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Pediatric colloid cysts: a multinational, multicenter study. An IFNE-ISPN-ESPN collaboration

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OBJECTIVE Colloid cysts (CCs) are rare at all ages, and particularly among children. The current literature on pediatric CC is limited, and often included in mixed adult/pediatric series. The goal of this multinational, multicenter study was to combine forces among centers and investigate the clinical course of pediatric CCs.

METHODS A multinational, multicenter retrospective study was performed to attain a large sample size, focusing on CC diagnosis in patients younger than 18 years of age. Collected data included clinical presentation, radiological characteristics, treatment, and outcome.

RESULTS One hundred thirty-four children with CCs were included. Patient age at diagnosis ranged from 2.4 to 18 years (mean 12.8 ± 3.4 years, median 13.2 years, interquartile range 10.3–15.4 years; 22% were < 10 years of age). Twenty-two cases (16%) were diagnosed incidentally, including 48% of those younger than 10 years of age. Most of the other patients had symptoms related to increased intracranial pressure and hydrocephalus. The average follow-up duration for the entire group was 49.5 ± 45.8 months. Fifty-nine patients were initially followed, of whom 28 were eventually operated on at a mean of 19 ± 32 months later due to cyst growth, increasing hydrocephalus, and/or new symptoms. There was a clear correlation between larger cysts and symptomatology, acuteness of symptoms, hydrocephalus, and need for surgery. Older age was also associated with the need for surgery. One hundred three children (77%) underwent cyst resection, 60% using a purely endoscopic approach. There was 1 death related to acute hydrocephalus at presentation. Ten percent of operated patients had some form of complication, and 7.7% of operated cases required a shunt at some point during follow-up. Functional outcome was good; however, the need for immediate surgery was associated with educational limitations. Twenty operated cases (20%) experienced a recurrence of their CC at a mean of 38 ± 46 months after the primary surgery. The CC recurrence rate was 24% following endoscopic resection and 15% following open resections ($p = 0.28$).

CONCLUSIONS CCs may present in all pediatric age groups, although most that are symptomatic present after the age of 10 years. Incidentally discovered cysts should be closely followed, as many may grow, leading to hydrocephalus and other new symptoms. Presentation of CC may be acute and may cause life-threatening conditions related to hydrocephalus, necessitating urgent treatment. The outcome of treated children with CCs is favorable.

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KEYWORDS colloid cyst; hydrocephalus; endoscopy; oncology

Colloid cysts (CCs) are benign cystic lesions typically located at the upper anterior part of the third ventricle, adjacent to the foramina of Monro. Their location can cause obstruction of both foramina of Monro, leading to bilateral hydrocephalus. CCs usually present with symptoms related to increased intracranial pressure (ICP) due to obstructive hydrocephalus. These symptoms usually appear acutely, although a subacute and even a chronic presentation over weeks or longer may occur.[1–6] Not all CCs cause symptoms, as some may not lead to hydrocephalus, while others may lead to hydrocephalus with a paucity or even absence of any symptoms.[7–10]

Given the strong potential for the development of acute hydrocephalus and even life-threatening conditions and

ABBREVIATIONS CC = colloid cyst; ESPN = European Society for Pediatric Neurosurgery; EVD = external ventricular drain; ICP = intracranial pressure; IFNE = International Federation of Neuroendoscopy; IQR = interquartile range; ISPN = International Society for Pediatric Neurosurgery.

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herniation with CCs,[11] they should be treated, especially if they are observed to grow over time or if they lead to hydrocephalus.[8] Treatment usually includes resection, either via a craniotomy through various microsurgical approaches,[2,12] or endoscopically.[7] CSF drainage with a shunt, and often a septostomy, is another treatment alternative, especially in the elderly or in instances of CCs that may not be safely resected. Currently, there is no single accepted surgical approach for CC resection, as much depends on the size of the ventricles as well as the surgeon's experience.[13–18]

CCs presenting during childhood are rare. They usually present with hydrocephalus but may also present incidentally.[6,19–26] A few case reports describing deaths related to CCs have been published, even during childhood.[27–33] Thus, awareness about this rare pathology by the treating teams should be increased. This study focuses on understanding pediatric CCs in the context of the presenting symptoms, radiological findings, natural history of nonoperated cases, surgical approach, and outcomes. As the experience of individual centers treating pediatric CCs is limited because of the relative rarity of the diagnosis, we organized an international collaboration among medical centers and retrospectively collected pediatric CC data.

Methods

This is a multinational, multicenter, retrospective study. Following IRB approval, we retrospectively reviewed the files of all children who were treated (or followed) since 2010 for a CC at the Department of Pediatric Neurosurgery of Dana Children's Hospital, Tel Aviv Medical Center. Patient or caregiver consent was waived. An introductory letter and study protocol were distributed via the IFNE (International Federation of Neuroendoscopy), ISPN (International Society for Pediatric Neurosurgery), and ESPN (European Society for Pediatric Neurosurgery) mailing lists to all their members, offering them the opportunity to join this study. Additional centers were recruited via direct contact with pediatric neurosurgeons from around the world. Anonymized patient clinical data were sent to the central office (Dana Children's Hospital) for analysis.

Inclusion Criterion

The inclusion criterion was children younger than 18 years of age when diagnosed with a CC. CC diagnosis was based on one or more of the following: typical MRI findings, intraoperative findings, or pathological confirmation.

Data Collection

We collected the following data: 1) patient demographics and symptoms, including presenting symptoms (or indication for imaging), symptom acuteness (no symptoms, chronic [months or more], subacute [approximately 2 weeks], acute [days or less], and acute on chronic), level of presenting symptoms (intact, consciousness, confused state, and other [specified]), and specific presenting symptoms; 2) imaging (MRI-based) data, including T1- and T2-weighted images (hypo-, iso-, or hyperintense), enhancement, maximal cyst size, and presence of hydrocephalus (none, unilateral, or bilateral); 3) treatment-related data, including treatment methods (surgical or conservative), timing of surgical treatment, surgical technique, surgery-related complications, cyst recurrence (radiological), and need for further surgeries; and 4) functional outcome as reported by each center based on patient follow-up charts, including statements regarding limitations in the following areas: daily function, education, academic difficulties, and permanent memory problems.

Contributing Centers

A total of 134 cases were recruited from 33 centers, each contributing 1–20 cases (mean 4 ± 4 cases). Only 2 centers contributed more than 10 cases (12 and 20 each). Centers were distributed over 5 continents (Table 1).

Statistical Analysis

Data were tabulated in a Microsoft Excel spreadsheet. IBM SPSS Statistics software (version 25, IBM Corp.) was used for all statistical analyses. Categorical variables were reported as number and percentage. Continuous variables were reported as median and interquartile range (IQR). Correlations between continuous variables were evaluated using Spearman's correlation coefficient. Associations between categorical variables were assessed using Fisher's exact test. Associations between categorical and continuous variables were assessed using a Mann-Whitney or Kruskal-Wallis test. All statistical tests were two-tailed and a p value < 0.05 was considered significant.

Results

A total of 134 children (74 boys and 60 girls) with CCs were reported and included in this study. Patient age at diagnosis ranged from 2.4 to 18 years (mean 12.8 ± 3.4 years, median 13.2 years, IQR 10.3–15.4 years). Table 2 summarizes the ages of the patients in the study, organized according to age group.

Clinical Presentation

Table 3 summarizes the presenting symptoms. Twenty-two cases were diagnosed as incidental CC. Indications for imaging in the incidental cases included traumatic brain injury (n = 7), skull lesion (eosinophilic granuloma, n = 2), learning difficulties and/or developmental delay (n = 3), unknown (n = 3), and other (scoliosis, ruptured arteriovenous malformation, endocrine workup, retinal hemorrhages, fever workup, cholesteatoma, follow-up of postmeningitis hydrocephalus, n = 1 each).

Twenty-two patients presented with decreased sensorium. In 8 patients this condition presented as a syncope or seizure in the absence of other symptoms. In 8 cases the patient presented as lethargic, in some cases with pupil dilation. In 1 case (a 6.8-year-old), the patient presented in a coma with dilated and fixed pupils. This patient died, despite insertion of an urgent external ventricular drain (EVD). The vast majority of the patients were intact at diagnosis, experiencing various symptoms. Twenty patients had no presenting symptoms and were all neurologically intact. Table 4 presents the main signs at presentation for

TABLE 1. Number of contributing centers and cases, organized according to continents and countries

Continent/ Region	Country (no. of centers)	No. of Cases	Open/Endoscopic Surgery*
Africa	Algeria (1)	7	7/0
Asia	India (1)	9	9/0
	Pakistan (1)	3	1/2
	Israel (1)	8	1/5
Europe	France (1)	2	0/2
	Germany (4)	10	2/6
	Italy (5)	23	1/22
	The Netherlands (1)	1	0/1
	Spain (2)	2	0/1
	Switzerland (1)	1	0/0
	Turkey (1)	4	1/3
	United Kingdom (2)	4	3/1
	Belgium (1)	5	4/0
North America	Canada (2)	5	0/3
	USA (5)	44	10/10, 2 unknown
South America	Argentina (1)	3	0/2, 1 unknown
	Brazil (2)	2	1/1
	Paraguay (1)	1	0/1
Total	33 centers	134	103

* The open/endoscopic column states the number of craniotomy (open) surgeries versus endoscopic resections among these centers.

the 114 symptomatic patients, organized according to the acuteness of symptom occurrence.

There was a significant correlation between age at diagnosis and occurrence of any symptom. Younger children were more commonly diagnosed with an incidental CC: 48.3% of children younger than 10 years had no symptoms, compared to 5.7% of children older than 10 years ($p < 0.001$). Older children more commonly presented with headaches ($p < 0.001$). There was no significant correlation between age and presentation with specific symptoms of nausea/vomiting, visual complaints, decreased consciousness, memory decline, or presence of papilledema. There was no significant correlation between the age at presentation and acuteness of symptoms (chronic, acute, acute on chronic, subacute); however, the number of children younger than 6 years of age (n = 6 children) was too small to make any definitive conclusions (Table 5).

TABLE 2. Number of patients according to various age groups

Age (yrs)	No. (%)
0–6	6 (4)
6–12	44 (33)
12–18	84 (63)
<10	30 (22)
>10	104 (78)

TABLE 3. Presenting symptoms

Presenting Symptom	No. (%)
Headache	100 (75)
Nausea/vomiting	52 (39)
Decreased sensorium	22 (16)
Behavioral changes	20 (15)
Visual complaints	31 (23)
Memory decline	2 (1.5)
Incidental	22 (16)

MRI Characteristics

We identified the following MRI characteristics: 1) 82% of the cysts were iso- or hyperintense on T1-weighted imaging; 2) 75% of the cysts were iso- or hyperintense on T2-weighted imaging; 3) 15% of the cysts had some enhancement; and 4) 55% of the patients presented with some form of hydrocephalus (8% unilateral and 47% bilateral). Cyst size ranged from 2 to 40 mm (mean 12.6 ± 7.3 mm, median 11 mm, IQR 7–17 mm).

There was no significant correlation between age at presentation and radiological appearance (T1-weighted/T2-weighted/enhancement) or maximal cyst size. There was no significant correlation between MRI appearance (T1-weighted/T2-weighted/enhancement) and type of presenting symptoms, papilledema, presence of hydrocephalus, or acuteness of symptoms. There was a significant correlation between maximal cyst size and acuteness of symptoms, as well as presence (and type) of hydrocephalus ($p < 0.001$ for both). Generally, larger cysts were correlated with more acute symptoms and with more severe hydrocephalus (bilateral > unilateral > no hydrocephalus). Larger cysts were also correlated with headaches ($p = 0.03$), nausea/vomiting ($p = 0.001$), decreased consciousness ($p < 0.001$), papilledema ($p < 0.001$), and any symptom ($p < 0.001$, as opposed to incidental CC), reflecting secondary effects of hydrocephalus.

Need for Surgery

Overall, 103 patients underwent a cyst resection, 75 at presentation. The remaining 59 children were initially followed. Of these 59 children, 28 had a resection at some point from 1 to 106 months after presentation (mean 19 ± 32 months, median 4.5 months, IQR 2–20.7 months). Reasons for delayed surgery included new symptoms (12 cases), cyst growth (8 cases, 2–106 months after diagnosis, mean 56 ± 40 months), ventricular enlargement (9 cases), and family decision or time to referral to neurosurgical care (3 cases, 1–106 months after diagnosis, mean 28 ± 46 months); some had several causes.

Nine patients underwent shunt surgery. Eight shunts were placed as the primary treatment for CC-related hydrocephalus, and 1 had a shunt for post-prematurity intraventricular hemorrhage (his cyst was never operated). Of the 8 treated for the CC, 3 patients were subsequently referred to another neurosurgical facility for cyst resection, and 5 were initially followed. All underwent delayed resection due to cyst growth or new cyst-related symptoms.

TABLE 4. Presenting signs and acuteness of symptoms in 114 symptomatic patients

Presenting Sign	Chronic	Subacute	Acute	Acute on Chronic	Total	Papilledema
Intact	37	27	19	3	86	21
Decreased consciousness	0	2	8	3	13	9
Confused state	0	0	7	0	7	2
Other*	0	5	3	0	8	6
Total	37	34	37	6	114	38
Papilledema	5	14†	17	2	38	

* Four patients had a squint, 2 had nystagmus, 1 psychiatric illness, and 1 ataxia.
† Two patients had unknown fundus examination.

The range of the follow-up period for the 31 nonoperated cases was 0–132 months (mean 48.6 ± 44 months, median 32.7 months). The range of the follow-up period for the entire group was 0–244 months (mean 49.5 ± 45.8 months, median 34 months, IQR 13–72 months). Two variables were correlated with the need for surgery at any time (initially or subsequently): 1) cyst size, i.e., larger cysts were associated with need for surgery ($p < 0.001$); and 2) older age at presentation ($p = 0.002$). There was no significant correlation between MRI appearance (T1-weighted/T2-weighted/enhancement) and a need for surgery.

Surgical Technique

For 100 of the 103 operated cases, the surgical technique was identified in the patient records. There were 62 endoscopic approaches (2 converted to open microsurgical resection), 16 transcortical transventricular approaches, 16 interhemispheric transventricular approaches, 5 interhemispheric interforniceal approaches, and 1 occipital transtentorial approach. We were unable to find any clear correlations between the contributing centers and surgical techniques (Table 1). Many different endoscopic systems of different sizes were used, from various companies. A septostomy was performed in 45 patients (48% of 93 reported cases), an endoscopic third ventriculostomy in 8 patients (9% of 90 reported cases), and an EVD in 41 patients (41% of 99 reported cases). A small number of surgeons reported using an endoscopic ultrasonic aspirator or a side-cutting aspirator, and a few reported using an endoscopic holder.

Surgical Outcome

There were 10 cases (10%) with 1 or more complications reported. Meningitis was reported in 2 cases, and infarction, seizures, minor hemorrhage, bone flap migration, acute hydrocephalus requiring an EVD, transient hemiparesis, strokes following herniation at presentation, and wound infection in 1 case each. One patient operated endoscopically had an intraoperative bleed; thus, the surgery was aborted and the cyst was uneventfully resected via an open approach 10 days later. Seven cases needed a new shunt following surgery (7.7%). CC radiological recurrence was identified in 20 patients (20%) at 0.3–178 months (mean 38 ± 46 months) after resection, of which 17 underwent an additional resection. The recurrence rate was 24% following endoscopic resection and 15% following open resections ($p = 0.28$). One death occurred in a 6.8-year-old who presented in a deep coma with fixed, dilated pupils, and who subsequently died despite an EVD. No other deaths were reported.

Functional Outcome

Table 6 summarizes the functional outcome as a function of the need for surgery. The data are subdivided based on whether the surgery was immediate or delayed. There was no significant correlation between a need for surgery

TABLE 5. Correlation between acuteness of symptoms and age at presentation

Age at Presentation	Symptoms				
	None	Chronic	Subacute	Acute	Acute on Chronic
Age, yrs					
Mean ± SD	9.1 ± 3.6	13.3 ± 2.7	13.9 ± 3.1	13.3 ± 2.9	12 ± 4.4
Median (IQR)	8 (7–12.4)	13.2 (11.2–15.8)	14 (12.5–16.8)	14 (11.5–15.7)	13 (8.7–15.2)
Minimum age, yrs	2.4	7	5.5	6.7	4.3
% <6 yrs	60	0	20	0	20
% 6–12 yrs	27.3	27.3	11.4	31.8	2.3
% >12 yrs	5.9	29.4	32.9	27.1	4.7
% <10 yrs	48.3	20.7	13.8	13.8	3.4
% >10 yrs	5.7	29.5	28.6	31.4	4.8

TABLE 6. Functional outcome as a function of the need for surgery, and whether it was immediate or delayed

Need for Surgery	Daily Function	Education	Permanent Memory Problems	Academic Difficulties
Immediate surgery	67 normal, 5 limitations	66 normal, 5 special education	58 no, 11 yes	56 no, 8 yes
Delayed surgery	27 normal	27 normal	25 no, 1 yes	26 no, 1 yes
No surgery	27 normal, 4 limitations*	19 normal, 4 special education*	26 no, 1 yes	23 no, 4 yes

* All 4 cases were the same patients, and all had a premorbid neurodevelopmental delay unrelated to the CC.

at any time and any outcome decline. There was a slight correlation between immediate surgery and memory decline ($p = 0.03$), and a slight correlation between delayed surgery and educational limitations ($p = 0.038$). Of the 7 cases presenting with lethargy or pupillary dilation who survived the acute phase, 1 had limitations in all outcome variables, whereas the remaining 6 had no reported functional limitations. All nonoperated cases with functional impairment had a premorbid neurodevelopmental delay unrelated to the CC explaining their limitations.

Discussion

This is the largest series to date focusing on pediatric CCs, the main presenting symptoms, radiological characteristics, treatment, and outcomes. CCs are rare among children; only by collaborating with 33 centers from 5 continents were we able to reach the relatively large number of 134 cases. Most centers contributed small numbers of fewer than 10 cases.

The main take-home messages from this study are that CCs may present even in young infants, and most symptomatic cysts present after the age of 10 years. Headaches were the most common presenting symptom, although other symptoms of increased ICP (nausea/vomiting, visual complaints, behavioral changes, and decreased sensorium) were reported as well. For the symptomatic group, 62% had hydrocephalus (uni- or bilateral) and 35% had papilledema. Approximately 20% of all children were asymptomatic. Of the symptomatic group, symptom occurrence subdivided relatively evenly, occurring acutely, subacutely, and chronically (about one-third each). Approximately 77% of the patients were treated with surgery at some point, 60% of which were endoscopic resections. Of the children who were only followed after diagnosis, about 50% eventually underwent surgery due to new symptoms, cyst growth, or developing hydrocephalus. The most important risk factors in the need for surgery were cyst size and older age. Generally, the functional outcome reported was good in the vast majority of cases, with the most common limitations related to memory decline. Children undergoing urgent treatment were more likely to develop functional limitations.

These results emphasize the importance of early referral for children of all ages who appear with new-onset neurological symptoms, or symptoms related to increased ICP, for urgent evaluation and imaging. Our study clearly indicates that although rare, CCs may present acutely even at very young ages, and should lead to early diagnosis and treatment.

Several publications regarding pediatric CCs have been published since 1933.[34] As the use of MRI for various indications has increased, and the threshold for cranial scanning has become lower over the years, incidental brain lesions are more commonly diagnosed,[35] potentially leading to diagnosis of more incidental CCs compared to previous historical series.[26] Since the year 2000, a total of 94 pediatric CCs have been reported in the literature, including 63 males and 31 females.[6,19–26,36–39] Age at presentation was 3–18 years (about 8.5% were younger than 10 years of age). Note that 7 cases (7.5%) were diagnosed incidentally in this earlier study (compared to the 20% incidental findings in our study). The majority of patients presented with increased ICP-related symptoms associated with the secondary hydrocephalus. Other series have included children and adults together, usually with small numbers of pediatric cases, and have not focused on the unique clinical or radiological features of the pediatric patients.[4,5,40–42] Of course, incidental CCs are common in adults too, found in large natural history series.[8]

Interestingly, drop attacks and syncope have been described in pediatric and adult CCs, often but not always in association with hydrocephalus.[6,19,22] In the current study, in 134 patients we found 13 instances (10%) of patients presenting with seizures or syncope. Death related to CC is probably secondary to acute hydrocephalus and may present in childhood.[33] The vast majority of patients have symptoms preceding death, usually associated with increased ICP. It is important to increase awareness of this pattern, because in children, especially compared to adults, these symptoms last longer prior to death (a mean of about 6 days).[33] However, an ultrafast course of deterioration over several hours, and even a true sudden death, has been described as well.[30,31,37] Some reports state that pediatric CC may present in a more aggressive manner and thus may more often lead to sudden death compared to adult cases.[21,31,32] In a large meta-analysis, however, age was not associated with a bad neurological outcome.[43]

Treatment of CCs includes both open approaches and endoscopic resections,[2–4,6,7,23,25,40] all with good functional outcome. There is no clear advantage of one technique over another,[40] and there is no unique treatment strategy for pediatric versus adult cases. Generally speaking, en-

doscopic resections have been advocated in the presence of hydrocephalus, but endoscopy has also been used in the absence of hydrocephalus, with good results.[7,42] The goal of surgery is complete removal of the cyst and its capsule; recurrence may occur in incomplete resections.[4] Similar to a recent series,[26] the results of the current multicenter series share a favorable outcome following endoscopic resections. Conversely, the radiological recurrence rate of this series appears to be relatively high for both surgical approaches, i.e., 24% following endoscopic resection and 15% following open resections ($p = 0.28$). We do not have an explanation for this recurrence rate; possibly it reflects the rarity of this disease and its treatment. Our series also stresses the role of shunt surgery in the presence of acute hydrocephalus, when CC resection is not feasible, later referring the patients for further evaluation and treatment to experienced centers.

For asymptomatic cysts, follow-up is a valid option, with periodic clinical and radiological evaluation, as these patients may develop progressive (and even acute) symptoms. Based on the current series, we are unable to state the length of follow-up needed, or whether there are any radiological risk factors for cyst growth, development of hydrocephalus, or symptom progression.

Study Limitations

This study has all the relevant limitations of a retrospective study. Potentially, nonoperated cases may have been underreported if they were not followed by the neurosurgical teams participating in this study. In addition, because this was a multicenter study, and cases were treated by various surgeons and teams, there were no unified indications for treatment. Data were reported by each team, with no central review of images, and no objective and absolute definition of complications. The diagnosis of CC based on radiological findings may mislead, as other pathologies such as low-grade astrocytoma, which are more common in children, may mimic CC.[44,45] The results of this study are biased by the experience of the treating teams, i.e., whether to treat endoscopically or via various open microsurgical approaches. The surgeon's experience may have also affected results and complications. A few cases also received shunts as their primary treatment. In at least some cases, the shunt was reported to have been placed at other medical centers (probably less experienced) to treat the acute life-threatening condition. These patients were later referred to tertiary centers for treatment of their cyst. Outcome assessments were not objective, and were determined based on the surgeon's clinic notes, using very simplistic measures. The absence of formal neuropsychological evaluations of CC patients in this series (before, during follow-up, and after surgery) is common in most CC series. We recommend that surgeons treating and following patients with CCs send these patients for formal evaluations.

Conclusions

CCs may present in all age groups, although most symptomatic ones present after the age of 10 years. Even if cysts are incidentally discovered, they should be followed, as many may grow, leading to hydrocephalus or causing new symptoms. The presentation of CC may be acute, and may cause life-threatening conditions related to hydrocephalus, necessitating urgent treatment. Outcomes are favorable in treated children with CCs.

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Appendix

Pediatric Colloid Cyst Study Group

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Roth. Acquisition of data: Roth, Perekopaiko, Kozyrev. Analysis and interpretation of data: Roth. Drafting the article: Roth. Critically revising the article: Roth, Constantini. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Roth. Statistical analysis: Roth. Administrative/technical/material support: Roth, Perekopaiko, Kozyrev. Study supervision: Roth.

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