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Second impact syndrome

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Article abstract—Diffuse cerebral swelling with delayed catastrophic deterioration, a known complication of brain trauma, has been postulated to occur after repeated concussive brain injury in sports—the "second impact syndrome" (SIS). Certain current concussion management guidelines are contingent upon this assumption. We established criteria for definite, probable, and possible SIS and analyzed all published cases. A total of 17 cases were identified in which the reports described the cases as being consistent with SIS. Of these, only five probable cases of SIS were found based on our diagnostic criteria. We also studied the accuracy of recalled episodes of minor concussion in football players by their teammates because the diagnosis of SIS is usually based on such accounts. We found overreporting of recalled episodes of concussion in teammates when compared with self reports and videotape analysis. Based on case reports, the claim that SIS is a risk factor for diffuse cerebral swelling is not established. Prevention strategies for sports-related cerebral swelling are difficult to implement in the absence of established risk factors.

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Diffuse cerebral swelling is a rare but well recognized cause of delayed catastrophic deterioration resulting in death or persistent vegetative state after an apparently minor head injury. Risk factors for this posttraumatic complication have not been clearly established, although most cases have occurred in children and adolescents.[1-8] This phenomenon has also been observed in collision sports. It has been postulated that a specific form of cerebral swelling may be the consequence of a repeated minor head injury. Specifically, the "second impact syndrome" (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" (p. 27).[9] It is postulated that this second impact sets in motion the rapid development of cerebral vascular congestion which in turn causes increased intracranial pressure, usually resulting in brainstem herniation and death.[9]

Documentation of a witnessed initial impact is crucial to the central issue as to whether repeated

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brain injury is a risk factor for the subsequent deterioration. For documentation of the concept of SIS, medical review following this initial injury is critical in ruling out a more significant intracranial injury and to verify the presence of ongoing postconcussive symptoms.

If SIS represents a real clinicopathologic entity, then there are potentially major consequences for the management of minor head injury in sports and implications for the innumerable amateur and professional athletes who sustain such injuries. In some centers, belief in the concept of SIS currently dictates management strategies for use in all minor sports-related injuries.[2,10,11] Conversely, if SIS is not a real entity, such management strategies may be inappropriate. Moreover, study of the causes of posttraumatic cerebral swelling, which undoubtedly does occur, could be misdirected. Given the rarity of these conditions, a case-control study would be the only feasible means to establish the risk factors.[12]

The concept of SIS rests on the interpretation of case reports. In addition to the published cases, a further 35 cases from the U.S. National Center for Catastrophic Sport Injury Research have been cited as probable cases of SIS, but not published due to lack of confirmatory details.[9,13] We have reviewed the published cases.

Methods. *Analysis of published cases.* To provide a consistent framework for analysis of published case reports, we defined four diagnostic criteria based on the clinicopathophysiologic features of the putative entity of SIS. Although arbitrary in nature, they provide a precise description of the expected temporal sequence of this entity.

These criteria are: (a) medical review after a witnessed first impact; (b) documentation of ongoing symptoms following the initial impact up to the time of the second impact; (c) witnessed second head impact with a subsequent rapid cerebral deterioration; and (d) neuropathologic or neuroimaging evidence of cerebral swelling without significant intracranial hematoma or other cause for cerebral edema (e.g., encephalitis).

All published cases of catastrophic brain injury and SIS in sports were extracted using a literature review approach and computerized database searches (Medline, Embase, Sport Discus). Further published or unpublished cases were sought through personal contact with acknowledged experts in this field. All published reports described or quoted as examples of SIS were classified according to the listed criteria as:

Definite SIS criteria: (a), (b), (c), and (d)

Probable SIS criteria: (c) and (d) plus either (a) or (b)

Possible SIS criteria: (c) and (d) only

Not SIS criteria: (c) or (d) absent

The extracted case details were compared by two independent reviewers to determine if the cases fulfilled the criteria listed for inclusion into the different categories.

Table 1 *Number of cases satisfying diagnostic criteria*

Criteria	Definition	Number
(a)	Medical review after a witnessed first impact	5/17
(b)	Documentation of ongoing symptoms following the first impact up to the time of the second impact	7/17*
(c)	Witnessed second head impact with a subsequent rapid cerebral deterioration	6/17*
(d)	Neuropathologic or neuroimaging evidence of cerebral swelling without significant intracranial hematoma or other cause for edema	13/17

* Includes four boxers.

Recall of previous head injury. To test the assumption that teammate recall of head injury is reliable, we performed a retrospective recall study involving 102 football players participating in elite Australian rules football. Individual players were questioned about the presence of major (involving loss of consciousness [LOC]) or minor (no LOC) concussive episodes in their teammates during the preceding 8 weeks. Accuracy of the player's recalled information was compared with the involved teammate's recall of self-reported episodes of injury and game videotape analysis. Differences between the reported and actual number of concussive episodes were analyzed using Student's *t*-test.

Results. *SIS criteria study.* Seventeen published cases were described[2,8,9,14-16] or subsequently quoted[1,17] as examples of SIS. The number of cases satisfying our diagnostic criteria are shown in table 1. The amount of clinical documentation varied considerably in the reports. In most cases, evidence of previous trauma was based on teammate-recalled episodes rather than videotape-documented reports. In two cases, immediate medical evaluation after the initial impact was documented in the reports, but these two cases failed to fulfill the other criteria of SIS. Surprisingly, there was no evidence of a "second" impact in 11 cases, including four of the cases described by Schneider that are frequently cited as classical examples of SIS.[17] Diffuse cerebral swelling was documented in 14 cases; however, in one case, there was another plausible neuropathologic cause for brain swelling (encephalitis), leaving 13 cases satisfying criterion (d).

Under our classification, there were no cases of definite SIS. There were five cases of probable SIS; the remaining 12 cases were not SIS. Tables 2 and 3 show detailed analysis of all cases that we classified as probable SIS and not SIS, respectively. SIS was excluded in these 12 cases on the basis of absence of neuroimaging or neuropathologic evidence of unexplained cerebral swelling (criterion d) in 4/12 cases and absence of a witnessed second impact (criterion c) in 11/12 cases. Both criteria (c) and (d) were lacking in 3/12 cases.

The five probable SIS cases were males aged 16 to 19 years and included one ice-hockey player, one American football player, and three boxers. In addition to these five probable cases, the nine non-SIS cases with cerebral swelling but without a documented second impact were also

Table 2 *Probable second impact syndrome cases*

Ref	Age (y)	Sport	First episode	Ongoing symptoms	Delay	Second episode	Pathology	Outcome	Criteria satisfied
Fekete, 1968[1]	16	Ice hockey	Struck back of head on ice; brief loss of consciousness; eyewitness description	Headache and unsteadiness	4 days	Checked heavily, struck left temple on ice causing loss of consciousness (duration not stated)	Occipital contusion (days), cerebral edema; small SDH, SAH	Died, 2 h	b, c, d
Kelly et al., 1991[2]	17	American football	Cantu Grade I concussion during football game; no loss of consciousness; headache postgame	Headache	1 week	Head struck during successive plays; briefly stunned after first contact but cleared quickly; light head contact during next play and collapsed	Cerebral swelling, obstructive hydrocephalus, small SDH, SAH	Died, 15 h	b, c, d
Cantu and Voy, 1995[9]	17	Amateur boxing	Headache after boxing match 2 days prior; using aspirin ++; motor vehicle accident causing head impact on morning of fight	Yes; no details given	2 days	Collapsed round 2; few minor head blows but no knockdowns in fight; seizure then rapidly decerebrate	Small left frontal SDH, cerebral edema	Died, 1 week	b, c, d
	19	Amateur boxing	Knocked down in fight; postfight headache	Yes; no details given	1 day	Collapsed round 2 after "minor" blows; seizure then decerebrate	Small right SDH cerebral edema ++	Died, day 6	b, c, d
	17	Amateur boxing	Several standing counts after being stunned by head blows; postfight psychiatric disturbance	Yes; no details given	6 hours	Fight stopped in round 2 after several "standing counts," collapsed minutes later; rapid coma	Cerebral edema with brainstem herniation	Died, day 2	b, c, d

Other papers with reported cases of SIS: Cantu 1992[48] and 1995[9] quotes Fekete's case[1]; McQuillen 1988[14] quotes Saunders case.[15]
All cases were male.
SDH = subdural hematoma; SAH = subarachnoid hemorrhage; ++ = marked, prominent.

young males, aged between 16 and 24 years, with both of the cases older than 20 years being boxers.

Recall study. Australian football players consistently overreported recalled episodes of major (associated with LOC) and minor (no LOC) concussive brain injury in their teammates when compared with self-reported and videotape-documented episodes. There was no significant difference between self-reported and videotape-documented episodes of major or minor concussive injury (table 4).

Discussion. The medical literature clearly describes many causes of delayed cerebral deterioration after traumatic brain injury. The earliest description of such a syndrome is credited to Otto Bollinger, who in 1891 coined the term "traumatische spät-apoplexie."[18] Patients who suffer a delayed deterioration or who "talk and die" after closed head injury represent approximately 15% of all patients sustaining severe head injuries. Intracranial hematoma is the cause of this syndrome in approximately 75% of these patients.[19-24] In some cases, hematomas are evident on initial imaging studies but, in other cases, hematomas develop after a delay.[25,26] There is a smaller subgroup of patients who deteriorate due to causes other than mass lesions who have evidence of posttraumatic diffuse cerebral swelling.

The pathophysiology of posttraumatic brain swelling. Posttraumatic cerebral swelling may be due to two separate pathophysiologic mechanisms. The first is thought to be due to increased cerebral blood volume secondary to a failure of cerebral vascular autoregulatory mechanisms.[3,4,19,27] Animal models and evidence from human cases show the extreme rapidity by which these vascular changes can occur.[28,29] In one case report, massive traumatic cerebral swelling documented on CT scanning occurred within 20 minutes of cerebral injury.[30] This entity is sometimes loosely called diffuse or "malignant" cerebral edema.[3,14]

The second mechanism of posttraumatic brain swelling is due to true cerebral edema. The characteristic feature of this entity is that the cut brain at autopsy "wept fluid."[31] The classic study of Klatzko identified two forms—vasogenic and cytotoxic edema.[32] Experimental evidence shows that both of these entities can occur within hours of head trauma.[31,33,34] The precise contribution of each of these forms of cerebral edema to the morbidity and mortality of closed head injury remains unknown.

Does SIS exist? In the SIS literature, we found 13 reports that clearly describe sports-related catastrophic brain injury associated with unexplained cerebral swelling. In many of these cases, including the index case,[15] the players did not have a second impact; they either collapsed during sports participation or walked off and collapsed without any further cerebral injury occurring.[2,8,9,14-17] Our analysis of the published cases shows that by using our strict criteria for the definition of SIS, only five of the cases would be considered probable SIS, with the remain-

Table 3 *Non-second impact syndrome cases*

Reference	Age (y)	Sport	First episode	Ongoing symptoms	Delay
Schneider, 1973[17]	16	American football	Tackle and hit head on thigh; immediate loss of consciousness; progressive decerebration	NA	NA
		American football	No details given apart from "previous mild head injury"	NA	NA
	17	American football	Tackle with head clash; walked away and collapsed on-field	NA	NA
	17	American football	Headache for 1 week prior to game; no details given; no head injury apparent in game; collapsed 5 minutes later	NA	NA
Saunders and Harbaugh, 1984[15]	19	American football	Fistfight with blow to head resulting in brief loss of consciousness; seen by doctor following day with headache and nausea	Headache for 3 days	5 days
McQuillen et al., 1988[14]	18	Downhill ski racing	Fall in practice; no obvious head injury	No	2 weeks
	24	Boxing	Sparring contest; dazed after hit to head; no loss of consciousness; was wearing helmet; collapsed several minutes later	NA	NA
Shell et al., 1993[16]	17	American football	Two Cantu grade 1 concussions over 1 week during football games; recovered without problems and normal examination by team doctor	No	5 weeks
Cantu and Voy, 1995[9]	21	Boxing	Several head blows in fight; no knockdowns; headache after fight	Yes	2 days
	24	Amateur boxing	Fight stopped in round 4 after several standing counts; collapsed minutes later after walking to dressing room	NA	NA
CDC, 1997[8]	17	American football	Tackled during first half of game and struck head on ground; felt ill and had headache at halftime	Headache and ill during break	<60 minutes
	19	American football	Complained of headache after practice; no reported head injury	Not stated	1 day

All cases were male.
NA = not applicable; SDH = subdural hematoma; CDC = Centers for Disease Control and Prevention.

der being excluded. None of the published cases fulfilled our criteria for definite SIS. In many published case reports, there was a paucity of medical details presented.

In most cases, evidence of previous trauma is based on recalled eyewitness accounts or circumstantial evidence. The proposed criterion of an initial documented witnessed impact, although strict, emphasizes the fundamental issue. This degree of diagnostic certainty may seem unrealistic to some observers; however, the central basis of this condition rests on the verification of this particular aspect

Table 3 Continued

Second episode	Pathology/imaging	Outcome	Criteria satisfied	Comments
No	Pathology: Right hemispheric edema; brainstem hemorrhage; thin SDH	Died 8 hours	d	No second impact
No injury seen; was confused on-field and collapsed during play	Pathology: Pontine hemorrhage; secondary pressure effects noted in brainstem only	Died	None	No second impact
No	Pathology: Acute left SDH, cerebral edema; midbrain hemorrhage	Died day 3	d	No second impact
No	Pathology: Not done; midbrain injury on clinical signs	Recovered over 3 weeks	None	No second impact
Involved as a blocker; no head injury noted; after game walked off field and collapsed; immediate coma.	Pathology: Right frontal contusion (days), cerebral edema	Died day 4	a, d	No second impact
Jarred on mogul; no head injury; collapsed several minutes later	Imaging: Left hemispheric edema on CT scan	Persistent vegetative state	d	No head injury apparent
No	CT demonstrated cerebral edema and small right SDH; Pathology: lymphocytic infiltrate ? encephalitis; flu 2 weeks prior	Died day 6	a	No second impact; ? encephalitis
Collapsed while running in play; no head trauma; rapidly decerebrate	Pathology: small right frontal SDH with left midline shift; evidence of old brain contusion	Survived, no neurologic deficit	a, d	No second impact
Collapsed after light sparring for 2 minutes, no head blows apparent	Details not stated	Died in minutes	a, b, c	Cerebral pathology unknown
No	Pathology: Cerebral edema; brainstem herniation with midbrain necrosis	Died in hours	a, d	No second impact
No; collapsed on-field in third quarter; was involved in routine blocks/ tackles but no obvious head injury	CT: diffuse brain swelling and small SDH; Pathology: Diffuse brain swelling; subcortical ischemia; SDH	Died 4 days	b, d	No second impact or initial medical assessment
No; collapsed on-field 2 minutes after a tackle	CT: diffuse brain swelling and thin SDH	Died 3 days	d	No second impact

of the published cases. It is assumed that other team players' recall of head injury events in such circumstances will be reliable. The limitations of this form of retrospective case ascertainment should be obvious. Our recall study demonstrates the limitations of using teammate-recalled injury.

In our study, teammates recalled episodes of major and minor concussions at a higher rate than self-reported or videotape-documented brain injury. In the 3-month period tested, an episode of recalled cerebral trauma occurred in every teammate. Although this is not a surprising result in a collision sport such as Australian football, it suggests that the accuracy of recalled data in cases of fatal SIS must be questioned.

In contrast to our view that SIS probably does not exist or has been overdiagnosed, there has been suggestion that the rarity of this condition does not

Table 4 *Recalled concussive episodes (n = 102)*

Concussion type	Mean events/ 12-week period	95% CI
Major		
Self-reported	0.12	0.002–0.20
Teammate-recalled	1.54	1.01–2.06
Video-documented	0.18	0.16–0.21
Minor		
Self-reported	0.53	0.25–0.80
Teammate-recalled	2.14	1.63–2.67
Video-documented	1.03	0.66–1.41

Statistical analysis showed a significant ($p = 0.001$) difference between teammate-recalled and self-reported/video-documented episodes of major and minor concussion and no significant difference ($p = 0.22$) between self-reported and video-documented episodes of major and minor concussion.

reflect its true incidence, with cases going unreported.[13] This seems implausible as most sports-related deaths in children and adolescents are likely to be investigated or the subject of coronial inquests. Given that these episodes seem noteworthy in their own right, one can assume that virtually all cases would be documented.

Risk factors for cerebral swelling in sports. Are boxers at greater risk? Particular note of the cases of cerebral swelling reported in boxers should be made. With the propensity of numerous head impacts during a single bout, determining what is a "first" or "second" impact is difficult. Some published cases suggest that both may occur during the course of a single bout.[9] Should these cases be included with other sports? If SIS is a real entity, the repetitive head impacts in boxing should make boxers much more likely to suffer from this entity. Boxers do experience other forms of catastrophic brain injury, such as subdural hematoma, more often than participants in other sports.[35-40] Given that concussive episodes occur in virtually every bout fought, why is SIS not more frequently seen in boxing?

Are children at greater risk? The striking feature of these published cases of SIS is that virtually all are adolescents. Excluding boxing, only two cases of probable SIS exist, one in in a 16-year-old ice hockey player and the other in a 17-year-old gridiron football player.[1,2] In boxing, the majority of cases are also noted in teenagers. In children, given the apparent higher risk of cerebral swelling after minor head injury and the propensity for structural injury (e.g., subdural hematomas) with relatively mild injury, some authors have argued that there may be a different cerebral autoregulatory response to trauma in children than in adults.[3,7,27]

Is there a gender bias? All reported cases of SIS are in young males. Whether this represents a true gender difference or an exposure bias has not been clarified. Given the nature of the sports from which cases are reported (gridiron, ice hockey, and boxing), the male bias is not wholly unexpected. In the related medical literature on neurosurgical catastrophic brain injury after minor trauma, approximately 30% of the cases were female.[16,19-22,24,36] Once again, given that motor vehicle accidents, gunshot trauma, and sports are the major patient sources, the male predominance is not surprising. Whether a true gender difference exists in terms of cerebral response to trauma remains unsubstantiated at this stage.

Prevention. Although extremely rare, sports-related diffuse cerebral swelling has a mortality approaching 100%. Many of the published case reports[14,15] and most notably the guidelines of the Colorado Medical Society and the American Academy of Neurology suggest that prevention of this syndrome should be based on a policy of not allowing individuals to return to sports until postconcussive symptoms have fully resolved.[2,11,41] In addition, the Colorado and Academy guidelines define arbitrary periods of exclusion from sports following concussive injury. The reasons for these practices relate to the belief that "individuals who are symptomatic from a concussion, even without LOC, are at risk for developing diffuse brain swelling after a second impact to the head" (p. 2869) and that the risk of cerebral swelling is lessened with time.[2] No data is provided as to the rationale by which arbitrary exclusion periods were established.

We agree that athletes should not return to sports until all postconcussive symptoms have resolved. The danger of prematurely returning to sports relates to the risk of sustaining further injury. Neuropsychologic measures of speed of information processing and reaction times are slowed in the early stages post injury.[42-47] In this setting, an athlete participating in a collision sport (such as football) or high-risk sport (such as motor car racing) may not be able to respond appropriately to dangers in the sporting situation and hence sustain further injury. There is no evidence that these strategies reduce the risk of posttraumatic cerebral swelling.

The risk factors for posttraumatic acute brain swelling are not currently understood. Our limited knowledge suggests that children and adolescents are at higher risk; hence, increased clinical vigilance and perhaps more aggressive investigational strategies may be necessary after all head injuries in this age group.

Diffuse cerebral swelling is a rare complication of mild traumatic brain injury in sports that occurs predominantly in male teenagers. Its causes are unknown but may involve disordered cerebral vascular autoregulation. Most cases have no prior evidence of head injury with ongoing symptoms that would support the concept of SIS. In those cases that are presumed to represent SIS, the evidence that a prior head injury is a risk factor for this pathophysiologic entity is not compelling. Case-control studies are required to determine if prior head injury is relevant in

some instances of posttraumatic cerebral swelling and to identify other risk factors so that correct preventative strategies can be instituted.

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Second impact syndrome

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