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The Sinking Bone Syndrome?

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Abstract

Bone resorption is a known complication of cranioplasty after decompressive craniectomy (DC). A peculiar group of insidious, progressive, invalidating neurological symptoms was observed in patients presenting with incomplete resorption and abnormal mobility of the re-implanted bone. Such symptoms were similar, but with time more severe, to those encountered in the sinking flap syndrome. Are we facing a sort of Sinking Bone Syndrome? We accurately analyze these cases and review the literature. Over a 7-years period, 312 DCs were performed at our Institution. In 7 patients, headache, vertigo, gait ataxia, confusion, blurred speech, short-term memory impairment, hemiparesis, sudden loss of consciousness, and third cranial nerve palsy were observed in a time period ranging from 18 months to 5 years after cranioplasty. Clinical and neuroradiological examinations were performed to disclose the possible etiopathogenesis of this condition. Collected data showed partial resorption of the repositioned bone and its unnatural inward movements during postural changes. Bone movements were interpreted as the major cause of the symptoms. A new cranioplasty was then performed in every case, using porous hydroxyapatite in 6 patients and polyetherketone implant in the other. Full resolution of symptoms was always obtained 3 to 20 days after the second surgery. No further complications were reported. We believe that long-term follow up in patients operated on by cranioplasty after DC will be needed regularly for years after skull reconstruction and that newly appearing symptoms should never go underestimated or simply interpreted as a long-term consequence of previous brain damage.

Key words: cranioplasty, decompressive craniectomy, intracranial pressure, sinking flap, syndrome

Introduction

In the last few years the use of decompressive craniectomy (DC) in everyday neurosurgical practice has largely increased, even though the effectiveness of this procedure is still uncertain.[1)] Patients surviving from DC need a second operation to repair the bone defect.[4)] Commonly, this surgery consists in the repositioning of the previously removed autologous bone flap. When it is not available, different artificial materials, appropriately shaped, may be used as substitutes.[5)] The common use of the autologous bone primarily relies on anatomical needs thanks to the optimal fitting of the removed bone to the skull defect. Furthermore, it is the best scaffold for bone regeneration providing a relatively low infection rate when compared to prostheses. However, after the autologous bone replant, the formation of the initial, small bony bridges between the implant and the surrounding cranial vault can sometimes not occur. This condition can lead to an incomplete re-ossification up to, in a still undefined number of cases, an almost complete resorption of the re-implanted bone.[6)] The reasons and the true incidence of this phenomenon are still largely unknown. Some authors focus on the suboptimal methods of bone preservation now available (cryopreservation versus storage within an appositely created abdominal pouch). Numerous adjuncts (e.g., the interposition of biological scaffolds such as granular hydroxyapatite or the local use of growth factors) have been proposed to minimize the risk of resorption, but their definitive validation is still lacking. Bone resorption seems to be a gradual phenomenon, but once started, it can potentially lead to a complete disappearance of the implanted bone. Bone resorption frequently occurs in a short time interval after

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cranioplasty (3–9 months) but occasionally requires years to develop, with a progressive loss of the normal connections between the re-implanted bone and the skull vault. In such cases, because of the free micro-motion of the bone over the underlying dura and brain, progressive insidious neurological symptoms may develop which could be misinterpreted. In the last few years we observed a small group of patients operated on by cranioplasty which have gradually developed neurological symptoms similar to those occurring in the sinking flap syndrome.[5,11] Are we facing a sort of ''Sinking Bone Syndrome''? We present these cases discussing the possible etiology and its potential correlations with the sinking flap syndrome as well as searching for literature support.

Materials and Methods

From January 2003 to January 2010, 312 DCs were performed at our Institution. One hundred eighty-nine patients had severe head trauma, 52 had subarachnoid hemorrhage, 45 had spontaneous intracerebral hemorrhage, 3 had bleeding from an arteriovenous malformation (AVM), 4 had tumors with sudden hemorrhagic onset, 7 had acute meningoencephalitis, and 14 had acute brain ischemia. One hundred eighty-six patients survived from DC and underwent cranioplasty. At the moment of bone repositioning, the autologous bone was always fixed using titanium miniplates and screws that were placed circumferentially. Moreover, before the bone flap was repositioned, the borders of the craniectomy were freed from the scar tissue and than slightly drilled in order to increase the potential for osteogenesis. In the time period between March 2007 to December 2010, 7 patients, operated on by cranioplasty, came back to our attention because of a history of unexplained, progressive, severe neurological deterioration. They were treated in a time interval from 2 to 5 years before. Mean age was 49 years (ranging from 42 to 60). The clinical onset, as referred either by the patients either by their relatives, was insidious and nonspecific, frequently characterized only by a positional headache without specific localization. Within a short period of time, lightheadedness, confusion, short-term memory impairment and, in left side operated patients, blurred speech appeared each time the patient assumed the upright position. In a few more months, patients were able to rise from bed only for a short period of time, then hemiparesis contralateral to the cranioplasty developed. In 2 cases, third cranial nerve palsy was associated with contralateral facio-brachio-crural hemiparesis. Recumbent position completely relieved the symptoms in 5 cases, and partially in 2. At inspection, free bone flap micromovements and evident asymmetry in the cranial conformation were observed in every patient.

Serial computed tomography (CT), magnetic resonance (MR) imaging, and electroencephalography were performed in all patients, and the only abnormality disclosed was partial resorption of the re-implanted bone. Cerebrospinal fluid (CSF) dynamic was studied in only 3 patients who presented with minimal to moderate enlargement of the ventricular system. This was investigated by a lumbar infusion test that resulted negative in all patients. In the remaining 4 cases, in whom the bone resorption was more advanced and the dimensions of the ventricular system were in the normal range, a lumbar infusion test was not considered useful neither predictive. In one case, MR imaging tractography was performed to disclose eventual abnormalities of the motor fibers. The pyramidal pathway lying on the operated side showed a smaller number of fibers than the contralateral one, but no clear distortion of their distribution was evidenced. Obviously, this could be related to the recumbent position assumed by the patient during the examination and to the impossibility of performing a dynamic observation. Unfortunately, no methodologies for the study of brain blood flow or metabolism (i.e., single photon emission computed tomography, xenon CT) were performed. All patients underwent a second surgery to insert a porous hydroxyapatite implant in 6 cases and polyetherketone implant in the other.

Results

No postoperative complications occurred. Symptom improvement was seen within 3 days from surgery in every case. Full resolution of all disturbances was always observed within 20 days. We report in detail the two most representative cases.

Case 1: On November 2008, a 45-year-old male was admitted to our hospital after a car accident. At arrival he was intubated and sedated. Left pupil was dilated and minimally reactive to light, and right pupil was promptly reactive. Glasgow Coma Scale (GCS) score before intubation was 7. CT disclosed a left acute subdural hematoma, with a midline shift of 1.2 cm and uncal herniation (Fig. 1A). A left fronto-temporo-parietal DC was performed in emergency and the subdural hematoma was evacuated (Fig. 1B). Ten days later he was transferred to our department from the intensive care unit. He was fully awake with a mild, right brachio-crural hemiparesis. On February 2009 cranioplasty using the cryopreserved

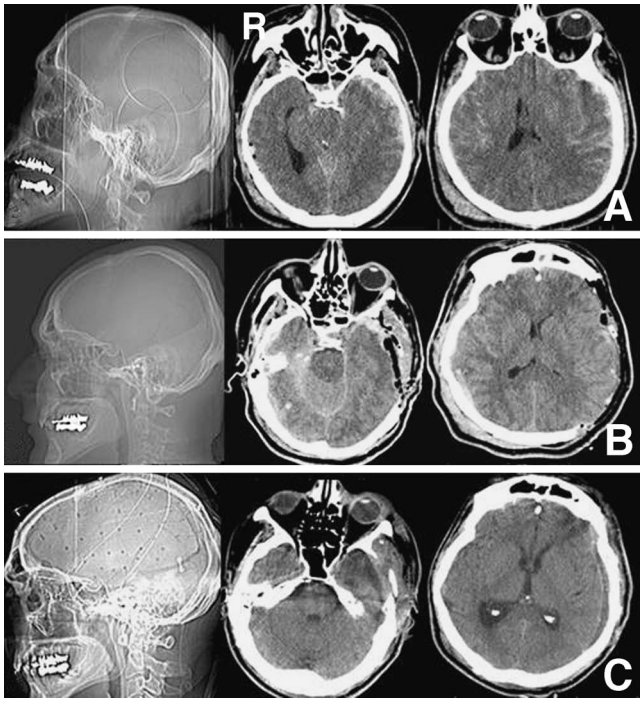

Fig. 1 Case 1. A: Computed tomography (CT) scout view and axial CT scans on admission showing a left acute subdural hematoma with multiple internal herniations. B: Postoperative CT scout view and axial CT scans demonstrating a large fronto-temporo-parietal decompressive craniectomy, subdural hematoma evacuation, and complete midline realignment with resolution of the intracerebral herniations. C: CT scout view and axial CT scans after cranioplasty showing the full coverage of the bone defect.

autologous bone was performed (Fig. 1C). One month after the second surgery, the residual hemiparesis further improved, leaving only minimal difficulties in distal fine hand movements.

Regular follow-up examinations and CT were performed every 6 months until March 2010. In this period the patient started to complain of a transient headache immediately after leaving the bed. At neurological evaluation, temporo-spatial orientation was normal and no motor or sensory deficits were observed. Reflexes were symmetrical. Symptoms were initially considered as a long-term sequel of the severe brain injury, similar to the post-concussion syndrome. Symptomatic treatment was started, initially with good results. Three months after, headache was still present on a daily basis. A few minutes after rising from bed, the patient reported an increasing feeling of confusion associated with the appearance of blurred speech and impaired autonomous walking. In August 2010, he was confined at home, unable to leave bed for long intervals and needing two people to help him move even from one room to the other.

At neurological evaluation, the patient showed severe compromise of the temporo-spatial orientation, speech was barely comprehensible, and he was unable to perform simple motor tasks. When asked to walk, he needed assistance to get up and when he maintained the upright position for more than a minute, left third cranial nerve palsy with ptosis associated with severe right brachio-crural hemiparesis appeared (Fig. 2A). In this position, the re-implanted bone flap collapsed within the borders of craniectomy. After 30 minutes in the supine position, ptosis and hemiparesis improved, as well as the state of consciousness, although the patient was still confused (Fig. 2B). Moreover, in this position cranial contour became regular again. Repeat CT evidenced partial resorption of the re-implanted bone and a gap of about 1 cm between it and the borders of the craniectomy (Fig. 2C).

On September 2010, he underwent reoperation. At surgery the resorbed bone, still kept in place by the titanium plates, moved freely up and down over the dural layer. It was removed (Fig. 2D) and replaced by a porous hydroxyapatite implant fully covering the defect (Fig. 2E). Three days after surgery, while still lying in bed, the patient was alert and well reactive, able to interact with the observers. One week after surgery, he was able to rise from bed autonomously. Hemiparesis and ptosis did not appear any more (Fig. 2F). Short-term memory impairment progressively resolved and the patient was fully able to perform the activities of daily living within 2 months. No further modifications of neurological conditions have been noted until now.

Case 2: On January 2003, a 35-year-old woman was admitted to the emergency department of our hospital because of the development of a comatose state. Her husband reported the appearance of left hemiparesis, followed by sudden loss of consciousness. At arrival she was intubated and sedated. Assigned GCS score was 5. The right pupil was dilated and nonreactive to light, and the left one was normally reactive. CT disclosed a large, right temporo-parietal intracerebral hemorrhage with midline shift over 1 cm and multiple intracerebral herniations. Digital subtraction angiography documented a right fronto-parietal AVM (Fig. 3A). She was treated through a right fronto-temporo-parietal craniotomy. After hematoma evacuation and AVM removal, the brain was still tense, so the bone flap was not repositioned (Fig. 3B). An intracranial pressure (ICP) sensor was left in place for future ICP monitoring. Because of the development of untreatable, persistent intracranial hypertension, 4 days later she

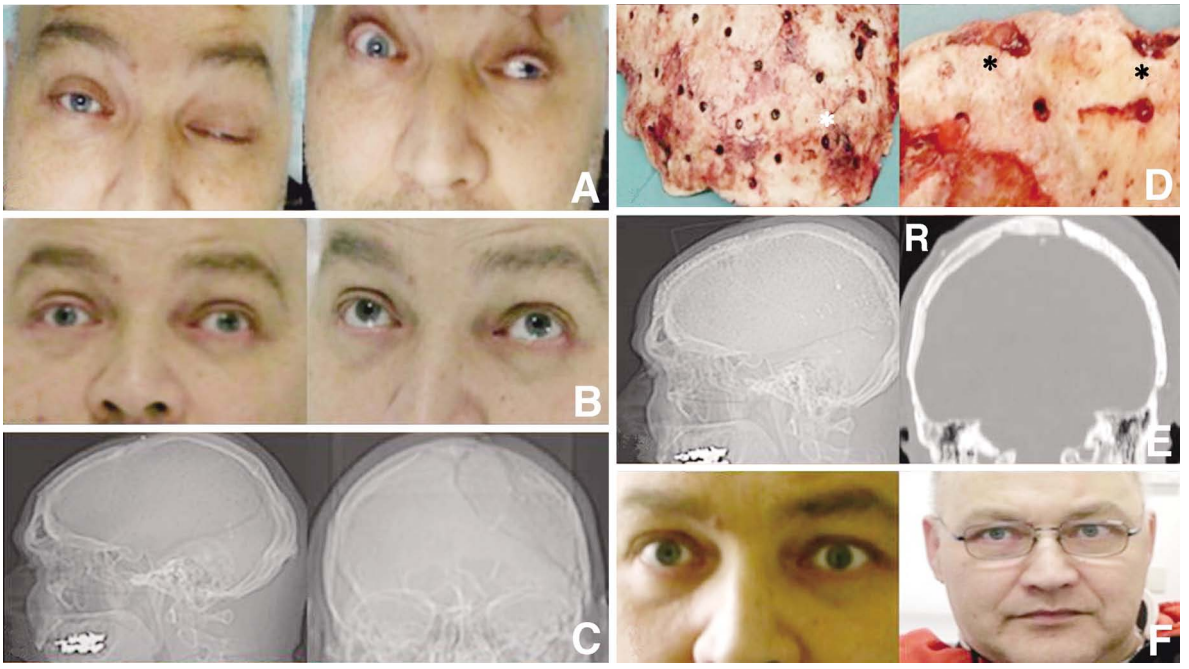

Fig. 2 Case 1. A, B: Neurological examination before sinking bone correction showing left ptosis and complete left third cranial nerve palsy appearing after a few minutes in the upright position (A), and ptosis regression and normal ocular movements during the supine position (B). C: Computed tomography (CT) scout views showing incomplete resorption and minimal inward retraction of the re-implanted bone. D: Intraoperative photographs of the removed bone confirming resorption both on the external surface (*white asterisk*) and on the borders (*black asterisks*). E: CT scout view and coronal CT scan after porous hydroxyapatite cranioplasty showing regular skull borders. F: Photographs after one month showing the left ptosis and third cranial nerve palsy had fully regressed, also in the upright position.

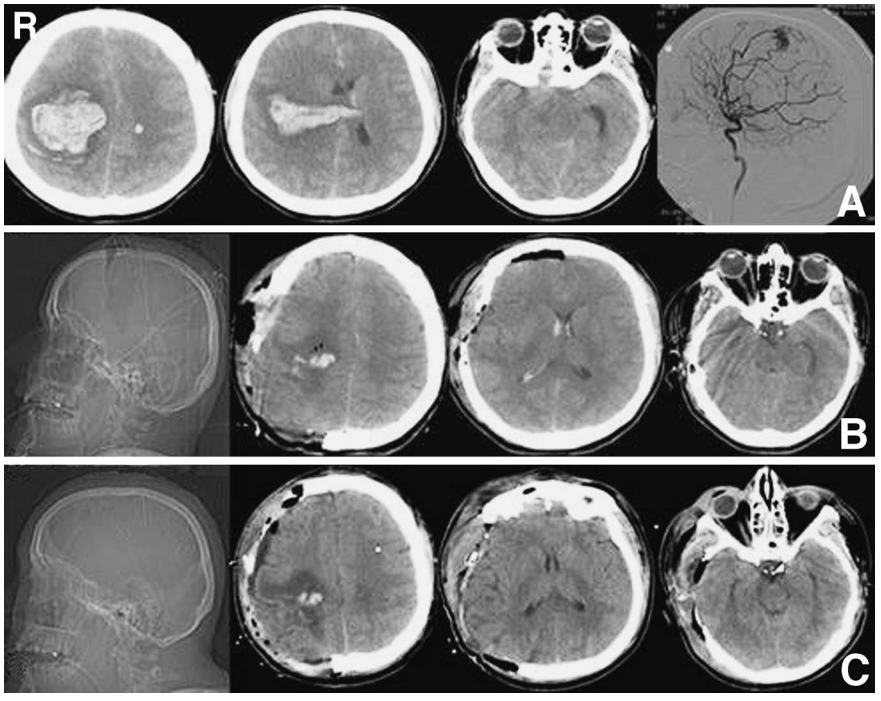

Fig. 3 Case 2. A: Axial computed tomography (CT) scans on admission and subsequent right carotid angiogram disclosing a large right fronto-parietal hematoma related to a fronto-parietal arteriovenous malformation. B: Postoperative CT scout view and axial CT scans showing a fronto-parietal craniectomy, intracerebral hematoma evacuation, and immediate midline realignment, but the persistence of perimesencephalic cistern effacement. C: CT scout view and axial CT scans after craniectomy demonstrating better visualization of the perimesencephalic cisterns.

underwent a second operation for enlargement of the previous craniectomy. After surgery, ICP immediately dropped into the normal range (Fig. 3C). She slowly regained consciousness and a tracheostomy was performed.

Two months after the DC, she underwent cranioplasty. Postoperatively, global cognition improved and she was fully awake with a mild, left brachio-crural hemiparesis. These condition remained unchanged for 4 years, during which the patient underwent neurological examinations every 6 months and CT once a year. Neuroradiological studies showed a progressive partial resorption of the re-implanted bone, that was already present on CT performed 6 months after cranioplasty but initially underestimated. On September 2008, the patient started to complain of fatigue, confusion, and difficulties in concentration, which were interpreted as the effect of a depressive syndrome, so pharmacological treatment with escitalopram was started, without benefits. On February 2009, short-term memory was clearly impaired and the preexisting mild hemiparesis worsened, so that she was no longer able to perform most of the common daily activities, reporting sudden falls when trying to walk by herself. Symptoms immediately disappeared when she was lying on the bed. On May 2009, she presented with double vision and incomplete right ptosis immediately after assuming the upright position. At follow-up evaluation, symptoms were considered as the long-term consequence of the brain damage and the ineffective antidepressant therapy was interrupted. Evaluated by an oculist, a diagnosis of medial rectus muscle dysfunction was made and she underwent surgery for shortening of the external rectus muscle, with slight vision improvement.

On August 2009, she finally came to our attention. She was almost completely bedridden, unable to focus attention on the examiner and to perform simple motor tasks. During examination she frequently fell asleep. She suffered from urinary incontinence too. An incomplete deficit of the right third cranial nerve was observed as well as severe left facio-brachio-crural hemiparesis (Fig. 4A). To help her assume the upright position, two people were needed and she immediately tended to bend toward the hemiparetic side. In this position massive sialorrhea developed and the hemiparesis turned to plegia of the arm and leg. On inspection, the bone flap had fallen inside the borders of craniectomy and was freely moving. CT largely confirmed these findings (Fig. 4B). On September 2009, she was re-operated on. At surgery the bones were resorbed and the dura layer was extremely adherent to it. The bones were removed and a preformed, porous hydroxyapatite implant was positioned (Fig. 4C). Postoperative course was regular. Eight days after surgery, the patient was fully awake, she promptly executed verbal commands, and the hemiparesis markedly improved. On day 15, she was able to rise from bed without any help, uri-

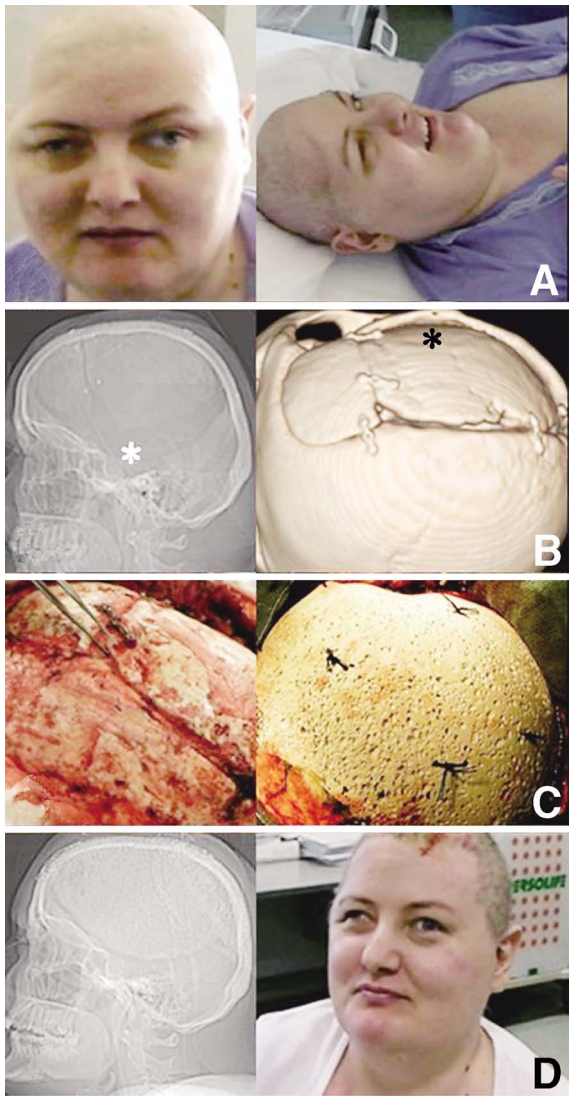

Fig. 4 Case 2. A: Neurological examination before sinking bone correction showing right ptosis during the sitting position and its regression in the supine posture. B: Computed tomography (CT) scout view and three-dimensional CT scan demonstrating partial resorption (*white asterisk*) and sinking (*black asterisk*) of the re-implanted bones. C: Intraoperative photographs showing the re-implanted bones were thinned and freely moving over the dural layer, so they were removed and replaced with a porous hydroxyapatite implant fully covering the cranial defect. D: Post-cranioplasty CT scout view showing the correct implant positioning, and photograph showing right ptosis regression also in the upright position.

nary incontinence was resolved, and the double vision recovered as well as the right ptosis (Fig. 4D). Unfortunately, presumably because of the previous ocular surgery, the globe was unable to assume the physiological symmetrical position. The patient has been regularly evaluated every 6 months since the second surgery and no further modifications have been observed so far.

Discussion

The increasing number of DCs performed in the last few years all over the world has led to a proportional increase in cranioplasty procedures.[1,3–6] The use of preserved autologous bone in these surgeries is universally considered the first and best option for skull reconstruction.[4] It grants optimal functional and aesthetic results, particularly when bone destruction is minimized during craniectomy. Risks of infection are lower and potential for bone regrowth is higher when autologous bone is compared to artificial implants. Unfortunately, bone resorption is one of the possible complications of autologous bone cranioplasty.[4,6] There is no definitive certainty about the exact percentage of cases in which this phenomenon occurs, although it seems to be rather unusual in most of the largest reported series.[6] Furthermore, there is no adequate information about the causes which ultimately lead to resorption. It is a common issue that the re-implanted bone should be put adherent to the skull contour in order to increase the potential for bone consolidation. This process may be also facilitated by removing the scar tissue covering the borders of the craniectomy to promote the activity of osteoblasts and osteointegration. Large gaps and excessive implant fragmentation will almost inevitably lead to resorption. The relationship between the method of bone flap storage and bone resorption has not yet been fully investigated, but there is no evidence of any significant difference in the overall complication rates when comparing series where the bone was cryopreserved or stored in the patient's abdominal wall.[7,10] Another factor to be considered is the time interval between bone removal and bone repositioning. Theoretically, the longer is the time between the removal and reconstructive procedure, the higher is the possibility of developing bone resorption. Even about this topic, no definitive information emerges from reports.[2,9] It is a common experience that patients undergoing autologous bone cranioplasty will develop a remodeling of the re-implanted bone. This process leads to minor irregularities of the cranioplasty profile, which can be easily disclosed at a close head inspection. In these subjects, serial CT scans are an essential part of the follow-up process, because it is necessary to be aware if the bone is ''adapting'' to the new condition or is ''disappearing.''

Bone resorption is an unpredictable process. Sometimes it may be almost complete in a few months, alternatively it may happen in years. In case of a partial resorption, bone width reduces without becoming critical. This minimal skull deformity is considered normal by the patients, but they are more exposed to the development of neurological symptoms. In this situation the bone is loosely attached or completely detached by the rest of the skull, so that it freely moves over the dural layer, depending on postural changes. The longer the time from cranioplasty, the stronger the adhesion will be between the dural layer and the mobile bone. Moreover, the excavated contours of craniectomy will act as a chute, allowing inward movements of the bone. Starting from these considerations, the leading question was why these patients developed such a peculiar group of symptoms and what caused their progression. Examining the literature, there is only one condition which can be assimilated to what we observed, that is the sinking flap syndrome.[5,11] In such patients the precise clinical onset is difficult to appreciate and they commonly present with undue fatigability, headache, dizziness, vague discomfort at the site of cranial defect, feeling of apprehension, insecurity, depression, followed by disturbances of sensation, hemiparesis/hemiplegia, poor cognition, lethargy and, if left untreated, death. The unopposed effect of atmospheric pressure over the unprotected brain would initially lead to a displacement of CSF toward the spinal canal, then, when this compensation mechanism is exhausted, to a direct displacement of the brain itself. However, sinking flap syndrome develops in patients waiting for cranioplasty and preoperative flap condition seems to be the most important aspect related to prognosis, as patients with significant sinking skin over the decompressed area usually have a good outcome after cranioplasty.

We were able to find only one previous report of neurological symptoms directly related to the free movement of a bone flap. In 1979, a 60-year-old patient was operated through a right temporoparietal craniotomy for an acute subdural hematoma.[8] One year after surgery he started to complain of dizziness, gait disturbance, memory impairment, and difficulty in following the right direction. At this time a depression of 1.5 cm was observed in the area of the previous craniotomy. The neurological symptoms and flap depression were fluctuating. The depression was not noticeable early in the morning after overnight recumbency, while worsened in the evening after he had been ambulating most of the

day. Additionally, the patient reported that he could think and concentrate better at certain times during the day. He was re-operated and the bone was fixed with an adjunct of methacrylate to fill the gap. After surgery, symptoms resolved promptly. The cases we report in this paper are similar, but the time period between cranioplasty and symptom exordium was sometimes much longer (up to 4 years).

We strongly believe that the symptoms essentially rely on the same mechanism proposed for the sinking flap syndrome, but with a striking difference. In patients still harboring the bone, though partially reabsorbed and thin, the weight of a solid body must be directly added to the effect of the atmospheric pressure. This can create a more severe mass effect when the implant is pushed inward at the assumption of the standing position, with massive distortion of the dural layer and subjacent brain. This mechanical effect might be relieved by the assumption of the supine position, allowing the re-implanted bone to return to a physiological seat if it is still attached to the surrounding skull borders by titanium plates. Once the bone gains complete free motion, the pressure cone on the brain parenchyma in the upright position could be so high as to cause a ''transient'' uncal herniation, explaining the appearance of the ipsilateral third cranial nerve palsy and the contralateral hemiparesis. This condition could be named the ''Sinking Bone Syndrome.'' In our series, complete neurological recovery was always observed after the new solid cranioplasty. This is encouraging, because surgery seems to be always able to address the potential ''Sinking Bone Syndrome'' regardless of severity and duration of the neurological symptoms. Nonetheless, a prompt diagnosis should be obtained in the preliminary phases of the disease. This is the leading reason why we currently ask the patients, their relatives or, when institutionalized, the attending physicians, to report any unusual long-term modification of neurological conditions, particularly when unexplained worsening of a preexisting relatively good neurological status or even small modifications of cranial conformation take place.

In conclusion, we believe that the clinical history of patients undergoing DC cannot be considered definitively closed once cranioplasty is performed. Because of the potential for long-term resorption of the re-implanted bone, follow-up examinations and regular CT should never be discontinued in order to early diagnose this insidious but severe syndrome related to bone resorption aiming at promptly scheduled re-surgery.

Conflicts of Interest Disclosure

The authors have no personal financial or institutional interest in any of the drugs, materials, or devices in the article.

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