi B, Vagnozzi R, Signoretti S, *et al*. Temporal window of metabolic brain vulnerability to concussions: oxidative and nitrosative stresses — part II. *Neurosurgery.* 2007; 61:390–5.
25. Vagnozzi R, Signoretti S, Cristofori L, *et al*. Assessment of metabolic brain damage and recovery following mild traumatic brain injury: a multicentre, proton magnetic resonance spectroscopic study in concussed patients. *Brain.* 2010; 133:3232–42.
26. Vagnozzi R, Signoretti S, Tavazzi B, *et al*. Temporal window of metabolic brain vulnerability to concussion: a pilot ^{1}H-magnetic resonance spectroscopic study in concussed athletes — part III. *Neurosurgery.* 2008; 62: 1286–95.
27. Vagnozzi R, Tavazzi B, Signoretti S, *et al*. Temporal window of metabolic brain vulnerability to concussions: mitochondrial-related impairment — part I. *Neurosurgery.* 2007; 61:379–88.
28. Wako N, Shima K, Marmarou A. Time course of brain tissue pressure in temporal fluid percussion injury. In: Hoff J, Betz A, editors. *Intracranial Pressure VII*. Berlin (Germany): Springer-Verlag; 1989. p. 593–7.
29. Zazryn TR, Finch CF, McCrory P. A 16 year study of injuries to professional boxers in the state of Victoria, Australia. *Br. J. Sports Med.* 2003; 37:321–4.
30. Zazryn TR, McCrory PR, Cameron PA. Neurologic injuries in boxing and other combat sports. *Neurol. Clin.* 2008; 26:257–70; xi.