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ORIGINAL ARTICLE

Mild trigonocephaly associated with microcephaly: surgical outcomes for 15 cases

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Abstract

Background and importance Surgical treatment for mild trigonocephaly associated with microcephaly is often attempted if neuroradiological studies show evidence of increased intracranial pressure. However, it is difficult to decide how to approach surgically these patients. Herein, we report the surgical outcomes of the patients we have treated surgically in our center.

Clinical presentation We performed surgery on 15 patients (ten girls and five boys) who were all diagnosed as microcephalic during infancy. All patients presented clinical symptoms and evidence of short stature. Symptoms included mental retardation, language delay, hyperactivity, motor dysfunction, and self-mutilation (head banging). Head circumferences were > 2 standard deviations below the normal range for their sex and age at the time of surgery. All patients were diagnosed with mild trigonocephaly based on three-dimensional computed tomography (3D-CT). No abnormal findings could be observed in the brain of 14 patients, as assessed by magnetic resonance imaging (MRI). One patient showed brain atrophy. 3D-CT showed marked digital markings in all. Intracranial pressure (ICP) was measured under normocapnia. Increased ICP could be observed in 13 patients. Decompressive cranioplasty was performed in all patients. After surgery, evidence of enlargement of the head circumference could be observed in six patients. Some degree of intelligence problems remained. However, every patient made some improvement in at least one of the other symptoms.

Conclusion We suggest that decompressive cranioplasty may be indicated in patients with mild trigonocephaly associated with microcephaly, if pre-surgical evaluation shows high ICP and no abnormal brain findings can be identified on MRI.

Keywords Microcephaly · Mild trigonocephaly · Developmental delay · Decompressive cranioplasty

Introduction

Our surgical team has reported on the problems associated with symptomatic mild trigonocephaly since 2000 [1–5]. Sometimes, these cases are complicated with microcephaly. Microcephaly is highly probable when craniosynostosis is associated with the ossification of multiple sutures; however, surgery is often unwarranted when the condition is associated with mild trigonocephaly. Surgical treatment of microcephaly became popular in the second half of the nineteenth century; however, this approach was later criticized due to the associated risks and poor outcomes observed during long-term follow-up [6, 7]. Advances in diagnostic radiology in the 1920s allowed doctors to characterize synostosis with greater accuracy and detail. This knowledge has led to the development of more targeted treatments for microcephaly. In this manuscript, we report the clinical features and surgical outcomes of 15 children diagnosed with both mild trigonocephaly and microcephaly that we treated surgically in our center. This subject was previously reported in a Japanese journal in 2010 [8]. Since then, case numbers have been increasing; therefore, we considered it would be important to report our now enlarged sample. The present findings were obtained from a long-term follow-up and are accompanied by detailed neuroradiological imaging data.

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Cases

From January 2001 to March 2015, we operated on 15 children with mild trigonocephaly associated with microcephaly at the Okinawa Prefectural Nanbu Medical Center & Children's Medical Center. The cohort consisted of five boys and ten girls, ranging in age from 1 to 8 years. All children presented with clinical symptoms. Physical tests, EKG, and chest X-rays revealed no other physical anomalies.

All patients were karyotyped before surgery. Chromosomal abnormalities were observed in two children: terminal deletion of the long arm of chromosome 7 (7q35-qter) in case 2 and asymptomatic Robertsonian translocation of the long arms of chromosomes 13 and 14 (rob(13;14)) in case 10. MRI revealed brain atrophy in one child; no brain abnormalities were observed in the other 14.

Clinical symptoms

In terms of appearance, the children generally had mild forehead bossing, a narrow forehead, and indented temples (Fig. 1). All children had intellectual disabilities. Delayed language development was observed in all patients. To analyze language development, we used the National Rehabilitation Center Sign-Significance Test (NRC S-S test) [9]. Eight children could not produce any meaningful words (cases 3–5, 7–10, 13), two less than 20 words (cases 11, 15), and one less than 100 (case 1); two could produce two-word phrases (cases 2, 12), and two could produce three-word phrases (cases 6, 15). We identified hyperactivity in six children (cases 2–3, 8, 12, 14–15), delayed motor development in eight—i.e., "inability to walk" (cases 3, 5, 8–10) and "walking difficulties" (cases 2, 7, 13)—and self-injurious behavior in two (cases 5, 6). Five children were still not toilet-trained by 4 years of age (cases 1, 2, 4, 6, 9) (Table 1).

Head circumference

At the time of delivery, head circumference measurements were within standard deviations of normal for 10 children, greater than two standard deviations below normal for four, and unknown for one. By 1 year of age, three more fell within the ± 2 SD of normal range. All children fell within this range at the time of surgery (Fig. 2). In addition, nearly all were below standard age-adjusted ranges for normal body weight and height.

Neuroradiological diagnosis

Skull morphology was imaged using 3D computed tomography (3D-CT) for all patients. Images commonly exhibited metopic ridge, sunken temples, narrow anterior cranial fossa and vault, and significant digital markings (Fig. 3a).

All patients were subjected to MRI scans to check for brain pathologies. One child exhibited brain atrophy. In addition, narrowing of the frontal lobes was observed in all patients.

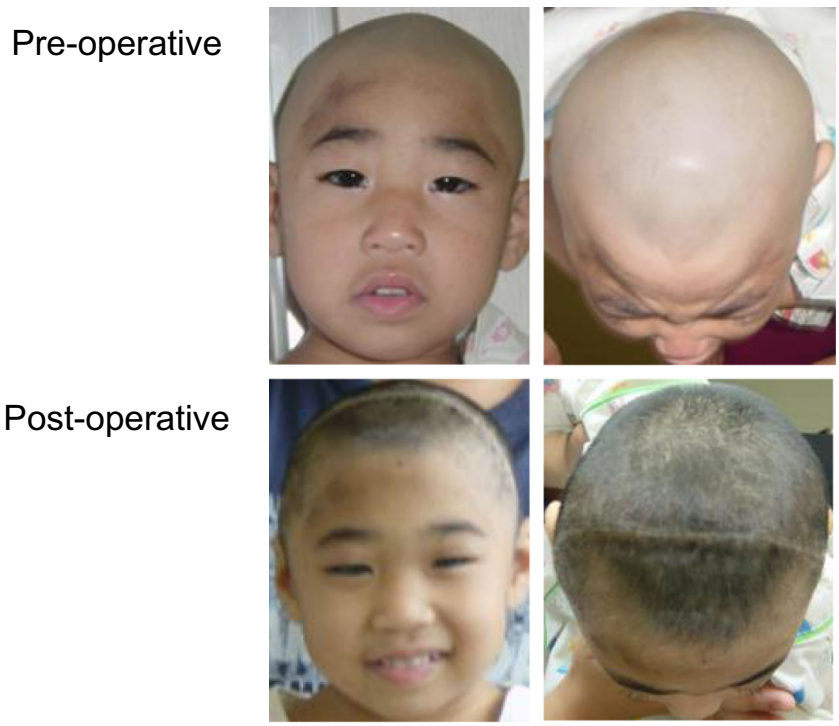

Fig. 1 Morphological aspect of the facial configuration before and after surgery. Upper column, pre-operatory (note bilateral temples decompression and heel-shaped forehead). Lower column, post-operatory (note improved depressed temples and wider and flatter forehead resulting in bigger frontal area) (from *Shouni No Nousinkei*. 2010 35: 100–112. Reprinted with permission) (with permission by parents to show the child's face)

Table 1 Summary of the description of all cases

	Sex	Age at surgery	Age today	Duration of follow-up	Date of surgery	Pre-operatory symptoms	Post-operatory changes in few years	Current status
1	F	5.5	22.8	17.3	01.01.2001	Able to say something but unable to hear; Toilet training not accomplished	Able to make conversations using 2-word sentences 2 months after surgery; Toilet training accomplished after 2 months; DQ, 28 (6 years old)	Graduated from a school for students with special needs; Spending a calm daily life at home; Deficits in intelligence; Good cooperative movement
2	F	6.8	23.9	17.1	04.23.2001	Able to speak using 2-word sentences at most; Hyperactive; Problems in balance—falling down easily; Chromosomal abnormality; Toilet training not accomplished	Able to use long sentences and able to make simple conversations 2 months after surgery; Hyperactivity improved 2 months after surgery; Good balance, no more falling down; Talkative 4 years after surgery; Toilet training not accomplished 1 year after surgery; DQ, 28 (9 years old)	Graduated from a school for students with special needs; No problems in daily conversation; No problems in daily life
3	F	2	17.2	14.9	06.30.2003	No meaningful words and problems with comprehension; Hyperactive; Unable to walk; Sleeping disturbance; DQ, 50	Language not changed even after 6 years; Comprehension improved; Listened to her mother; Running but unstable walk 4 months after surgery; No sleep disturbances after 4 months	No meaningful words; Unable to write and read even her name; In a school for students with special needs; IQ, 15
4	F	4.5	18.8	14.4	12.22.2003	No meaningful words; Did not care about parents; Toilet training not accomplished; DQ, 37	Panic disappeared in a couple of months; No meaningful words even after 5 years; Toilet training accomplished after 1 year; DQ, 36	Able to speak simple words; Good understanding; In a school for students with special needs
5	F	3.1	17.1	14	04.19.2004	No meaningful words; Standing with help; Self-mutilation worsening day after day; Sleeping disturbance	No meaningful words after 5 years; Walking several steps after 1 month; Self-mutilation disappeared in 1 month; Sleeping disturbance disappeared in 1 month	No meaningful words; Walking without help since 12 years old; Comprehension still with deficits; In a school for students with special needs
6	F	6.3	19.6	13.3	01.31.2005	Difficulty in conversation; Self- mutilation; Toilet training not accomplished	Conversation improved; Much better comprehension after 1 month; Telling her mother what happened in the school; Self-mutilation disappeared in 1 month; Toilet training accomplished in 1 month; No problems in daily conversation after 6 months	Graduated from a school for students with special needs and now working in a care unit for elderly
7	F	2.6	15.1	12.5	10.31.2005	No meaningful words; Difficulties in eye contact and playing with other children; Unstable walk; DQ, 46	No meaningful words; Better comprehension; Eye contact improved and started to play with some specific children; Walking became relatively stable; DQ, 35 (4 years old)	Difficulty in expressing her feelings; Able to communicate using words; Unable to jump; In a school for students with special needs
8	F	1.7	14	12.3	01.05.2006	No meaningful words; Unable to walk; Hyperactivity worsening; Sleeping disturbance (nightmares); Seizures occurring every few months	No meaningful words after 3 years; Walking without support in 6 months; Hyperactivity improved after 1 year; Sleeping more than 8 h; Seizures ceased	No meaningful words; Reacting to what have been told; Toilet training not accomplished; In a school for students with special needs

Table 1 (continued)

	Sex	Age at surgery	Age today	Duration of follow-up	Date of surgery	Pre-operatory symptoms	Post-operatory changes in few years	Current status
9	M	5.2	16.8	11.7	09.11.2006	No meaningful words; Unable to walk; Drooling saliva; Respiratory distress needing admission frequently; Seizures (drop attacks); Toilet training not accomplished	No meaningful words after 2.5 years; Walking after 2 months; Drooling saliva disappeared; Respiratory distress disappeared; Seizures did not occur after surgery; Toilet training not accomplished in 1 year	Only a few words; Running at the moment; In a school for students with special needs
10	M	1.5	11.8	10.3	02.07.2008	No meaningful words; Control of the head movements not accomplished; Drooling saliva in abundance; Respiratory distress; Chromosomal abnormality	Several words in 1 year; Comprehension improved; Drooling much less saliva; Respiratory distress improved; Standing with support after 6 months; Walking with crutches in 2 years	Using several words; Able to communicate with family; Walking without help but unsteady; In a school for students with special needs
11	M	2	12.5	9.7	08.28.2008	Language delay (only few words at 2 years old)	Vocabulary increased in few months after surgery; Comprehension improved; DQ, 56 (4 years old)	No problems in communication; In a class for students with special needs; IQ, 72 (12 years old)
12	F	3.4	12.5	9.1	03.19.2009	2-word sentences; Problems with pronouncement; Hyperactive	Increased words in 1 month; Better pronouncement; Hyperactivity improved; Talkative after 2 years; IQ, 59 (6 years old)	No problems in daily conversation; Able to play with other children; In a class for students with special needs
13	F	1.7	10.6	8.9	06.04.2009	No meaningful words; Able to walk only a few steps; DQ, 60	Comprehension became better after 2 months; Walking normally in 1 month; DQ, 65 (2 years old); Able to make conversations using 2-word sentences; Running in 1 year; Using more than 3-word sentences in 2 years; DQ, 73 (4 years old)	In a class for students with special needs; No problems in communication; IQ, 71 (6 years old)
14	M	8.9	15.2	6.3	02.02.2012	Talkative but behaving like an infant; Hyperactive; Diagnosed with ADHD and prescribed atomoxetine; Drooling saliva; IQ, 60	Drooling saliva disappeared in 1 month; Hyperactivity subsided without taking atomoxetine in 6 months; IQ, 57 (9 years old)	In a class for students with special needs; Living a calm daily life; IQ, 47 (12 years old)
15	M	2.7	5.9	3.2	03.12.2015	Only a few words; Hyperactive; Nightmares; Unable to play with other children	Able to use 100 words and some 3-word sentences, better comprehension; Hyperactivity decreasing in 3 months; Nightmares disappeared in 1 month	In a nursery school; Able to make conversations using childish language; Difficulties in playing with other children; DQ, 60 (5 years old)

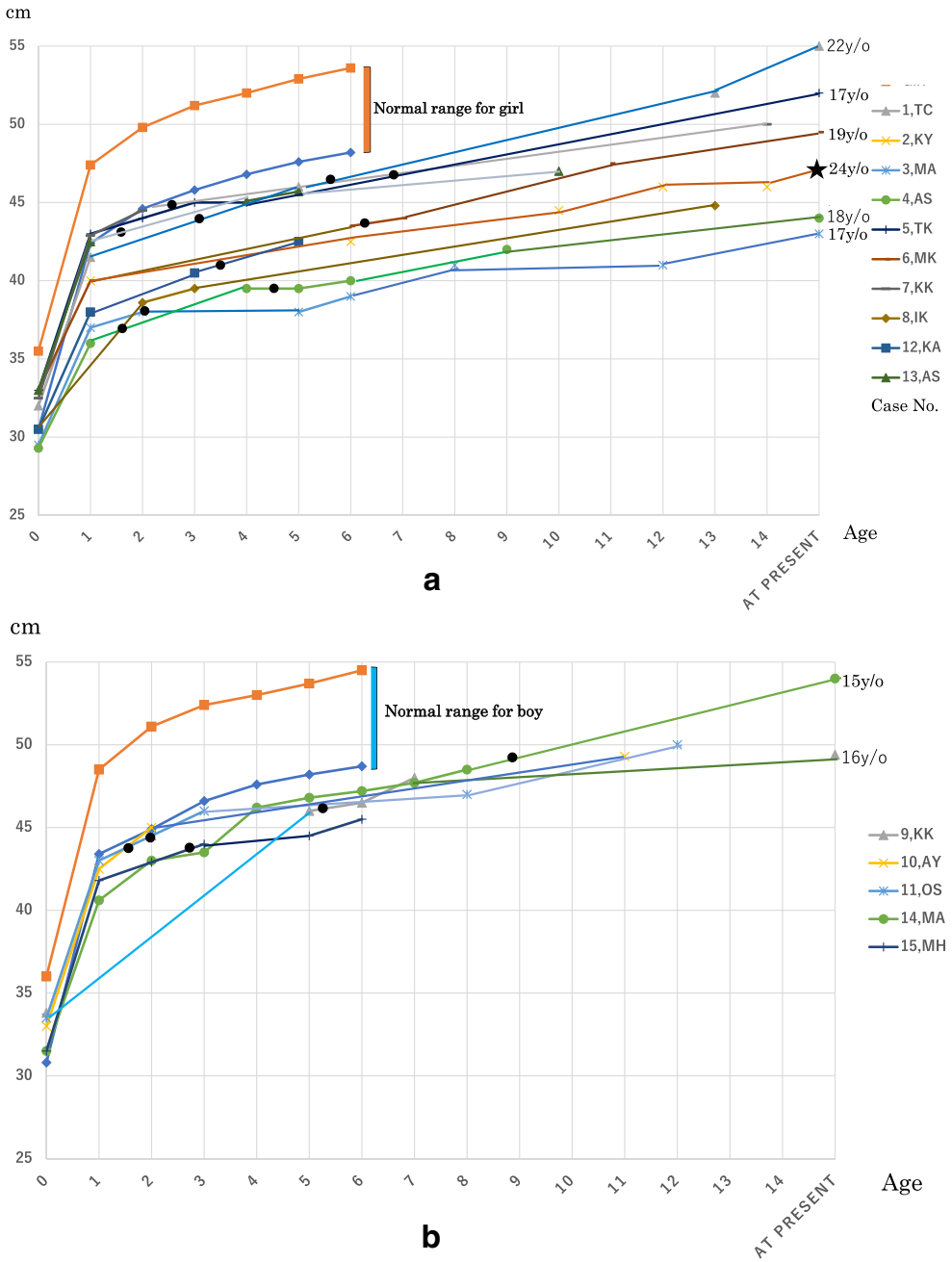

Fig. 2 Chronological evolution of the head circumferences (**a** girls, **b** boys) (all patients presented small head circumferences during infancy, which became lower than 2SD from the normal range before taking surgery—black circles). A star refers to case 2; numbers refer to the number of each case as presented in Table 1

Otherwise, no physical brain abnormalities were observed in the other children (Fig. 3b).

Intracranial pressure

Patients were put under general anesthesia using sevoflurane via endotracheal tube, with peak inspiratory pressure maintained at 18 mmHg. A single burr hole was opened in the frontal skull, and a sensor inserted extradurally (Camino multiparameter monitoring system, Integra NeuroScienses, USA). First, measurements were made while keeping partial CO_2 pressure (PCO_2) around 30 mmHg, then a second run between 38 and 42 mmHg. Measurements could not be obtained for two children whose PCO_2 exceeded 42 mmHg. Valid data was acquired for the other 13.

Surgery

Before surgery, we confirmed that patients' condition had not changed or deteriorated in follow-up observations for a minimum of 6 months. We discussed our grounds for performing decompressive cranioplasty at length with families, emphasizing the significance of the digital marking, and obtained informed consent for all children.

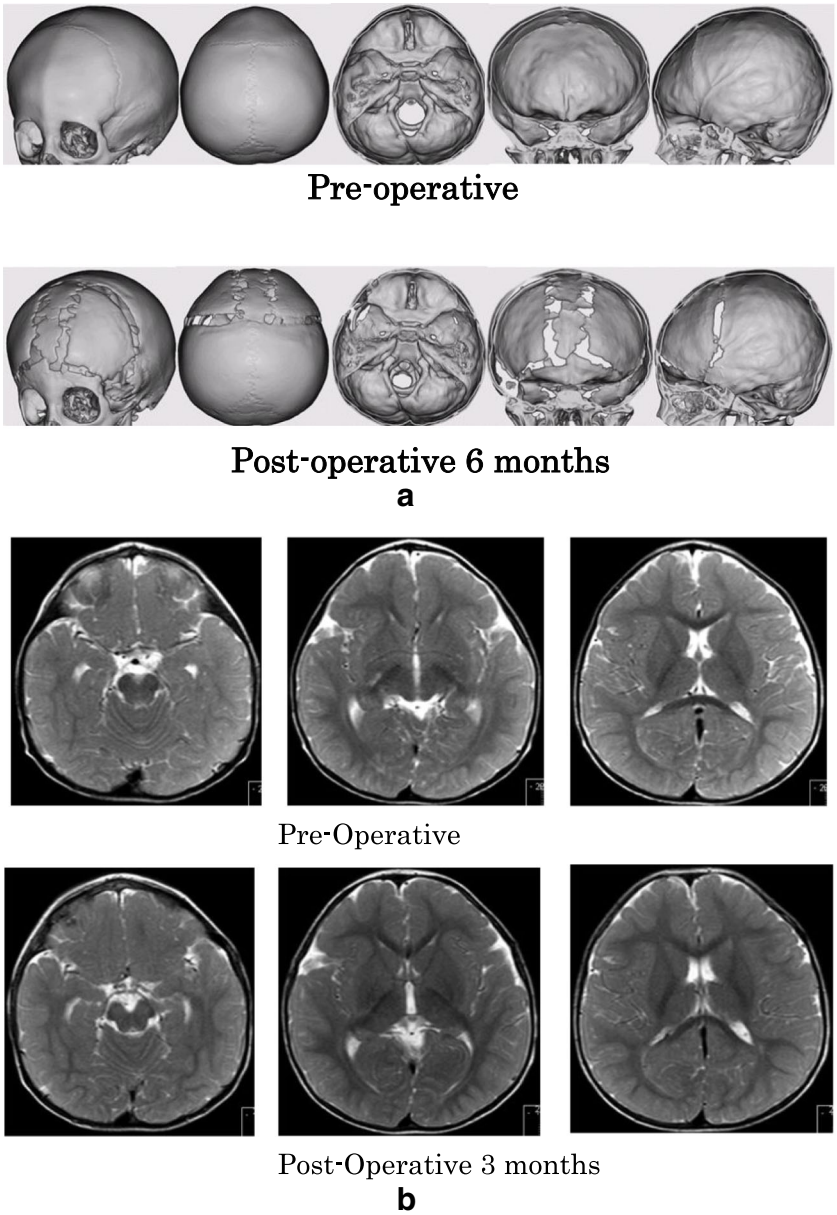

Fig. 3 Findings of 3D-CT and MRI imaging. **a** Upper column, pre-operatory (3D-CT showed smaller frontal area and anterior fossa; marked digital markings). Lower column, post-operatory (note the enlargement in the frontal area and the anterior fossa, markedly decreased digital marking). **b** Upper column, pre-operatory (MRI showed no abnormal findings except smaller frontal lobes). Lower column, post-operatory (MRI showed an increase in the frontal lobes) (from *Shouni No Nousinkei*. 2010 35: 100–112. Reprinted with permission)

We have described the surgical protocol elsewhere [2]. Briefly:

1. The frontal bone was removed whole.
2. Major sections of the greater and lesser wings of the sphenoid were removed, and the sphenoid ridge removed to the meningo-orbital band.
3. The frontal-orbital bar was dissected in one piece; during reconstruction, it was re-set approximately 5 mm anterior to its original position.
4. The dissected coronal bone was cut and trimmed into strips, which were replaced with approximate bilateral symmetry on the frontal lobes without fixation (floating method).

This protocol adequately reduces intracranial pressure while completely freeing the frontal base from the anterior cranial fossa (Fig. 4).

Results

Patients were followed up for between 3 and 17 years (Table 1). In terms of appearance, all children exhibited temple widening, forehead flattening, and anterior cranial cavity expansion (Fig. 1).

While all patients still had intellectual disabilities ranging from mild to severe, all of them improved in terms of their clinical symptoms in at least one domain. Three of the eight

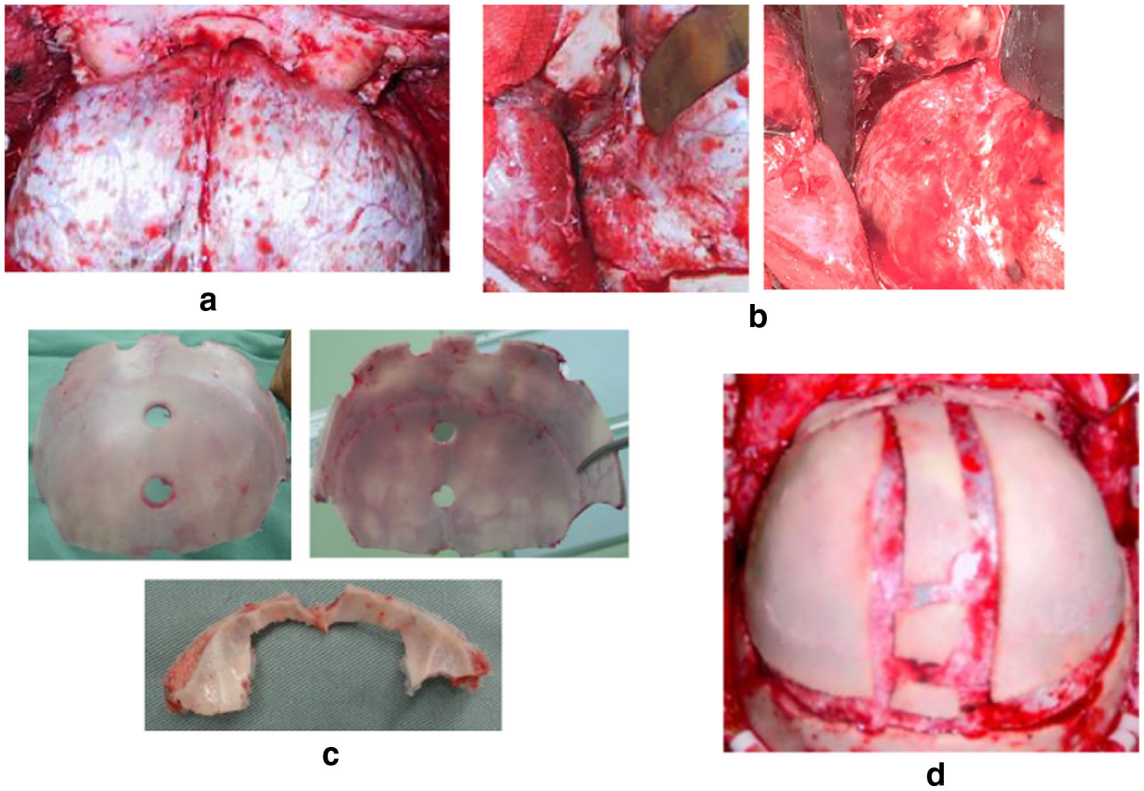

Fig. 4 Operative views. **a** Bilateral frontal craniotomy was carried out behind the coronal sutures. **b** The greater and lesser wings of the sphenoid bone were removed using a rongeur. **c** Note the digital marking on the calvarium. The orbital bar was removed with orbital roofs. **d** The orbital bar was replaced with one stay suture at each side of the lateral orbital rim. The trimmed frontal bones were replaced in a floating fashion

children with severe language impairment (i.e., no significant words) did not improve during long-term follow-up (cases 3, 5, 8). However, two increased their vocabulary to ≤ 20 words (cases 4 and 9), and another two up to 100 (cases 7 and 10). Cases 15 and 11, who could speak no more than 20 words before surgery, can now speak three-word phrases (case 15) and hold conversations without issue (case 11), respectively. Case 1, who could not speak more than 100 words, can likewise have a conversation normally today. All four children who could only speak two- or three-word phrases before the operation became capable of having normal conversations (Fig. 5). In addition, post-operative testing found every child's verbal comprehension to have improved.

Hyperactivity had abated to varying degrees in all six affected children, based on reports from their parents and medical observations in hospital. Three of the five motor-disabled children who were unable to walk before the surgery could ambulate independently within 1 year (cases 3, 8, 9). One motor-disabled patient improved enough to take a few steps shortly thereafter, but it took her 9 years (age, 12 years) to become able to walk without assistance (case 5). Likewise, case 10 was unable to support his head before surgery, but 6 months later he could pull himself up to stand, and 2 years later could walk using crutches. He finally became able to walk independently, albeit with unstable gait, 9 years after the operation (age, 10 years; Fig. 7). The three children rated as having "walking difficulties" became able to walk independently shortly after surgery (cases 2, 7, 13). Self-injurious behavior extinguished shortly after surgery in both affected children (cases 5 and 6). In terms of toilet training, three out of the five children still not toilet-trained by 4 years of age accomplished toilet control between 1 and 6 months post-operatively (cases 1, 4, 6); the remaining two are still untrained today (cases 2 and 9; Table 1).

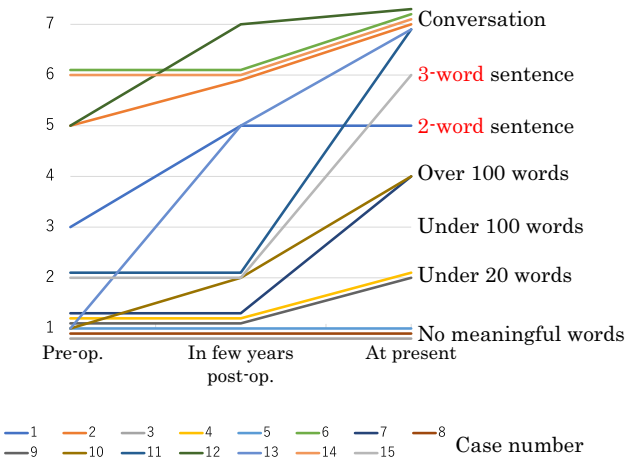

Fig. 5 Changes in language use and acquisition after surgery

Head circumference was continuously tracked after the operation and recorded in a growth chart (Fig. 2a, b). Six children exhibited cranial cavity growth sufficient to put them close to the normal range for their gender (cases 1, 5, 6, 7, 11, 14), the remaining nine stayed in the microcephalic range throughout development.

Neuroradiological changes

On 3D-CT, anterior cranial fossa extension as well as forehead and anterior cranial cavity expansion was observed in all cases. Convolutional digital marking had largely disappeared after 6 months (Fig. 3a). Frontal lobe volume appeared enlarged on MRI in all cases (Fig. 3b).

Average intracranial pressure was 16.4 mmHg in all patients (range 9–22 mmHg).

Next, we will describe the clinical features and postoperative course in detail for one young girl whose condition was complicated by the presence of a chromosomic 7q35-qter deletion (case 2). This young girl was seen by doctors at the age of 6 years, after 2 months with chief complaints of developmental (primarily language) delay. She could produce three-word sentences with difficulty, but not engage properly in normal conversations; her pronunciation was indistinct and her listening comprehension poor. She was also highly restless and would reportedly leave the family's house without permission. Motor skills were underdeveloped: her parents mentioned that she would frequently fall due to balance problems. She had not accomplished toilet training in terms of either urination or defecation. Her general developmental quotient (DQ) was 28 (revised Kyoto-form developmental test). Physical characteristics included small head circumference indicative of microcephaly (42.5 cm, marked by ★ in Fig. 2), and body weight and height more than two SDs below the normal range for her age. She underwent a battery of tests in our pediatrics clinic to determine the pathology of her short stature; however, her bone age and somatomedin levels, and her responses to hormone and growth-hormone-stimulation tests, were all normal.

3D-CT images showed the metopic suture had fused into a ridge and significant narrowing of the anterior cranial fossa, leading to a diagnosis of mild trigonocephaly (Fig. 6a). Severe digital marking on the skull interior was also observed. No abnormal findings were observed on brain MRI. Due to her microcephaly, we opted to monitor her clinical course in the short-term without surgical intervention. Her condition was stable in the subsequent 6 months. Encouraged by our institution's successful surgical record for mild trigonocephaly, her parents expressed a strong desire for decompressive craniectomy. Preoperative karyotyping revealed 7q35-qter deletion (i.e., deletion of the long arm of chromosome 7 from the q35 locus) (Fig. 6b). We performed the procedure 8 months

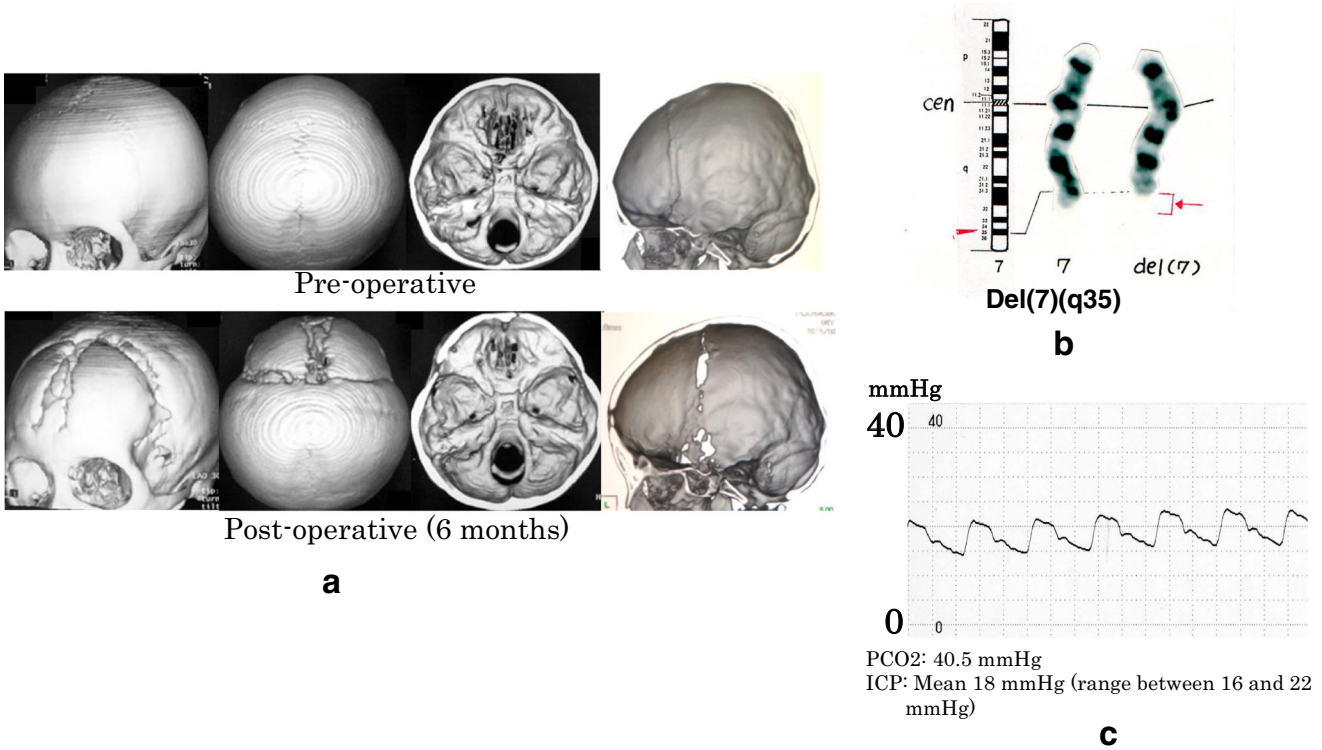

Fig. 6 Case 2 presentation. **a** Patient's 3D-CT (pre-operatory). Upper column, apparent ridge of the metopic suture, heel-shaped deformity of forehead, and smaller anterior fossae indicated mild trigonocephaly (note the enlargement of the frontal area and anterior fossa on 3D-CT in the post-operatory evaluation). **b** Karyotype abnormality—Del [7](q35). **c** Representative graph of the ICP monitoring during surgery—high ICP (mean, 18 mmHg) in normocapnia (from *Shouni No Nousinkei*. 2010 35: 100–112. Reprinted with permission)

after her initial diagnosis. Intracranial pressure measures during surgery were high—mean 18 mmHg (range between 16 and 22 mmHg).

By 2 months after the operation, the girl could converse normally. Anecdotally, her mother said she became more responsive and playful, with better motor coordination and infrequent falls. Seven months after surgery, she could engage with others normally: her pronunciation improved, she no longer fidgeted restlessly during movements, and she could climb stairs one leg at a time. Her DQ remained unchanged at 29 1 year after surgery. Her vocabulary had markedly improved by 2 years post-operation, and she could construct phrases as long as three words. Her conduct could be described as well-behaved, mature, and talkative by 5 years after surgery. She was enrolled in a special needs school at the age of 15. Today, she can converse without problems and is independent in activities of daily living. Post-operative 3D-CT images showed obvious expansion of the anterior cranial fossa and cavity and disappearance of digital marking (Fig. 6a).

Her head circumference remained small (47.7 cm), still two standard deviations below normal for her age; however, her continuous growth after the operation, as depicted in Fig. 2 (denoted by ★), indicates some minor improvement in this respect. However, her height and weight remained unchanged.

Discussion

Historically, surgical interventions for microcephaly date back to Dr. Odilon Marc Lannelongue's series of reports in 1890, where he firstly described craniectomy to treat the condition [10]. Similar protocols were developed and started in North America by Drs. William Williams Keen [11] and Levi Cooper Lane [12] at around the same time. In Montreal in the 1880s, Dr. William Fuller independently applied craniectomy or trepanation to treat microcephalic patients with intellectual disability and reported improvements in intellectual function after the operation. Many doctors would adopt his methods, leading some contemporary commentators to consider him the founder of the surgical approach. Dr. Lane would later proclaim that Fuller had successfully "unlocked" the brain [12]. These innovators paved the way for a craniectomy boom in Europe and America, buoyed by the hope of curing microcephalic children with mental disabilities.

However, Dr. Abraham Jacobi, the so-called father of pediatrics, would criticize the procedure at an international conference in Rome in 1893 as ineffective: he would formalize his concerns in a paper published the following year [13]. Specifically, Jacobi noted the high mortality rates associated with craniectomy and the procedure's failure to enhance intellectual development (Feinsod and David have well summarized his critiques in a recent review paper) [7]. Surgical interventions to treat microcephalic children with intellectual disability fell out of favor after this report. Their demise is well illustrated by Dr. Harvey Cushing's *Surgery of the Head*, a classic surgical textbook published in 1908, which cites Dr. Keen himself, one of its original pioneers, in describing the protocol's inefficacy [6].

A diagnosis of microcephaly alone was no longer a valid indication for craniectomy. Attitudes began to change in the 1920s, driven by case reports by Drs. Mehner in Germany [14] and Faber and Towne in the USA [15], which described positive outcomes for patients with a craniosynostosis diagnosis clearly validated by X-ray findings. Surgical interventions became now popular again, albeit strictly for patients diagnosed with craniosynostosis.

We started performing decompressive craniectomy to treat children with mild trigonocephaly in 1994. The number of cases has continued to increase since 1998 thanks to coordination with other care facilities for handicapped children throughout Okinawa Prefecture. Our research efforts have focused on elucidating the therapeutic mechanism underlying the procedure, and quantitative studies to validate its efficacy [1–5]. We have hesitated to treat the condition in cases when it is clearly associated with microcephaly. We observed serious digital marking in most cases, but no abnormal brain structures on MRI (excepting one child with brain atrophy). While most pediatric neurosurgeons have, at some point, encountered microcephaly as a consequence of multi-suture craniosynostosis (e.g., acrocephaly), it is rarely present in patients with single-suture fusion. The pathology is defined as a growth defect of the central nervous system, with many possible causes: failure of the cranial bones to grow and "stretch" normally at the sutures results in an abnormally small head circumference throughout development. Typical physical findings include thickening of the calvarial bone and excessive enlargement of the paranasal cavities (e.g., the frontal sinuses); digital marking is not present. Despite our reservation about surgical interventions to treat children with both microcephaly and mild trigonocephaly, our decision for each child was bolstered by several criteria: notably, the lack of developmental changes during at least 6 months of observation, the absence of abnormal imaging findings in the skull or brain, and the presence of significant digital marking. Patients' families were all fully apprised of the difficulties that comorbid microcephaly would pose to the operation. Our findings show that clinical symptoms improved to some degree in all cases. Head circumference increased in six patients, albeit not enough to put them in the normal range; in the other nine, the growth was slow and moderate over time.

As far as we know, there have been no recent reports of surgical intervention performed explicitly to treat combined microcephaly and single-suture craniosynostosis. Decompressive craniectomy in the 1880s and 1890s, at the peak of its popularity, was undertaken to treat not only

craniosynostosis but also many other intracranial abnormalities alike, since the limitations of diagnostic technology at the time did not allow doctors to confidently differentiate between microcephaly and other pathologies. The heterogenous composition of this cohort, including patients with organic brain disorders besides microcephaly, was likely responsible for the poor surgical outcomes identified by Jacobi [13]. Alternatively, even hypothetically assuming that all these historical patients did indeed have craniosynostosis, it is possible that cranial decompression was still insufficient because of the specific techniques used (linear craniectomy and trepanation) or the significant bone removal involved. McClintock [16] published pre- and post-operative pictures of a 4-year-old patient (reprinted here as Fig. 7a). The facial appearance in the picture certainly suggests that the patient's condition had improved by 2 months after the surgery, likely thanks to adequate decompression (we deeply suspected mild trigonocephaly in this case based on the metopic ridge seen in the middle forehead). In 2011, Cushing achieved substantial decompression using their protocol and tracked improvements in patients' clinical course in a chart [17].

One child (case 10) in our cohort was quite similar to McClintock's patient [16]. We diagnosed him with mild trigonocephaly based on 3D-CT findings and elected to perform surgery due to the high degree of digital marking despite brain atrophy apparent on MRI. Intracranial pressure measurements indicated final values of between 7 and 20 mmHg (mean: 13 mmHg), evidencing substantial and sufficient decompression. Enhanced motor development, improved respiratory status, and reduced drooling were observed after the surgery. In the course of over 10 years of follow-up, he became able to produce simple words and to walk independently (Fig. 7b).

All patients discussed above were diagnosed with mild trigonocephaly due to single-suture craniosynostosis; however, their symptomology resembles the historical patients presented in nineteenth-century reports. Table 1 contains a summary of our clinical findings before and after surgery and during the long-term observation period. Despite persistent intellectual disability, children's clinical condition improved in various dimensions, including vocabulary and speech production, leading us to conclude that their quality of life was indeed enhanced—or at least, increased independence in daily life could be achieved. We attribute these positive outcomes to the significant decompression of the opercular regions achieved after major reduction of the sphenoid bone. This

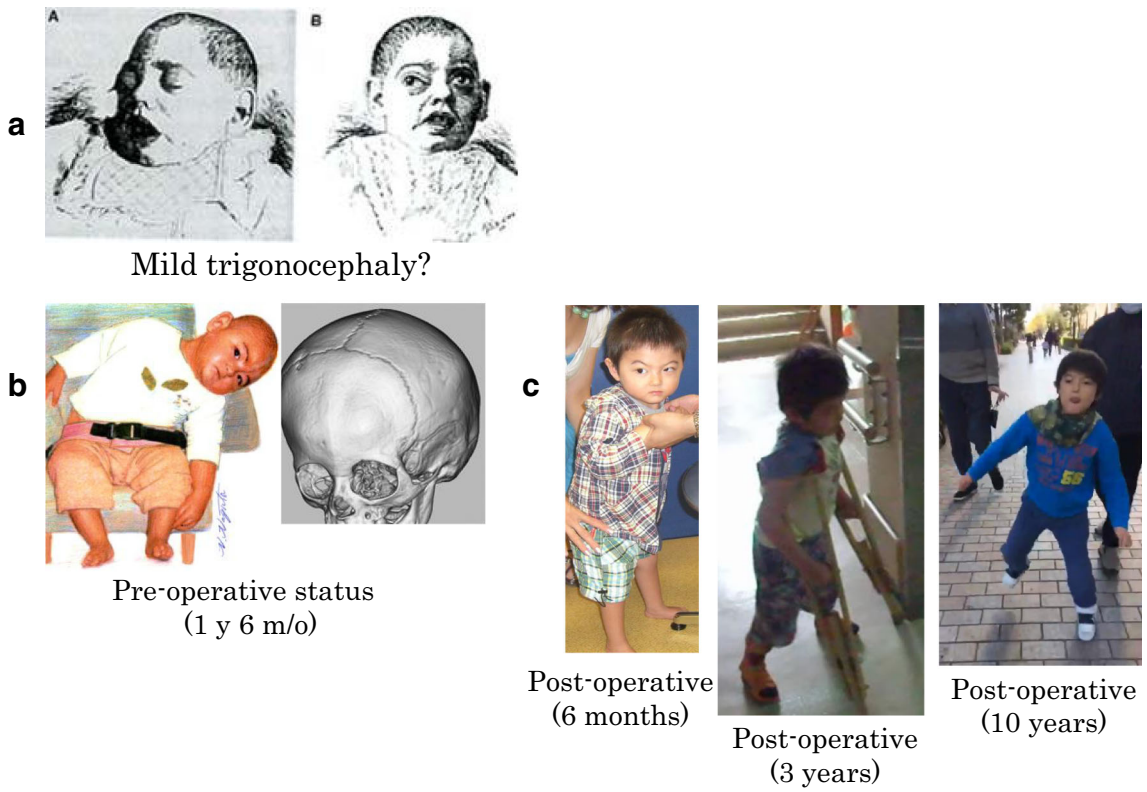

Fig. 7 Similarities between McClintock's patient and one of our patients. **a** McClintock's patient: left picture, pre-operatory expression (note the bony ridging at the midline of the forehead suggesting trigonocephaly); right picture, post-operatory expression (note the eyes clearly opened, suggesting improved conscious level—from Feinsod's paper [7]). **b** Our 1.5-year-old male patient. He did not accomplish neck control before surgery. 3D-CT presented bony ridging at the midline of the forehead. **c** Post-operatory improvement. He could stand with some support in 6 months and his motor function kept improving year after year (from *Shouni No Nousinkei*. 2010 35: 100–112. Reprinted with permission) (with permission by parents to show the child's face)

procedure aims to surgically expand the anterior cranial cavity, especially the anterior cranial fossa.

Diagnostic technology, pediatric care, and surgical principles are more advanced today than ever before. We continue to believe in the value of decompressive craniectomy when treating patients with high intracranial pressure in the absence of abnormal brain findings on MRI, even for cases of single-suture craniosynostosis complicated by microcephaly and intellectual disability.

Various clinical issues associated with 7q35 deletion are well known and documented [18]; however, even in such cases, surgical intervention is one treatment option for patients with suspected high intracranial pressure in the absence of abnormal findings on brain MRI. Further investigation appears necessary to clarify these points.

Conclusion

Surgical outcome of 15 patients with severe intellectual disabilities and various delays in developmental milestones associated with microcephaly and trigonocephaly was reported. They were diagnosed by 3D-CT and showed no abnormalities in the brain as assessed by MRI. All patients had marked digital markings suggesting increased ICP. They then underwent decompressive cranioplasty and each patient made some improvement in at least one of the symptoms.

We propose that in patients with trigonocephaly or other single craniosynostosis associated with microcephaly, surgical intervention may be tried when there are no abnormal findings in neuroradiological studies and a high ICP is observed.

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Compliance with ethical standards The hospital ethical committee approved the surgical treatment for mild trigonocephaly.

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

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