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Review Article

Locked-In Syndrome in Children: Report of Five Cases and Review of the Literature

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The locked-in syndrome is a rare neurologic disorder defined by (1) the presence of sustained eye opening; (2) preserved awareness; (3) aphonia or hypophonia; (4) quadriplegia or quadriparesis; and (5) a primary mode of communication that uses vertical or lateral eye movement or blinking. Five cases are reported here, and previous literature is reviewed. According to the literature, the most common etiology of locked-in syndrome in children is ventral pontine stroke, most frequently caused by a vertebrobasilar artery thrombosis or occlusion. In terms of prognosis, 35% of pediatric locked-in syndrome patients experienced some motor recovery, 26% had good recovery, 23% died, and 16% remained quadriplegic and anarthric. These findings raise important ethical considerations in terms of quality of life and end-of-life decisions in such challenging cases.

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Introduction

The development of hospital intensive care units has considerably increased the number of children surviving severe brain damage. In clinical practice, traumatic and nontraumatic coma is a frequent problem and, in this case, the main preoccupation of parents and physicians is the neurologic recovery, which may range from absence of cognitive and motor impairments to severe disability or death. Some children may awake from the coma in nearly complete paralysis, able to communicate only via small eye movements. This condition, termed the *locked-in syndrome*, is typically caused by a brainstem lesion [1].

The rarity of locked-in syndrome in children often results in the diagnosis being delayed or even missed entirely. Signs of consciousness, such as vertical eye movements in response to verbal commands, should be tested in any child apparently in a coma or in vegetative state, especially if a brainstem lesion is detected. Indeed, early detection of locked-in syndrome is important with regard to nursing (including adapted pain treatment [2]) and possible end-of-life decisions, especially in the case of children with potential long-term survival. However, there are no widely accepted guidelines for management of pediatric locked-in syndrome patients. Additionally, there is not much in the literature to inform pediatric physicians and other medical professionals about the management of locked-in syndrome in children.

Presented here are five cases of locked-in syndrome in children or adolescents. Patient 1 was hospitalized at the Liepe University Hospital. Patients 2-5 were members of the French Association for Locked-In Syndrome. This article contains a review of the available pediatric literature on this topic and a discussion of quality of life and end-of-life decisions in locked-in syndrome children.

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Cases

Patient 1

A 13-year-old girl with unremarkable medical history was admitted to the emergency department of Liepe University Hospital displaying left hemiparesis. On admission, her Glasgow Coma Scale subscores were Eye response 2, Verbal response 1, Motor response 2. She was intubated and mechanically ventilated. She remained comatose during the following 3 days, and then developed spontaneous eye opening and stereotyped extension movements in response to noxious stimuli. After awakening, she did not respond to simple auditory commands, but showed reproducible downward eye movements in response to written commands. She showed oral reflexive movements, vertical visual pursuit and fixation, and quadriplegia with bilateral Babinski sign and absent auditory startle response. Somatosensory evoked potentials showed bilateral N20 waves (although with delayed latency). Brainstem auditory evoked potentials demonstrated preserved I-III waves but absent IV-V components. Visual evoked potentials showed preserved cortical responses. Computed tomography and magnetic resonance imaging [3] (Fig 1) revealed an extensive circular ventral pontine lesion with a hemorrhagic component extending to the left tegmental area. Magnetic resonance angiography findings were normal, and electroencephalography (EEG) depicted normal background activity that was responsive to eye opening.

The parents asked for withdrawal of artificial respiration and denied tracheostomy. The medical team was divided, but decided not to follow the parents' wishes. Tracheostomy and gastrostomy were performed. After 1 week, the patient recovered functional hearing in one ear; after 2 weeks, she could use eye-coded yes/no communication, and she subsequently recovered voluntary control of cervical muscles while remaining mute and quadriplegic. The family now explicitly asked for euthanasia. On day 31, the patient was able to communicate via eye-coded movements and reported that she wanted continuation of care. She next started to communicate using the eye-coded alphabetic communication system (Table 1). Using this method she communicated that she left the decision concerning end-of-life issues to her parents. On day 37, the patient exhibited external signs of anxiety and was treated with alprazolam. On day 59, she was transferred to a rehabilitation center. She failed to show further motor recovery and 3 months after admission she became stuporous, then comatose, due to obstructive hydrocephalus. At the request of the family, it was decided not to continue treatment and she died on day 92 after the initial brain insult.

Patient 2

A 17-year-old boy with a history of head trauma and absence epilepsy (petit mal since age 4) showed acute-onset dizziness, vomiting, and inability to walk and speak. On admission to the hospital, he was comatose (with Glasgow Coma Scale subscores of Eye response 1, Verbal response 2, Motor response 1) and required intubation and mechanical ventilation. The computed tomography scan revealed an ischemic hypodensity of the brainstem, vermis, and right cerebellar hemisphere, attributed to an ischemic origin. After a 2-week period of pharmacologic coma, the diagnosis of locked-in syndrome was made based on the presence of preserved vertical eye movements and voluntary eye blinks. On day 15, he was fully awake and able to consistently and accurately communicate using an ocular code. On day 79, he was transferred to a rehabilitation center, where he manifested small-amplitude voluntary movements of the head, mouth, and left hand. Soon after, he started to communicate, using a chin-contactor that enabled him to use an adapted computer (Fig 2). The patient had bilateral central facial paralysis, aphonia, and spastic quadriplegia with bilateral Babinski sign. Deglutition reflex was preserved, but no oral feeding was possible. No pathologic laughter or crying were noted. On day 103, magnetic resonance imaging showed a large ischemic pontine lesion.

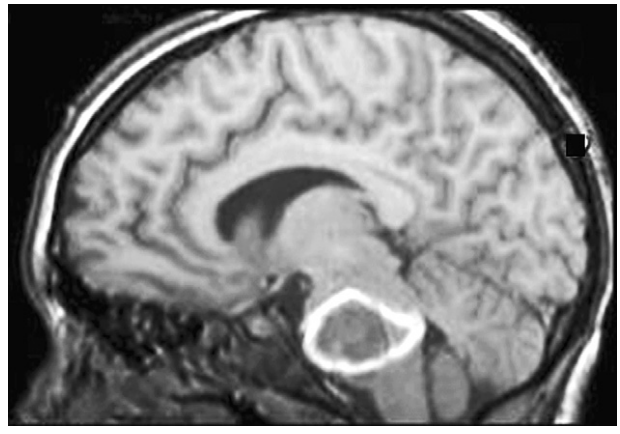

Figure 1. T_1-weighted magnetic resonance imaging (sagittal section) reveals a massive hemorrhage in the brainstem (circular hyperintense signal) (TR/TE = 1960/4 ms).

The patient returned home 10 months after his basilar artery thrombosis. Facial paralysis was significantly reduced but he remained anarthric and was fed through gastrostomy. He had voluntary control of micturition and intentional coughing. The patient was actively involved in family and personal decision making and spent much time praying and listening to religious radio programs. At $2\frac{1}{2}$ years after onset, the patient died of unknown cause; autopsy was refused by the family.

Patient 3

A 13-year-old boy with a history of epilepsy and brainstem astrocytoma (treated with radiotherapy at the age of 8) presented recurrence of generalized tonic-clonic seizures and was admitted comatose to the emergency department, where he was intubated and mechanically ventilated. In the following days, he regained the ability to spontaneously open his eyes, but remained quadriplegic and mute and failed to exhibit voluntary eye movements. The computed tomography scan documented the previously known brainstem lesion without

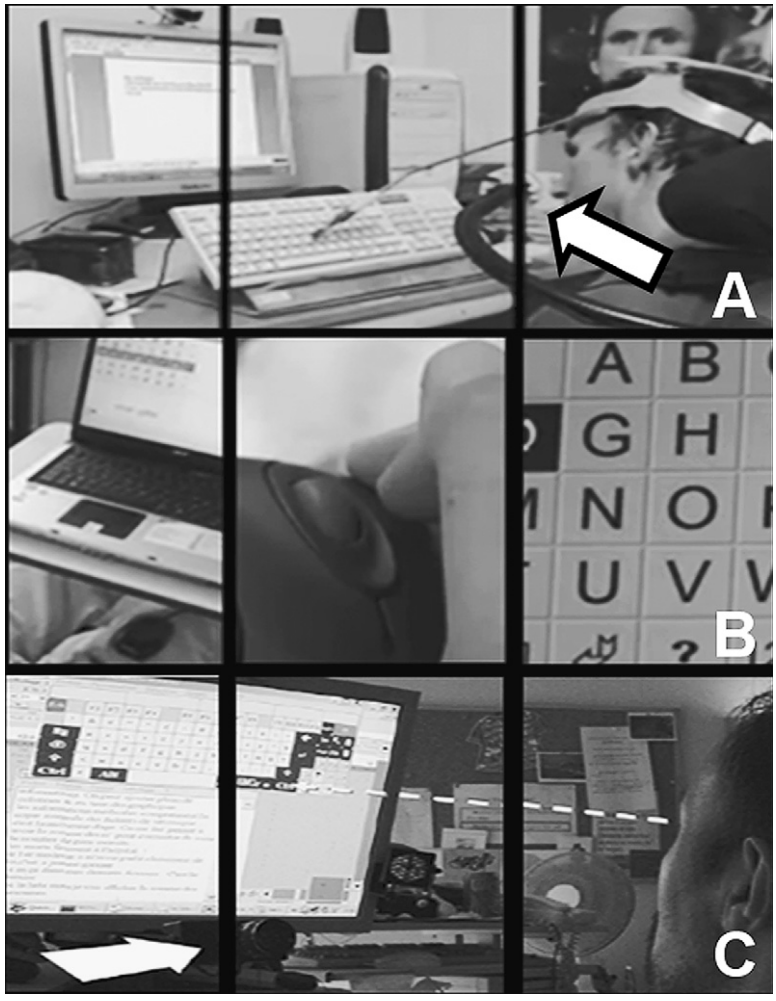

Figure 2. (A) A chin-contactor (white arrow) enabled patient 2 to control his wheelchair, and a head-mounted contactor allowed him to use an adapted personal computer. (B) A finger-controlled text-to-speech synthesizer, as used by patient 3. (C) An infrared eye-tracking device is coupled (white arrow) to a virtual on-screen keyboard; for patient 4, the device was incorporated into her glasses.

additional abnormalities. Magnetic resonance imaging and magnetic resonance angiography identified a ventral pontine ischemic lesion and a basilar artery occlusion, probably secondary to radiation-induced vascular changes. He was considered as being in a vegetative state until his transfer to a rehabilitation center 6 months after onset. There, he demonstrated consistent and reproducible voluntary eye movements, which led to the diagnosis of locked-in syndrome.

As of writing, 11 years later, the patient is staying at a nursing home. He remains fully dependent for activities of daily living, but can control his wheelchair (with his left arm and hand) and communicates using a finger-controlled text-to-speech synthesizer (Fig 2). He can eat, write, and read.

Patient 4

A 16-year-old girl with a history of classic migraine, cannabis use, and head trauma (aged 3 years) and a family history of cerebrovascular accidents was admitted to the emergency department after acute-onset dizziness and vomiting. She subsequently became stuporous and was intubated and sedated. Her Glasgow Coma Scale subscores were Eye response 1, Verbal response 1, Motor response 2. She remained in a pharmacologic coma for 3 days, and then responded with reproducible but fluctuating eyelid movements to commands, confirming the diagnosis of locked-in syndrome. The patient had aphonia, preserved voluntary vertical ocular movements (horizontal ocular movements restored after 2 months), preserved limited facial movements, and quadriplegia. After 3 months, she exhibited more prolonged periods of sustained vigilance and could use an eye-coded alphabetic communication system (Table 1); later on, she could vocalize.

As of writing, 6 months after onset, she is staying in a rehabilitation hospital, fully dependent for activities of daily living. She still has a spastic quadriplegia, aphonia (only recovered some tongue movements), and dysphagia (needing frequent aspiration) and exhibits pathologic laughter and crying with fluctuating emotional status. The patient performs no intentional coughing and has no voluntary bladder control. She reports normal sleeping patterns with preserved oneiric activity and communicates by means of an infrared eye-tracker (incorporated into her glasses) coupled to a virtual on-screen keyboard (Fig 2).

Table 1. Eye-coded alphabetic communication system, with language-specific options

Order	Letter of the Alphabet																								
Traditional	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y	Z
English*	E	T	A	O	I	N	S	R	H	L	D	C	U	M	F	P	G	W	Y	B	V	K	X	J	Q	Z
French*	E	J	A	R	I	N	S	T	U	L	O	M	D	P	C	F	B	V	H	G	Q	Z	Y	X	K	W

* The language-specific order reflects the frequency of letters (i.e., the rate of appearance in that language as written).

At last follow-up, the patient reported good social interactions with the family. However, when asked to self-score general well-being on the Anamnestic Comparative Self-Assessment scale [4] (in which the subjects' memories of the best and the worst time in their life experiences, on a scale from +5 to −5, define the present individual quality of life), she reported a score of −4 (i.e., ''almost as bad as the worst period in my life''). Occasionally, she considers herself as being depressed, but has never had suicidal thoughts and never considered euthanasia. She wants resuscitation to be attempted in case of cardiac arrest.

Patient 5

An 18-year-old girl with unremarkable medical history showed acute-onset dizziness and headache and was unconscious when admitted to the emergency department. Findings from a computed tomography scan were normal, but magnetic resonance imaging revealed an extensive ventral pontine ischemic lesion. The diagnosis of locked-in syndrome was made 8 hours after onset. The patient was intubated and remained comatose during 1 month, after which she exhibited spontaneous eye opening but was unable to make voluntary eye movements or blinks. After 3 months, she was transferred to a rehabilitation center where she exhibited aphonia and limited voluntary movements of the eyes, right hand, and right foot. The endotracheal tube was removed 1 year after onset. She did not have facial paralysis, and she exhibited pathologic laughter and crying. The patient began to vocalize after 2 years of speech therapy. Voluntary micturition control and intentional coughing were recovered 5 years after onset.

As of writing, 6 years after onset, pathologic laughter and crying have resolved and the patient has recovered limited oral feeding abilities but the dysphagia still requires gastrostomy. She can mime some words, but remains anarthric. The patient reports preserved sleep patterns and oneiric activity, but experiences from short-term memory deficits. For communication, she uses an eye-coded alphabetic system (Table 1). She can walk some steps, if assisted. When self-scored general well-being was assessed by means of the Anamnestic Comparative Self-Assessment scale [4], she reported a score of 0 (i.e., ''neither good nor bad''). She considers herself as being depressed occasionally, but reports good social interactions with family and friends and reports never having experienced suicidal thoughts or considered euthanasia. However, she answers negatively to the question ''do you want resuscitation to be attempted in case of cardiac arrest.''

Definition

In 1966, the term *locked-in syndrome* was first introduced by Plum and Posner [1] to describe the phenomenon of patients who are totally conscious and paralyzed, but able to use vertical eye movements and blinking to communicate. More recently, the American Congress of Rehabilitation Medicine [5] defined locked-in syndrome as a neurologic impairment characterized by the presence of sustained eye opening, aphonia or severe hypophonia, quadriplegia or quadriparesis, preserved cognitive functioning, and a primary and elementary code of communication that uses vertical eye movements or blinking. The locked-in syndrome can be subdivided on the basis of motor impairments: the *classic* locked-in syndrome is characterized by quadriplegia and aphonia, with preserved consciousness and vertical eye movements or blinking; the *incomplete* locked-in syndrome is characterized by remnants of voluntary motions other than vertical eye movements; and the *total* locked-in syndrome is characterized by complete immobility, including all eye movements, but preserved consciousness [6].

The first report of the occurrence of this syndrome in children was made by Latchaw et al. [7] in 1974. They reported the case of a 7-year-old boy with vertebrobasilar arterial occlusion who suddenly presented dizziness, headache, and stiffness of the neck. The follow-up examination 4 years later showed flaccid quadriplegia, aphonia, and eye-coded communication. Although the authors did not explicitly consider this a case of locked-in syndrome, all the symptoms correspond to the American Congress of Rehabilitation Medicine criteria [5]. In 1976, Golden et al. [8] reported three cases of children clearly diagnosed as having locked-in syndrome.

Etiology

In all the patients detailed in the Cases section, the locked-in syndrome was attributed to stroke in the brainstem. A review of the literature confirmed that the most common etiology in children is ventral pontine stroke (20 of 33 published cases, or 61%, including the 5 cases reported here), most frequently caused by a vertebrobasilar artery thrombosis [7-19] (Table 2). A previous review of locked-in syndrome etiology in adults identified 79% as following upon brainstem stroke [20]. Other causes are

Table 2. Literature on locked-in syndrome in patients aged 18 years or younger

Reference	Age/Sex	Etiology	Outcome	Follow-Up
Latchaw et al., 1974 [7]	7 yr/M	Thrombosis	Locked-in syndrome	4 yr
Golden et al., 1976 [8]	13 yr/M	Thrombosis	Locked-in syndrome	1 yr
Golden et al., 1976 [8]	5 yr/M	Thrombosis	Vocalizations and left arm movements	4 mo
Ackerman et al., 1977 [9]	10 yr/M	Thrombosis	Mild quadriparesis and dysarthria	3 days
Marés et al., 1987 [10]	7 yr/M	Thrombosis	Died due to tracheal bleeding	4 wk
Chatkupt et al., 1987 [11]	8 yr/M	Thrombosis	Locked-in syndrome	3 wk
Nakatomi et al., 1999 [14]	7 yr/M	Thrombosis	Mild paraparesis	10 mo
Verdú et al., 2001 [15]	9 yr/M	Thrombosis	Left hemiparesis	2 yr
Larner, 1998 [13]	18 yr/F	Thrombosis	Walks with supervision; mild dysarthria; normal affect	18 mo
Rosman et al., 2003 [16]	6 yr/M	Thrombosis	Spastic left hemiparesis	4 yr
Grigoriadis et al., 2007 [19]	6 yr/M	Thrombosis	Good outcome after 12 hours (oriented, restored speech, right hemiparesis that recovered completely after 1 month)	1 mo
Rosman et al., 2003 [16]	18 yr/F	Thrombosis	Left hemiparesis, non verbal communication	2 yr
Rosman et al., 2003 [16]	4 yr 9 mo/M	Thrombosis	Mild left hemiparesis, ataxia	2 yr
Kirton et al., 2003 [17]	15 yr/M	Thrombosis	Good outcome, left hand dysdiadochokinesia	6 mo
Zaidat et al., 2005 [18]	16 yr/M	Thrombosis	Good outcome, complete neurologic recovery	3 mo
Present study, case 2	18 yr/M	Thrombosis	Died	2 mo
Present study, case 3	18 yr/F	Thrombosis	Locked-in syndrome	6 yr
Present study, case 4	13 yr/M	Thrombosis	Locked-in syndrome	12 yr
Present study, case 5	16 yr/F	Thrombosis	Locked-in syndrome	6 mo
Present study, case 1	13 yr/F	Ventral pontine hemorrhage	Died due to obstructive hydrocephalus (treatment withholding)	3 mo
Golden et al., 1976 [8]	13 yr/F	Brainstem tumor	Died	10 mo
Masuzawa et al., 1993 [21]	17 years/NA	Brainstem tumor	Died due to pontine glioma	4 mo
Ockey et al., 1995 [22]	11 yr/M	Brainstem tumor	Good outcome, return of independent living.	14 mo
Tabarki et al., 1997 [12]	8 yr/M	Post-traumatic vertebral artery dissection	Good outcome, full neurologic recovery	6 mo
Landrieu et al., 1984 [23]	8 yr/M	Trauma	Good outcome, return of independent living, full motor recovery	4 mo
Lilje et al., 2002 [26]	15 yr/F	Central pontine myelinolysis	Good outcome. Full neurologic recovery	18 mo
Brito et al., 2006 [25]	15 yr/F	Central pontine myelinolysis	Died. Cause unclear (''metabolic stress'')	NA
Kotagal et al., 1984 [29]	12 yr/M	Reye's syndrome	Remained locked-in	10 mo
Habre et al., 1996 [27]	15 yr/NA	Meningitis	NA	
Belhadj et al., 1995 [28]	6 yr/M	Post-infection	Spastic gait, right facial paralysis	14 mo
Ortiz-Corredor et al., 2007 [32]	NA	Guillain-Barré syndrome	NA	
Echenberg, 1992 [31]	2 mo/F	Spinal muscular atrophy type I	Died due to cardiac arrest (resuscitation not attempted)	NA
Biyani et al., 2007 [30]	18 yr/F	Postoperative pneumocephalus	Good outcome, return of independent living, no significant neurologic deficits	1 day

Abbreviations:
F = Female
M = Male
NA = Not available

brainstem tumor (10%, as calculated from Table 2) [8,21,22], traumatic brain injury (6%) [21-24], central pontine myelinolysis [25,26], meningitis [27], encephalitis [28], Reye's syndrome [29], and brainstem tension pneumocephalus [30]. In addition to brainstem lesions, pediatric locked-in syndrome can also be caused by spinal muscular atrophy [31] or Guillain Barré syndrome [32]. Finally, *myorelaxing* agents can induce a transient locked-in state [33]. In adults, locked-in syndrome has also been reported in cases of subarachnoid hemorrhage and vascular spasm of the basilar artery, brainstem drug toxicity, hypoglycemia, or vaccine reaction (for a review, see reference [20]).

All our patients required intubation and mechanical ventilation reflecting involvement of the respiratory center in the medulla oblongata in the acute phase of the illness. Facial paralysis, in addition to the quadriplegia, is caused by a lesion of the VII nerve nuclei (for a review, see reference [6]). Aphonia may be due to a dissociation of the vocalization center in the midbrain and the retroambiguous nucleus in the lower medulla oblongata for actual execution of vocalization. Horizontal oculomotor disturbances encountered in locked-in syndrome are thought to be caused by damage of the paramedian pontine reticular formation [6].

Diagnosis

In patient 3, the diagnosis of locked-in syndrome was made only months after the brainstem stroke. A study

performed in collaboration with the French Association for Locked-In Syndrome (ALIS; http://alis-asso.fr/) indicated that, in 33% of cases, it was a relative of the locked-in syndrome patient and not the physician who first realized that the patient was conscious and could communicate via eye movements [34]. In that study, the time elapsed between the acute insult and the diagnosis of locked-in syndrome was 2.5 months on average [20]. This delay can be explained by the rarity of this syndrome; by the difficulty of recognizing unambiguous but limited signs of consciousness (i.e., voluntary eye movements or blinking) [35]; by a fluctuation of vigilance in the acute setting (as illustrated by patient 4); or by additional cognitive [36] or sensory deficits, such as deafness [37,38] or dysacousia (as illustrated by patient 1). Because locked-in syndrome infrequently occurs in children, pediatric patients may wrongly be considered as being in a coma, a vegetative state, or akinetic mutism.

The presence of a relatively normal and reactive EEG rhythm after a brainstem lesion should alert the physician (as illustrated by case 1), but heterogeneity of EEG findings suggests that this approach cannot by itself be used to reliably disentangle locked-in syndrome from postcomatose unconscious patients [39]. One study of EEG in locked-in syndrome indicated normal or minimally slowed EEG signal, with a predominance of reactive alpha activity [40], but other studies have reported EEG abnormalities such as slowed activity over the temporal or frontal areas [41], unreactive EEG [42], or an ''alpha coma'' pattern (i.e., alpha rhythm nonreactive to multimodal stimuli) [43].

Structural brain imaging (ideally, magnetic resonance imaging) typically reveals isolated lesions (bilateral infarction, hemorrhage, or tumor) of the ventral portion of the pons or midbrain (for a review, see reference [44]). Functional neuroimaging with positron emission tomography has indicated higher metabolic activity in locked-in syndrome than in vegetative state [45]. These studies also suggested that, in the case of classic locked-in syndrome, regional cerebral metabolic rates for glucose are not significantly different from those of healthy volunteers [45-47].

Prognosis

In two of the present cases, the patient died (in 3 months, with treatment withholding, and at 2.5 years after onset). The three who survived (one up to 11 years after the insult) remained with severe motor handicap. A review of the literature, and including the present five cases, indicates that most pediatric locked-in syndrome patients show some motor recovery: 11 out of 31, or 35%. In 26% of the 31 cases, ''good recovery'' (return of independent living) was reported; 16% remained quadriplegic and anarthric; and 23% died.

The prognosis for basilar artery occlusion is known to be poor in children, with a mortality of 25% and serious sequelae in survivors [48]. In adult locked-in syndrome, mortality is approximately 75% in the acute setting for vascular etiology, with nearly 90% of deaths occurring in the first 4 months [41]. Once a patient has been medically stabilized and the locked-in syndrome continues for more than 1 year, the probability of survival is reported to be approximately 80% during the 10 years after onset, and 40% during the 20 years after onset [49]. Classically, motor recovery is earlier and more complete in nonvascular locked-in syndrome, compared with vascular cases [41]. Return of horizontal visual pursuit within 4 weeks after onset is thought to be predictive of good recovery [50].

Recent studies indicate that intensive and early rehabilitative care improves motor outcome [51] (Pantke KH, unpublished data, 2005). These treatments, which rely on brain plasticity, are expected to be more effective early in life. Despite the severe persisting motor deficits, some patients may present some improvement (classically showing a distal to proximal progression) and may recover voluntary control of head, finger, or foot [52]. Surprisingly, many locked-in syndrome patients can return home (as illustrated by patient 2). In 2008, the French Association for Locked-In Syndrome database indicated that, out of 158 patients, nearly 65% could return home (8% remained in hospital setting, 11% in rehabilitation center and 16% in nursing home). Also, 58% had recovered limited but useful movements and monosyllabic speech, with 51% of the surveyed locked-in syndrome patients using some kind of technological communication device (data obtained on $n = 95$).

Cognitive Functioning

In clinical practice, neuropsychologic testing used to evaluate cognitive functioning classically needs written or verbal responses. Because of the severe motor and verbal impairments, no systematic neuropsychologic evaluation is possible in locked-in syndrome patients. Several case reports have emphasized that cognitive abilities remain intact in case of locked-in syndrome (for a review, see reference [20]). Recently, Schnakers et al. [36] assessed 10 adult locked-in syndrome survivors using a standardized neuropsychologic testing adapted to an eye-response mode (assessing sustained attention, short-term and long-term memory, executive functioning, phonologic and lexicosemantic processing and vocabulary knowledge). Cognitive deficits were not observed in locked-in syndrome patients with an isolated brainstem lesion; however, patients with additional thalamic or cortical lesions did show identifiable cognitive dysfunction [36]. Detection of cognitive deficits in locked-in syndrome survivors is critical to adjusting the communication mode and hence to facilitating communication and increasing the patient's autonomy [53].

Communication

Communication is a major challenge for locked-in syndrome patients. Especially in an intensive care setting, it is essential that medical staff establish communication as soon as possible with locked-in syndrome children. Usually, the first method of communication is an elementary yes/no

Table 3. Eye-coded communication method using the vowel-and-consonants system in a 4 × 7 grid

Group	Letter of the Alphabet						
Vowels	A	E	I	O	U	Y	
Consonants 1	B	C	D	F	G	H	
Consonants 2	J	K	L	M	N	P	Q
Consonants 3	R	S	T	V	W	X	Z

The alphabet is divided into four groups, first six vowels and then the consonants, in alphabetic order. The interlocutor says "Vowel" and then "Consonants 1, 2, or 3." The locked-in patient blinks to indicate the chosen group, blinking once for Vowels, twice for Consonants 1, and so on.

code based on preserved eye movements or blinks (e.g., look up for "yes" and down for "no"). In a next step, alphabetic communication methods may be used, permitting a higher level of communication with expression of more complex ideas. Many variants of these systems can be tailor-made to the patient's preferences and physical abilities. The simplest way is to list the alphabet and ask the locked-in syndrome patient to make a prearranged eye movement to indicate a letter (Table 1, first row). Some patients prefer a listing of the letters sorted in function of appearance rate in their usual language (Table 1 gives examples for English and French). Because of vigilance fluctuations, these methods may be time consuming. Variants on the alphabetic system use vowels and consonants in different grids (Tables 3 and 4). The rapidity in use depends upon practiced skill of both the patients and their interlocutors. These systems also rely on a good knowledge of written language. For young locked-in syndrome children or patients with poor written language, pictographic codes can be used that represent emotions, basic needs (e.g., eating, drinking, elimination), favorite positions (e.g., lying down, sitting), frequently needed sentences, and so on (Fig 3).

All of these systems require the intervention of an external aide. Recent technological developments are changing the lives of locked-in syndrome patients. Instead of passively responding to external requests, new computerized technologies allow patients to initiate conversation and to actively intervene and control their environment [20] (Fig 2). Experts in rehabilitation engineering and speech-language pathology are continuously improving patient-computer interfaces, including such devices as infrared eye movement sensors, or chin- or finger-contactors that can be coupled to virtual on-screen keyboards. This allows locked-in syndrome patients to use a word processor (which can be coupled to a text-to-speech synthesizer), to access the World Wide Web, and to use e-mail, all of which greatly improves their quality of life. In the future, brain-computer interfacing (i.e., modes of communication in which messages or commands are sent directly by the brain without intervention of motor or verbal responses [54]) could also offer a solution for cases of chronic complete locked-in syndrome [55].

As seen in patient 1, the locked-in syndrome can be complicated by deafness [37,38]. In this case, communication must be adjusted and adapted to cognitive and motor dysfunctions. Smart et al. [37] reported the case of a locked-in syndrome patient who presented with a hearing deficit. The authors developed an augmentative communication system designed to exploit the patient's preserved cognitive functions by using visual cues, written questions, an eye-gaze computer system, and speech-generating devices in whatever combination proved most useful to a given purpose.

Quality of Life

Limitations of communication make quality of life assessments in locked-in syndrome particularly difficult [56]. Some physicians who take care of both acute locked-in syndrome patients and generally healthy individuals may consider that the quality of life of a locked-in patient is very limited [20]. Studies have, however, established that patients with severe diseases or motor impairments do not necessarily self-report a poor quality of life. In one report, more than half of patients with moderate to severe disabilities experienced a good to excellent quality of life despite being socially isolated, having severe difficulties in performing daily tasks, and having limited incomes and benefits [57]. The links between symptoms and quality of life are neither simple nor direct [58].

To date, there have been no studies on quality of life in locked-in syndrome children. Both aspects of this proposition (i.e., the age and the condition) are problematic. Children are often considered as legally and mentally incompetent, or as unreliable respondents. Nonetheless, the wishes of the child should be taken into account in all decisions involving the child's health care, and should be given increasing weight in accord with the child's capacity for understanding. The mature child, in the judgment of the physician, is entitled to make her or his own decisions about health care [59]. If the child is of sufficient maturity and understanding, the informed consent for any procedure or therapy shall be

Table 4. Eye-coded communication method using the vowel-and-consonants system in a 7 × 4 grid

Group	Letter of the Alphabet			
Vowels 1	A	E	I	
Vowels 2	O	U	Y	
Consonants 1	B	C	D	F
Consonants 2	G	H	J	K
Consonants 3	L	M	N	P
Consonants 4	Q	R	S	T
Consonants 5	V	W	X	Y

The alphabet is divided into seven groups, for fewer letters per group than in the 4 × 7 grid (Table 3). As before, the vowels are given first, then the consonants, each in alphabetic order. To designate, for example, the letter *H*, the patient blinks four times (for the fourth group), pauses, and then blinks twice (to indicate second column).

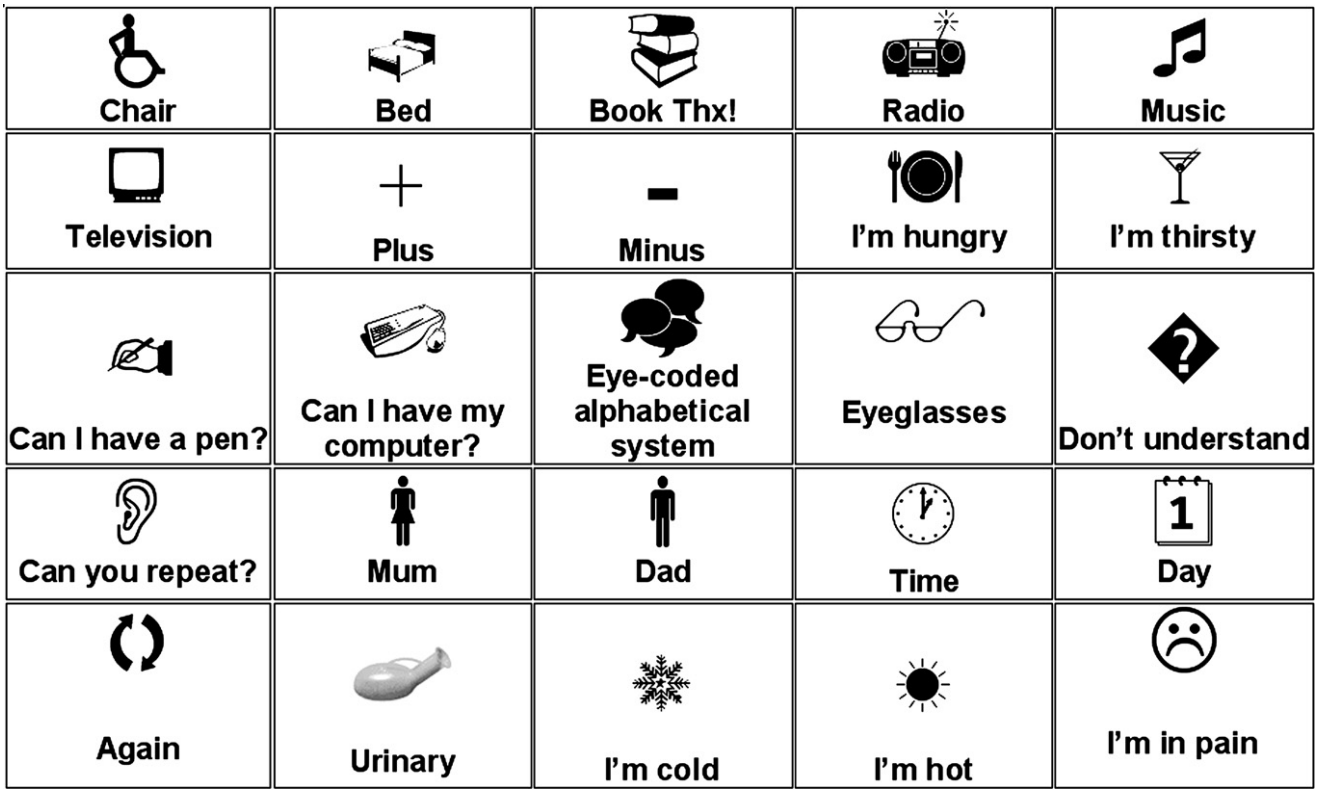

Figure 3. Pictograms permit the patient to choose from a limited number of messages.

obtained from the child himself or herself (see the Belgian Patients' Rights Act [60], sections 8, 12, and 15).

In chronic locked-in syndrome adults, studies indicate that most patients still maintain social activities and lead meaningful lives, and that their self-scored general well-being is not significantly different from matched healthy controls [20,53,61]. The cases reported here illustrate that quality of life can be measured also in children, by means of the Anamnestic Comparative Self Assessment scale. The scale estimates general wellbeing on a scale from −5 (corresponding to the worst period in the respondent's life) to +5 (corresponding to the happiest period in the respondent's life) [4]. The use of biographical references reduces the likelihood of falsely high ratings due to the 'given the circumstances' relativity bias [62].

Some health care professionals assume that most locked-in syndrome patients would choose to die. However, quality of life studies showed that most locked-in syndrome patients have a wish to live [20]. It is not unusual for health-care professionals to rate the quality of life of chronic illness or disability patients lower than do the patients themselves [63]. Similarly, in pediatrics, physicians tend to rate quality of life of children lower than do their parents [64]. When children with disabilities are given the opportunity to assess their well-being, they generally rate their quality of life as similar to that of ''normal'' children [65]. In the cases reported here, quality of life could be assessed in patients 4 and 5, in terms of the Anamnestic Comparative Self Assessment scale. These two patients reported no wish for euthanasia, nor had they suicidal thoughts.

End-of-Life Decisions

As stated by the American Academy of Neurology, adult patients with severe and permanent paralysis have the right to make decisions regarding their own health-care and to accept or to refuse life-sustaining therapy [66]. In 2005, Verhagen and Sauer [67] published the Groningen protocol, to define the circumstances under which applying euthanasia to an infant may be considered appropriate.

In Belgium, euthanasia is, for now, legally accepted only in adults. Euthanasia was partially legalized in Belgium in 2002 [68]. Two provisions under the current law are that a patient must be over the age of majority (18 years) and have a health condition without hope of improvement and in constant suffering in order to qualify for euthanasia (section 3 in reference [68]). The government of Belgium is considering different proposals to legalize euthanasia for children and youth up to age 18.

According to the Dutch Medical Treatment Contracts Act [69] and the Dutch Euthanasia Act [70], children older than 11 years have the right to make decisions on their medical treatment or to request euthanasia. Although any legal cutoff point for age seems arbitrary, according to one report pediatricians estimate that children 10 or 12 years old are often able to participate in important medical decisions [71]. In clinical practice, most children are too quickly considered to be unable to participate in the decision-making process (as illustrated by case 1). The active ending of life at the parent's request is more commonly practiced [71].

In accordance with the principle of patient autonomy, physicians should respect the right of locked-in syndrome patients to accept or refuse any treatment. At least two conditions are necessary for full autonomy: patients need to have intact cognitive abilities and they must be able to communicate their thoughts and wishes.

Conclusion

Because of the rarity of the condition in children, the diagnosis of locked-in syndrome may be missed and patients may wrongly be considered as being in a coma, vegetative state, or akinetic mutism. The data discussed here point to the need for pediatric physicians to carefully interpret signs and symptoms of locked-in syndrome. Good recovery of motor and speech function is very rare. Two of the five cases reported here died after the acute phase; the other three survived (one of them up to 11 years after the insult) but retained a very severe motor handicap. The literature review indicated that 35% of pediatric locked-in syndrome patients showed some motor recovery, 26% showed good recovery, 16% remained quadriplegic and aphonic, and 23% died.

Recent studies indicate that early rehabilitation can improve functional motor outcome and verbal communication. Several reports have emphasized that cognitive abilities remain intact in case of locked-in syndrome with an isolated brainstem lesion but that patients with additional lesions can show cognitive dysfunction. Identification of cognitive deficits permits adapting communication modes to better fit the patient's preserved cognitive abilities and thus facilitate communication and increase the patient's autonomy. In adults with chronic locked-in syndrome, studies have revealed that most patients can still maintain social activities and lead meaningful lives. In the future, more widely available access to adaptive communication computer equipment should additionally enhance the quality of life of locked-in syndrome patients.

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