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GRAND ROUNDS

Pure distraction injury of T1–2 with quad fever

Jun-Yeong Seo[1] · Chae-Moon Lim[1] · Young-Hoon Kim[2] · Kee-Yong Ha[2]

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Abstract

Introduction We report a pure distraction injury of the upper thoracic spine and uncontrolled hyperthermia without an infectious cause. Quad fever appears in the first several weeks to months after a cervical or upper thoracic SCI and is characterized by an extreme elevation in body core temperature beyond 40 °C without an infectious cause. Discriminating between infectious and noninfectious causes is important, and a thorough clinical assessment is required.

Materials and methods A 52-year-old male visited the emergency room complaining of back pain with complete paralysis [American Spinal Injury Association (ASIA) A] of both lower extremities after a pedestrian-motor vehicle accident. He had trouble breathing due to a hemothorax and flail chest caused by fractures of the right second to eleventh and left fourth to seventh ribs. A computed tomography scan revealed severe distraction of the T1–2 intervertebral space. A magnetic resonance image showed signal changes in the spinal cord and a clean-cut margin between the T1–2 disc and T2 body. The neurological level of injury was C8 upon the initial neurological assessment. Emergency surgery was performed. C6–T3 posterior instrumentation and an autologous iliac bone graft were performed.

Results After surgery, the core temperature increased gradually to above 38.0 °C on post-trauma day 4 and increased to 40.8 °C on post-trauma day 7. None of the repeated aerobic, anaerobic, or fungal cultures of the blood, tracheal aspirate, line tips, urine, or stool was positive until post-trauma day 21, when *Candida tropicalis* was identified in the urine culture. On post-trauma day 63, the blood pressure, pulse, and body temperature stabilized and the patient was transferred to the general ward. At post-trauma year 6, the injury state was still complete and the neurological level of injury was changed to C4.

Conclusions Based on the Grand Round case and relevant literature, we discuss the case of pure distraction injury of T1–2 with quad fever. Spinal surgeons should be knowledgeable regarding quad fever as well as the differential diagnoses and treatment strategies.

Keywords Upper thoracic spine · Distraction · Spinal cord injury · Hyperthermia · Fever of unknown origin · Quad fever

✉ Kee-Yong Ha
kyh@catholic.ac.kr

[1] Department of Orthopaedic Surgery, Jeju National University Hospital, School of Medicine, Jeju National University, Jeju, Korea

[2] Department of Orthopaedic Surgery, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, 222 Banpo-dae-ro, Seocho-Gu, Seoul 137-701, Korea

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Case report

A 52-year-old male visited our hospital after being hit by a car while jogging on the road. In the ambulance, dopamine was administered with fluid because of his low blood pressure. On admission, he had blood pressure of 61/40 mmHg, a pulse rate of 60 beats/min, and a body temperature of 36.6 °C. He presented with paraplegia [American Spinal Injury Association (ASIA) Impairment Scale A] with bladder and bowel dysfunction. His Glasgow Coma Scale (GCS) score was 15 on admission. The initial neurological assessment identified C8 as the neurological level of injury. He had trouble breathing due to multiple rib fractures and a hemothorax (Fig. 1). CT scans revealed severe distraction of the T1–2 intervertebral space. Magnetic resonance imaging (MRI) revealed signal changes in the spinal cord and a clean-cut margin between the T1–2 disc and T2 body (Fig. 2). A brain computed tomography (CT) scan did not reveal any abnormal findings. Emergency surgery was performed under general anesthesia with isoflurane and rocuronium bromide. The posterior ligamentous complex was disrupted completely in the surgical field. Posterior instrumentation was installed from C6 to T3 with posterior fusion by autologous iliac bone graft (Fig. 3). He was sent to the intensive care unit after surgery.

His core temperature increased gradually to greater than 38.0 °C on post-trauma day 4 and increased to 40.8 °C on post-trauma day 7, when his blood pressure dropped to 90/38 mmHg despite norepinephrine administration. His body temperature was persistently unresponsive to antipyretics or intravenous propacetamol, intravenous cold fluids, ice pack, and empirical antibiotics. On post-trauma day 8, a slight decrease was observed in his mental status, and he was unresponsive to external stimuli; a brain MRI was performed and showed a modest amount of subdural hemorrhage without mass effect. The serum cortisol level and thyroid function tests were normal (thyroid-stimulating hormone, 5 μIU/mL). We found no clinical evidence of myocardial infarction or deep vein thrombosis. None of the repeated aerobic, anaerobic, or fungal cultures of the blood, tracheal aspirate, line tips, urine, or stool was positive until post-trauma day 21, when *Candida tropicalis* was identified in the urine culture.

From post-trauma day 4 to 21, his core temperature remained at >38.0 °C with diurnal variation (Fig. 4). On post-trauma day 34, his body temperature temporarily surged to 42 °C, his blood pressure dropped to 53/43 mmHg, his pulse was irregular (from 96 to 190 beats/min), and his respiration rate was 42 breaths/min. This febrile episode was considered to be due to septic shock because *Enterococcus* and *Streptococcus* were identified in the blood cultures. He recovered with fluid, antibiotics, and inotropic agents. On post-trauma day 63, his blood pressure, pulse, and body temperature stabilized and he was transferred to the general ward.

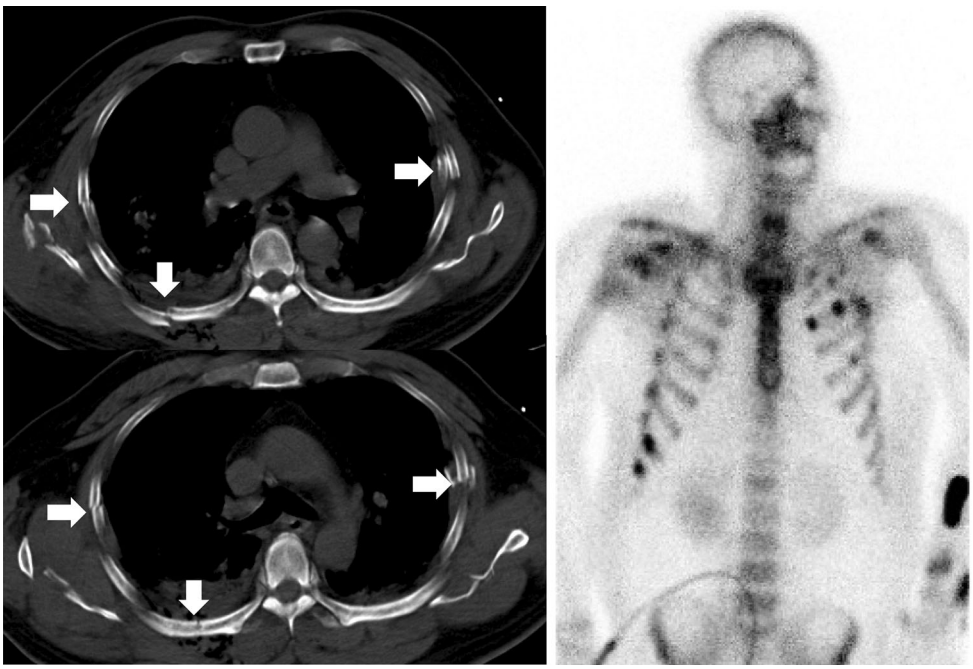

Fig. 1 (*Left*) chest CT showed multiple rib fractures with hemothorax. Both anterior and posterior arcs fractures were identified at right 5th to 8th ribs (*arrows*). (*Right*) multiple hot uptake sites suggesting rib fractures were identified on the bone scan

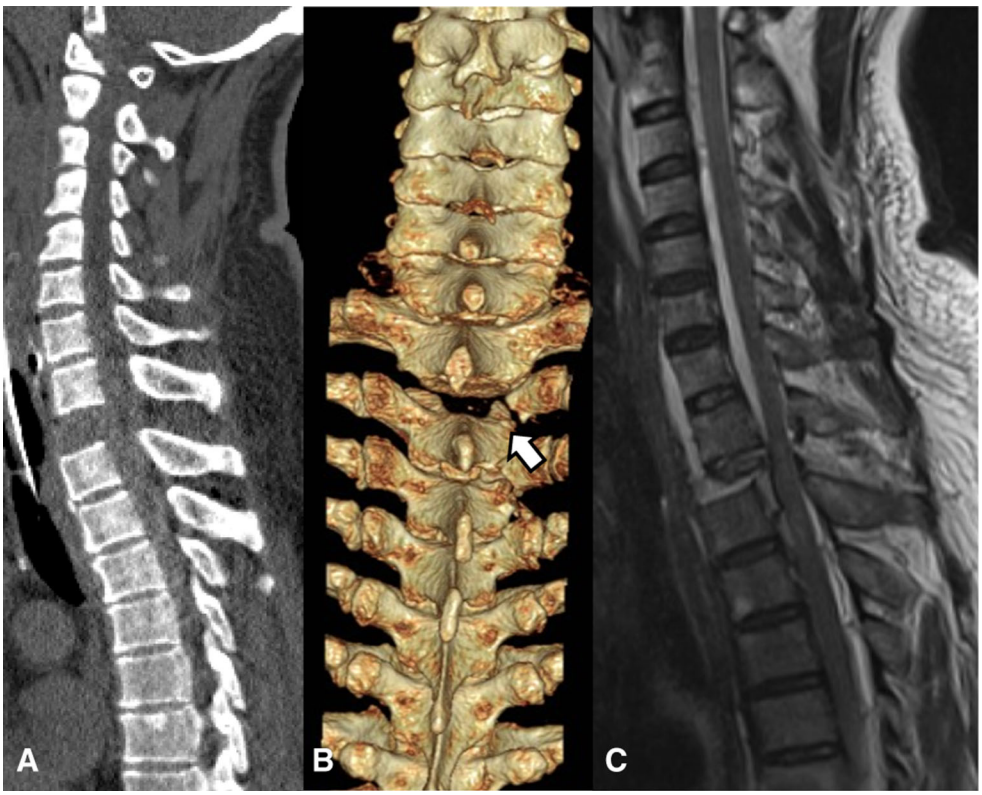

Fig. 2 Radiological examination of the case shows **a** widening of the T1–2 disc space on the computed tomography scan. **b** *Arrow* indicated fracture of the T2 right transverse process and lateral half of the superior articular process seen in three-dimensional reconstruction image of a computed tomography scan. **c** The spinal cord was compressed by the posteriorly displaced T1 and T1–2 disc on the magnetic resonance image

Diagnostic imaging section

Thoracic spine CT scans revealed severe distraction of the T1–2 intervertebral space (Fig. 2a, b). Chest CT showed multiple rib fractures with hemothorax. Multiple rib fractures were found at right 2nd to 9th and 11th ribs and left 4th to 7th ribs, especially both anterior and posterior arcs were fractured at right 5th to 8th ribs suggesting flail chest (Fig. 1a). Multiple hot uptake sites suggesting rib fractures were identified on the bone scan (Fig. 1b). Magnetic resonance imaging (MRI) revealed signal changes in the spinal cord and a clean-cut margin between the T1–2 disc and T2 body (Fig. 2c).

Historical review of the condition

Changes in autonomic function, such as severe hypotension or bradycardia, may be life-threatening in patients with acute cervical spinal cord injuries (SCIs). Hyperthermia due to autonomic dysfunction may contribute adversely to hemodynamic instability [1, 2]. In 1885, the earliest documented case of thermoregulatory dysfunction resulting in hyperthermia in the absence of infectious etiology was reported; [3] a man with an upper thoracic SCI and abrupt rising of body temperature, "On May 20, it rose to 109.2°, he was sweating profusely, and his face was dusky, but his pulse was only 80, and respiration 22. Half an hour afterwards, on his bowels being freely relieved, he said at once that he felt much better, and his temperature was found to have fallen to 97.8°". Sugarman et al. [4] referred "quadriplegia fever" as an unexplained fever in quadriplegics. He described a type of thermodysregulation observed after spinal cord injury as quad fever. Quad fever appears in the first several weeks to months after a cervical or upper thoracic SCI and is characterized by an extreme elevation in body core temperature beyond 40 °C without an infectious cause. Discriminating between infectious and noninfectious causes is important, and a thorough clinical assessment is required.

Rationale for treatment and evidence-based literature

Body temperature is under direct control of the thermoregulatory center located in the anterior hypothalamus [5]. The hypothalamic thermoregulatory center balances

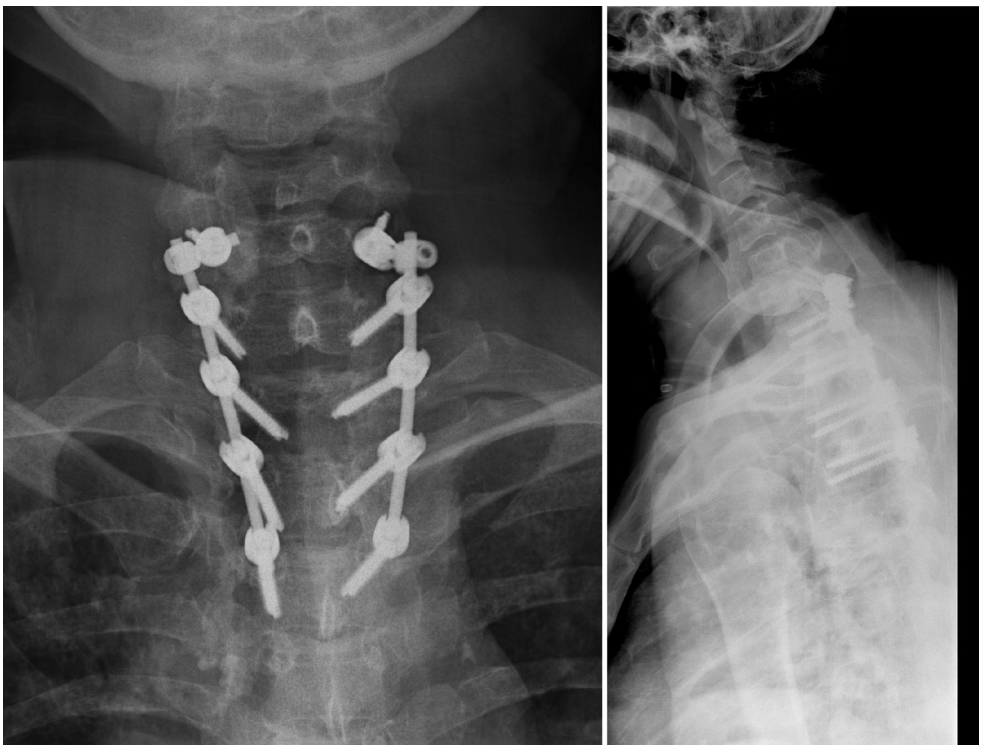

Fig. 3 Posterior instrumentation and fusion of C6–T3 on a cervico-thoracic roentgenogram

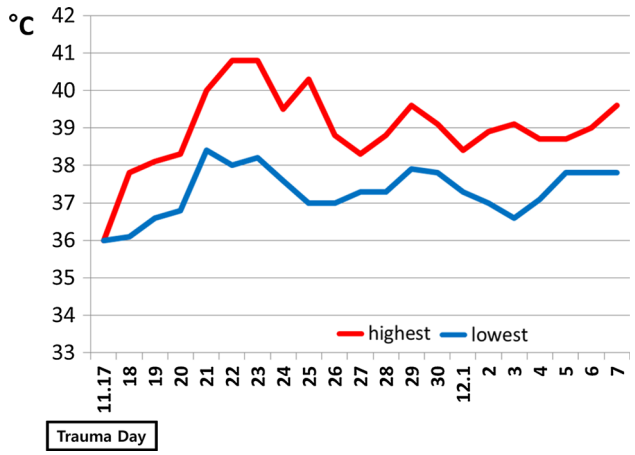

Fig. 4 Graph shows core temperature trends during the fever of unknown origin period

excess heat production, derived from metabolic activity in muscle and the liver, with heat dissipation from the skin and lungs [6]. Although central temperature mechanisms are unaffected by SCI, the ability to regulate body temperature is impaired due to the loss of hypothalamic thermoregulatory control below the level of the injury [7]. In addition, afferent pathways from the peripheral temperature receptors are interrupted below the level of the SCI [7].

Thermodysregulation after SCI falls into three categories based on the current literature [8]. The first is poikilothermia, often called "environmental fever". Some people with cervical SCI complain of feeling very cold. This is very marked after a shower, when the patient sometimes needs a heated quilt or a heater to feel comfortable. The ability to increase temperature by shivering is lost below the level of the lesion. Some patients suffer from feeling cold all the time [9]. The second is quad fever, a fever without an infectious source occurring in the first several weeks to months after SCI. The third is exercise-induced fever [8]. The presenting case experienced a pattern identified as quad fever during a febrile episode of unknown origin until a urinary tract infection was detected.

Sweating plays a key role in heat dissipation; for example, atropine interferes with thermoregulation by blocking sweating or vasodilation followed by raising core temperature. Autonomic dysfunction can result in sweating disturbances, which can render patients unable to get rid of excess heat by sweating, which may play a role in quad fever [8]. In individuals with SCIs above T6, shivering, thermoregulatory sweating, and peripheral circulatory adjustment below the lesion are completely lost [7]. The degree of temperature dysregulation appears to be related to the level of injury, and perhaps to the degree of the SCI completeness, similar to the pattern of autonomic dysfunction [10]. SCI completeness has not been correlated with autonomic completeness [8]. In the present case, severe distraction of T1–2 could have resulted in autonomic completeness and temperature dysregulation.

Quad fever is a diagnosis of exclusion when other causes are ruled out as sources of fever. There are noninfectious causes of severe hyperthermia, such as certain metabolic diseases (e.g., hyperthyroidism), and the effects of pharmacologic agents that interfere with thermoregulation (e.g., malignant hyperthermia, neuroleptic malignant syndrome, serotonin syndrome) [11]. The anesthetic agents administered in this case were isoflurane and rocuronium. Malignant hyperthermia had to be ruled out because of some of the clinical signs, such as increased muscle metabolism, muscle rigidity, and absence of rhabdomyolysis. In addition, the onset of malignant hyperthermia usually occurs within 1 h of administration of general anesthesia [12]. In this case, the body temperature increased above 38 °C 3 days after surgery.

Fentanyl and tramadol were used to control pain. Serotonin syndrome, a potentially life-threatening condition associated with increased serotonergic activity in the central nervous system, had to be ruled out as the cause of fever in this patient. Serotonin syndrome is characterized by a triad of mental status changes, autonomic hyperactivity, and neuromuscular abnormalities. To diagnose serotonin syndrome, a patient must have taken a serotonergic agent and meet one of the following conditions: spontaneous clonus; inducible clonus and either agitation or diaphoresis; ocular clonus and either agitation or diaphoresis; tremor and hyperreflexia; hypertonia; temperature above 38 °C; and either ocular or inducible clonus [13]. The temperature increase in serotonin syndrome is due to muscle activity, not the hypothalamic set-point [14]. The patient in this case did not have hypertonia or ocular or inducible clonus; therefore, he did not meet the diagnostic criteria for serotonin syndrome.

In the presented case, the initial GCS score was normal and the initial brain CT showed normal findings. On post-trauma day 8, the brain MRI showed delayed subdural hemorrhage; however, there was no mass effect or abnormal findings in the brain parenchyma. Diffuse axonal injury and frontal lobe injury are independently predictive of an increased risk of development of neurogenic fever following severe traumatic brain injury [15]. Therefore, the possibility of neurogenic fever after traumatic brain injury was low.

Patients with cervical SCI are prone to lung problems, such as atelectasis or pneumonia, especially in the basal segments of the lung [16, 17]. Atelectasis may also cause fever in patients, especially in the early postoperative period; however, such extremely high temperatures could not be explained solely by atelectasis. Pneumonic infiltration was not found in the chest CT or chest X-ray in this case; the chest X-ray was examined daily.

Ulger et al. [18] reported five fatal cases of quad fever in patients with cervical SCI. All cases died of uncontrolled quad fever of up to 44 °C followed by cardiac arrest. Fortunately, the patient in the present case survived despite the unstable, life-threatening situation. However, the neurological level of injury changed from C8 on initial assessment to C4 after a febrile episode. This indicates that secondary injury damaged the cephalad-level neuronal cells tremendously. Hyperthermia damages cells by the following mechanisms: increases in membrane fluidity and permeability, metabolic rate, and activity of the Na^+–K^+ adenosine triphosphatase pump; and decreases in cellular adenosine triphosphate content [19]. Therefore, controlling quad fever is essential for minimizing secondary injury to the spinal cord. Intravascular temperature modulation has been shown to be effective for preventing and controlling fever [20, 21]. However, the risk of catheter-related thrombosis is a potential problem. In addition, systemic hypothermia reportedly has complications, such as cardiac arrhythmia, coagulopathies, and a rebound increase in intracranial pressure [22]. Since quad fever itself is a very debilitating condition that has high mortality and morbidity, we did not try to lower the body temperature forcibly in this case. However, this is challenging because of its potential beneficial effects of preventing cellular damage from secondary injury. We supplied sufficient hydration, intravenous antipyretics, and body surface cooling with ice packs; however, the prognosis of the neurological deficit was not satisfactory. Controlling quad fever is clinically important not only to save a patient's life but also to protect the spinal cord from secondary injury. If a patient with quad fever is encountered in the near future, we will try to modulate the body temperature with the cooperation of the appropriate medical departments and the intensive care unit.

Procedure (surgery, intervention)

The posterior ligamentous complex was disrupted completely in the surgical field. The remained torn ligamentum flavum at T1–2 was clearly resected to prevent buckling of the ligament during in T1–2 reduction. Posterior instrumentation was installed from C6 to T3 with posterior fusion by autologous iliac bone graft (Fig. 2).

Outcome, follow-up

At post-trauma year 6, his injury state was still complete and the neurological level of injury was changed to C4. His shoulder elevation motor power was decreased to grade 3.

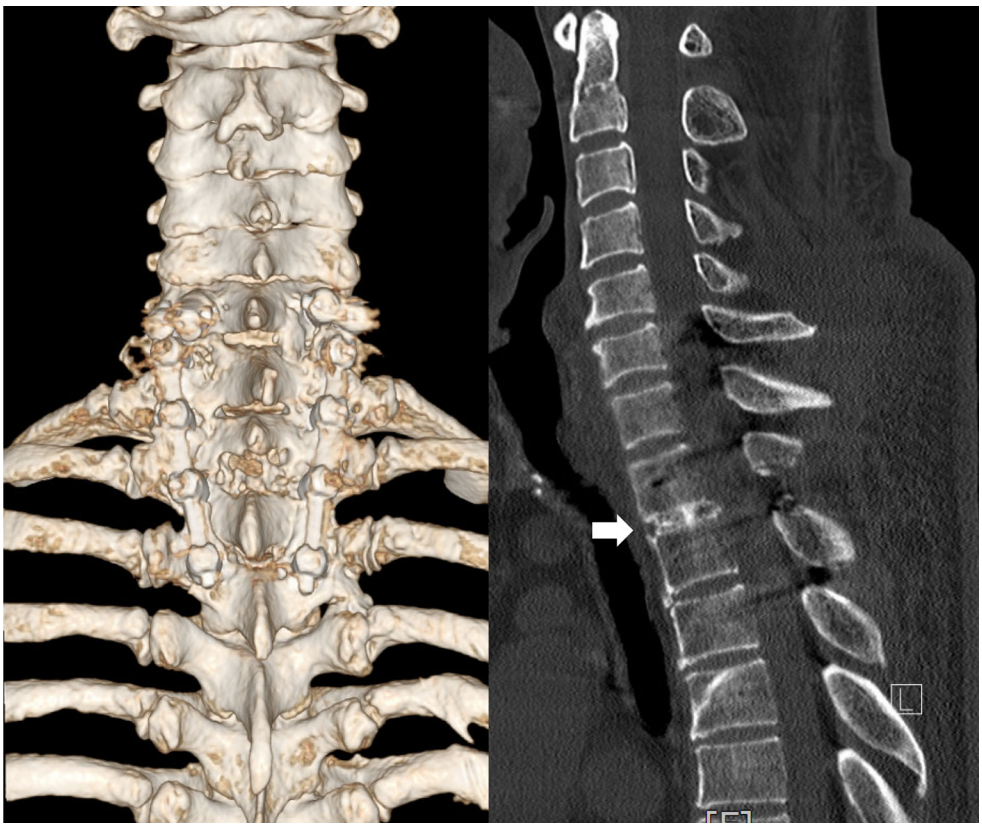

Fig. 5 **a** Three-dimensional CT scan showed solid union was achieved after 6 years post-trauma. **b** Spontaneous T1–2 interbody fusion was seen on sagittal CT images (*arrow*)

Fine hand movement was impossible. Solid instrumented fusion was achieved. Interestingly, spontaneous T1–2 interbody fusion was identified on the follow-up cervicothoracic CT scans (Fig. 5).

Compliance with ethical standards

Conflict of interest The authors declares that they have no conflict of interest.

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