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Current trends in the management of subependymal giant cell astrocytomas in tuberous sclerosis

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Abstract

Introduction The management of subependymal giant cells astrocytomas (SEGAs) has been traditionally represented by surgical treatment through an open craniotomic approach. Though open surgery still represents a major option in the management of this kind of tumors, the introduction of mTOR inhibitors in the clinical practice, technological advances in neuroendoscopy and the more recent use of laser interstitial therapy have significantly enlarged the range of available management opportunities.

Methods A thorough review of the literature has been performed. Accordingly, current views in open surgical treatment, medical therapy, endoscopic tumor removal and new trends (such as laser interstitial thermal therapy) are discussed.

Results The risk of significant neurological morbidity (5–50%) complicating open surgery has been for a long time representing a main drawback in the management of SEGAs. More recent series report a significant reduction of morbidity and mortality. The mTOR inhibitors have demonstrated efficacy in both warranting a tumor reduction by up to 60% of the tumor size and helping the control of seizures. However, the reported rate of side effects is as high as 30% and tumor recurrence is a documented occurrence at the time of mTOR inhibitor discontinuation. Endoscopic tumor removal has been more extensively considered an option due to the acquisition of new tools. Limits are still represented by tumor size (< 3 cm) and broad attachment of the tumor to the basal ganglia. Laser interstitial thermal therapy (LITT) is the more recently considered option. Though promising, only short follow-up is available so far, while data on medium- and long-term results of this treatment are completely lacking to date.

Conclusions Surgical treatment remains a mainstay of the management of SEGAs. The indication for an open craniotomic approach should be balanced with an endoscopic tumor removal or LITT according to patient conditions, presence or not of an active hydrocephalus and extension of the attachment of the tumor to the basal ganglia. The mTOR inhibitors do have a definite role both as primary and as adjuvant treatment, but consistent limitations are represented up to now by a not negligible rate of complications and the uncertainties related to the possibility of tumor recurrence once the medical treatment is discontinued.

Keywords Tuberous sclerosis · SEGA · Surgery · Endoscopy · Medical treatment · LITT · Personalized medicine

Introduction

The term "subependymal giant cell astrocytoma" (SEGA) was first coined by Russell et al., as it has been previously referred to as astrocytoma, ependymoma, spongioblastoma and possible ganglioglioma [1]. SEGAs represent 1–2% of all paediatric tumors, presenting almost exclusively in tuberous sclerosis complex (TSC), solitary SEGA anecdotally occurring due to somatic mosaicism involving the TSC gene. SEGAs are generally benign, slow-growing, non-infiltrative lesions, although they may be more aggressive from a clinical standpoint. Indeed, due to the localization mainly in the region of the foramen of Monro and the tendency to grow, they may cause obstructive hydrocephalus, focal neurological deficits and even sudden death [2–4].

SEGAs mostly occur in the first two decades of life and only occasionally in elder patients [5], with an average age at presentation of 11 years. However, thanks also to the diffusion of magnetic resonance imaging (MRI), they have also been reported in young childhood and even prenatally [6, 7].

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Common clinical presentation of patients with SEGAs includes seizures (generalized tonic–clonic seizures or focal motor seizures), psychomotor delay, visual disturbance (decreased vision, diplopia, or blindness), headache and vomiting. The latter are common presenting symptoms of hydrocephalus that results from the obstruction of CSF pathway by SEGAs. The growth of SEGAs may also cause the worsening of seizure burden, as well as learning or behaviour disabilities [8], that characterize TSC patients. Recent studies demonstrate that TSC2 mutation tends to be related with earlier and more severe clinical onset than TSC1 mutation [9]. Other radiological and clinical factors, such as size of tumor exceeding 2 cm and young age of the patients, have been recognized as predicting factors of an acceleration in growth of SEGAs [10]. Acute symptomatology is usually due to acute intratumoral haemorrhage or abrupt worsening of the obstructive hydrocephalus, which both may cause a life-threatening condition, imposing rapid surgical treatment.

The diagnosis of SEGA is mainly based upon MRI, although the differential diagnosis from subependymal nodules is not always straightforward. SEGAs are typically localized at the caudothalamic groove, and dimensions are usually bigger than 5–10 mm [3]. On the other side, SubEpendymal Nodules (SENs) are usually situated in the ependymal lining of the lateral ventricle along the caudate nucleus and they are usually non-enhancing lesions. Finally, they tend to remain stable in size [11]. Tumors appear iso- or hypo-intense on T1WI and iso- or hyper-intense on T2WI [6]. After the injection of gadolinium contrast, tumors markedly show homogeneous or heterogeneous enhancement. Progression in size is peculiar [3, 10].

As a result, the 2012 Washington Consensus Conference agreed on the working definition of SEGA as "a lesion at the caudothalamic groove with either a size of more than 1 cm, extended in any direction or a subependymal lesion at any location that has shown serial growth on consecutive imaging regardless of size" [3]. Accordingly, a growing subependymal lesion, even in the absence of enhancement on MRI, should be considered a SEGA.

The management of SEGAs has deeply changed through recent years. Surgical resection has represented the exclusive treatment for long time and still represents a safe and effective option nowadays. However, in the last decade the management of SEGAs has been deeply affected by the introduction of mTOR inhibitors in the clinical practice and by technological innovations.

Furthermore, many of these tumors were diagnosed late in the past, with patients presenting with symptoms of elevated intracranial pressure for obstructive hydrocephalus. On the contrary, many of these tumors are now diagnosed at an early stage, when still asymptomatic, as part of the screening process of TSC patients, with obvious management implications.

Surgery

SEGAs do not respond to traditional chemotherapy and radiotherapy may be associated with increased risk of secondary malignancy [12, 13]. Stereotactic radiosurgery arises similar concerns, though considered potentially beneficial for SEGAs not amenable to surgical resection. Thus, at present there are scarce data demonstrating its safety and efficacy [14]. On these grounds, surgery has played for long time an exclusive role in the management of SEGAs.

Unfortunately, retrospective surgical series provide inconsistent results concerning outcome, morbidity and mortality mainly due to the heterogeneity of studies population with regard to patients and tumor features (Table 1).

After the introduction of mTOR inhibitors in the clinical practice, several reviews have pointed out advantages and drawbacks of surgical versus medical treatment options. Basically, the surgical morbidity must be weighed against the potential long-term risk of the medical therapy that could be administered potentially lifelong. The problem is that surgical morbidity is not always clear from literature data, as stated before, and side effects of medical treatment may be unknown in the long term. As a result, current practice is based on the experience of single centres.

Surgery remains the only option in SEGAs presenting with acute clinical onset, namely with acute hydrocephalus or intralesional haemorrhage.

In asymptomatic patients, clinical and radiological follow-up is recommended. Current consensus guidelines recommend that neuroimaging should be performed every 1–3 years in patients with TSC, up to the age of 25 years [3]. The frequency of the scans needs to be determined based on clinical grounds, the main characteristics that should trigger an earlier scan being as follows: (i) asymptomatic SEGA in young patients, (ii) large or fast-growing SEGA, (iii) developmental delay or loss of skills (especially in patients with intellectual disability), (iv) new unexpected/sudden onset of symptoms related to raised intracranial pressure as well as an increase in seizure frequency or change in neurological status and behaviour [25].

The indications for treatment include new onset of symptoms or radiological evidence of tumor growth, according to the recommendations from the International Tuberous Sclerosis Complex Consensus Conference 2012 [26]. The choice between surgical and medical option is not univocally defined and may depend on several considerations, including the experience of the physicians.

Since the superiority of one treatment option over the other is not proven, a multidisciplinary team should discuss on a case by case basis the choice and propose both options to parents, thus illustrating advantages and drawbacks of each treatment in the specific case (Table 2).

Table 1 Review of surgical case series

First author, year	No. of pt (tumors)	Approach (transcallosal/ transcortical/ endoscopic)	Gross total resection	VPS	Recurrence	Complications	Death	Follow-up (months)
Giordano 2019 [16]	31	23/5/3	25	10	11	Hydrocephalus (8); Subdural hygroma (4); wound infection (1); brain edema due to thalamo-striatal vein throm- bosis (1); memory impairment (1) and hemiparesis (1)	1 (IMA)	29.7 m
Fohlen, 2018 [15]	18	0/17/1	16	6	3	Meningitis (1)	0	63.6
Harter, 2014 [17]	18 (22)	16/5/1	15 (+ 5 radical STR)	10	2 (STR)	Caudate edema (1), EDH (1), CSF leak (1)	0	52
Kotulska, 2014 [18]	57 (64)	56/5/3	58	13	5	Hemiparesis (14, 8/14 permanent), intracranial bleeding (9), cognitive decline (4, 3/4 permanent), meningitis (2), diabetes insipidus (2), new seizures or increased number of seizures (2), precocious puberty (1), neuropathic headache (1)	3 within 7 days postoperatively (1/3 drug-resistant status epilepticus, 1/3 massive intracerebral bleeding, 1/3 cardiac arrest)+ 1 3 months after partial tumor resection (tumor regrowth and acute hy)	63.7
Amin, 2013 [19]	16	2/14	13	4	1	Presumed ventriculitis (1)	0	40
Jiang, 2011 [20]	17	11/6	15	4	1 (STR)	Transient memory impairment (11)	1 (infarction and acute hy)	46
de Ribaupierre, 2007 [21]	19	19/0	15	4	4 (STR)	Meningitis (1), memory deficit (1)	2 (acute hydrocephalus)	77
Goh, 2004	11	ns	7	3	1	Hemiparesis (2)	0	2–36
Sharma, 2004	23	ns	10	ns	2		2	37.1
Cuccia 2003 [22]	15	9/6	12	1	3 (STR)	Subdural effusions (2), hemiparesis (3, 1/3 permanent), acute hy (1)	0	52
Torres, 1998	19	ns	18	ns	2	Complicated postoperative course (1)	1 (secondary GBM after RTx)	ns
Di Rocco, 1995 [23]	10	5/2/0	ns	3	ns	Complicated postoperative course (1)	0	69.6

Table 1 (continued)

First author, year	No. of pt (tumors)	Approach (transcallosal/ transcortical/ endoscopic)	Gross total resection	VPS	Recurrence	Complications	Death	Follow-up (months)
		(2 ns/1 only VPS)		(before tumor resection)		*Multiple shunt malfunctions in VPS before tumor resection*		
Sinson, 1994 [24]	10	4/6/0	9	7	2	Hemiparesis (1)	2 perioperative (1/2 acute hy, 1/2 intratumoral haemorrhage) + 1 after 5 days (hy) + 1 after 1 year (not dependent from surgery/disease)	80.4

ns not stated, *VPS* ventriculo-peritoneal shunt, *STR* subtotal resection, *GBM* glioblastoma multiforme, *RTx* radiotherapy, *hy* hydrocephalus

Table 2 Comparison of advantages and drawbacks of different treatment options of SEGA

	Microsurgery	mTOR inhibitors	Endoscopy	Laser interstitial thermal therapy (LITT)
Advantages	- Possible cure - Rapid relief for acute symptoms - Histopathological examination	- Might control systemic TSC (*if present*) - Epilepsy control	- Minimally invasive approach - Possibility to concomitantly treat the hydrocephalus (i.e. septostomy or ETV)	- Minimally invasive approach
Disadvantages	- Possible recurrence - Complications (*vision loss, DVP, Headache, memory deficits, damage to cerebral or vascular structures*)	- Indefinite treatment - Mild immune suppression - Drug interaction - Drug-related adverse events	- Limited by tumor size - Length of the operation - Possible recurrence	- Limited by tumor size - Complications (*possible acute hydrocephalus, focal neurological deficits, edema of basal ganglia*)
Indication	- Acute symptomatic SEGA - Asymptomatic SEGA with enlargement of ventricles - Residual tumor after mTOR inhib. treatment	- Not meeting the criteria for surgical treatment - Multiple organ TSC localization - Contraindications for general anaesthesia - Recurrence of SEGA - Neoadjuvant treatment	- Tumor size < 3 cm - Favourable (perpendicular) trajectory of the endoscope to the tumor base (rigid endoscope)	- Tumor size < 2 cm - Adjuvant to medical treatment - Clinical conditions not allowing to consider open surgery or endoscopic tumor removal
Contraindication	- Total resection not feasible (*relative contraindication*)	- Severe acute infection - Elevated blood levels of bilirubin	- Broad base of attachment to the basal ganglia - Tumor size > 3 cm	- Tumor size > 2 cm - Active hydrocephalus - Broad attachment of the tumor to the basal ganglia

Surgical morbidity and mortality widely vary across the literature and 2012 may be considered the turning point in our analysis. In fact, in earlier reports a high rate of postsurgical complications was described due to several reasons, such as symptomatic hydrocephalus, big size of the tumor secondary to late diagnosis, one-step bilateral resection, and acute postoperative hydrocephalus [15, 21–24, 27–29] leading even to death in a not negligible number of patients [20, 29].

In 2012, Sun et al. reported a rate of incomplete resection as high as 34% and a complication rate in the 12 months following SEGA surgery of almost 50% [30]. However, the methodology of this study is limited and these results should be viewed with caution. In fact, data were collected from medical insurance claims coming from 3 US national databases and the authors had no direct contact with any of the patients reported in this study so as they were not able to verify any of the clinical histories.

After 2012, most recent case series demonstrated that neurosurgical resection of SEGAs is an effective way of treating these lesions with acceptable morbidity and zero mortality, thanks to new surgical techniques and earlier surgery [15]. Indeed, the surgical morbidity in these series of patients is generally low, particularly in experienced high-volume centres [1, 18, 27].

In this context, the complications and mortality rate reported by Kotulska et al. in 2014 may appear in contrast with this observation. Actually, this large series includes as many as 57 but patients were operated in different centres in a period going from 1994 to 2011 [18].

The risk of permanent hydrocephalus, requiring VP shunting, largely varies among different series, the general evidence being that the risk of hydrocephalus is more significant when patients present with overt hydrocephalus at the time of surgery [17]. On these grounds, some authors propose to operate SEGAs when there is evidence of growth but before overt hydrocephalus complicates the picture, aiming to reduce the risk of permanent hydrocephalus [15].

Partial tumor resection is frequently associated with progression of the residual tumor. Redo surgery is feasible, but the risk of morbidity should be carefully assessed.

The choice of the surgical approach may partly affect the rate and type of complications.

Some considerations are common to other ventricular tumors. Indeed, the optimal surgical approach for the removal of these lesions is determined by their size, location within the ventricular system and laterality, with transcortical and transcallosal routes being the main options. The former is preferred when the ventricles are enlarged and the lesion is predominantly located in the body of a lateral ventricle. The latter is generally utilized for smaller lesions centred near the midline or involving the anterior third ventricle, in particular if the ventricles are not enlarged. However, in the most recent case series, transcortical route was used in all cases and was assisted by magnetic neuronavigation in the absence of ventricular enlargement [15].

The possibility to manage bilateral lesions has represented an argument orienting the choice of some authors towards the transcallosal route, since the removal of bilateral SEGAs with a unilateral single approach may increase surgical morbidity and in particular the risk of injuring the fornices. However, the resection of the largest side tumor in a staged procedure has been preferred in most recent series to further reduce surgical morbidity [15].

Other important considerations are specific to SEGAs. Their location immediately medial to the genu of the internal capsule increases the risk of motor deficits of the face or upper extremity, thus suggesting the use of intraoperative neurophysiological monitoring whenever feasible.

Considering the attachment of the tumor in the caudate nucleus region, surgical dissection of the tumor should identify firstly the free margins anteriorly, medially and posteriorly in order to protect the normal surrounding structures with cottonoid patties. The tumor is then truncated, and the portion projecting into the lateral ventricle is removed. The remaining tumor, in particular the tumor base, is commonly heavily calcified, and the use of an ultrasonic aspirator or microscissors may allow its cautious debulking lowering the risks connected to the dissection around the tumor interface into the basal ganglia [17].

Identification and preservation of the fornix are also important to prevent memory impairment. Venous anatomy deserves additional consideration, since surgical manipulation should aim to preserve it. The thalamo-striate vein is usually displaced inferiorly and posteriorly, eventually encased by the base of the tumor. If a small portion of tumor remains adherent, particularly when calcified, it is left behind. The caudate vein is usually stretched over the tumor, and occasionally encased. The smaller septal vein tends to be displaced medially and is easily separable from the tumor. On the contrary, the choroid plexus may be coagulated and divided without consequences. Microsurgical septostomy at the time of tumor resection is also performed to potentially simplify shunt procedures if eventually necessary [17]. Whichever approach is taken, a ventricular catheter is left in site to reduce the risk of CSF complications.

Medical treatment

In recent years, the most significant progress in the medical treatment of SEGAs has been obtained due to the identification of mTOR as the key protein kinase involved in the TSC [7].

Thus, mTOR inhibitors rapamycin (sirolimus) along with the prodrug CCI-779 (temsirolimus) and the analogue RAD001 (everolimus) have been actively investigated for a wide array of oncology indications, including the treatment of

TSC-associated SEGAs and as drug-resistant for TSC-associated epilepsy [31].

Rapamycin (sirolimus) is a macrolide compound isolated in 1975. The first study with Sirolimus in TSC patients was published in 2006 and demonstrated a significant reduction in SEGA volume, ranging from 46 to 63% (serum levels, 10 to 15 ng/mL) [32]. Its efficacy has been subsequently confirmed by further studies [28, 33].

Everolimus, that is derived from rapamycin, shows substantially more favourable pharmacokinetic characteristics (better absorption, oral availability, faster steady state levels after initiation, shorter half-life). In 2010 its use has been approved by the Food and Drug Administration for SEGAs associated with TSC that cannot be treated by surgery. Currently recommended drug dose titration ranges from 5 to 15 ng/mL serum concentration [33]. Once SEGA has been stabilized, the dose of the drug may be reduced in order to minimize long-term side effects [10].

Medical treatment may be indicated in either symptomatic or asymptomatic SEGAs.

Considering symptomatic patients, medical treatment is indicated in case of episodic headache with mild ventriculomegaly, in the absence of papilledema or cranial nerve dysfunction.

Medical treatment is also favoured in the case of recurrent tumors, as well as multiple tumors, which are often bilateral, and lesions not amenable to surgical resection or for which gross total resection is unlikely. Indeed, residual tumor will almost invariably regrow.

Systemic contraindications to anaesthesia and surgery may push the choice towards medical treatment.

In asymptomatic patients, medical treatment is indicated in case of tumor growth, even in case of ventriculomegaly. Another potential indication is as neoadjuvant treatment in SEGAs infiltrating deep structures, aiming to shrink the tumor size and accordingly decrease the risk of surgical morbidity that is related to the size of the tumor in many series. Young age, particularly under 3 years, has been also associated to poor outcome of SEGA surgery and proposed as a factor favouring medical treatment [18].

Finally, mTOR inhibitors may have beneficial effect in enlarging SEGAs with increased seizure burden.

In fact, although the main purpose of the medical treatment is the reduction of tumor volume, randomized controlled trials have shown other positive effects. In fact, it may improve seizure frequency [34–36], relieve CSF obstruction [2, 37], improve other systemic TSC manifestation (i.e. reduction in size of cardiac rhabdomyomas) [38, 39] and overall improve the quality of life of these patients with no interference on children growth [3, 10, 34].

These data encourage the debate on the specific indications for mTOR inhibitors with or without surgical excision to obtain optimal outcomes for TSC patients with SEGA [37].

Concerning the effect on seizure burden, mTOR inhibitors do not appear to act like standard antiepileptic drugs (AEDs), which decrease neuronal activity by the modulation of ion channels or neurotransmitter receptors. The mTOR inhibitor pharmacodynamic could be related to the regulation of the expression of ion channels via effects on protein translation, which might subsequently reduce neuronal excitability (increase the expression of potassium channels and decrease the expression of glutamate receptors). Everolimus and rapamycin are metabolized primarily by cytochrome CYP3A4 and P-gp.

Side effects are more prone to occur during the first year of treatment and then this risk decreases with time. The most common adverse reactions (at least 30%) are aphthous ulcers, acneiform rash, diarrhoea, arthralgias, nausea, anorexia, mucositis and impaired wound healing. Common laboratory abnormalities include anaemia, leukopenia, thrombocytopenia, hypercholesterolemia, elevated serum creatinine, alkaline phosphatase and aspartate aminotransferase. As a consequence, severe acute infections or elevated blood levels of bilirubin constitute the main contraindications to this treatment.

Also, the inducers of these enzymes, such as many AEDs (e.g. carbamazepine, phenytoin, phenobarbital) may decrease rapamycin and everolimus concentration, whereas inhibitors may increase their concentration. Thus, coadministration of rapamycin and everolimus with CYP3A4 inducers could result in lower than expected serum levels and consequently a lower response to the treatment. This evidence may partly explain cases presenting poor response to the treatment [3].

Finally, discontinuation of mTOR inhibitors is typically associated with regrowth of tumors [21, 40]. Hence, doubts on the optimal drug duration and dosage are still present. The treatment might be continuous in time until the patients reach 30 years, if these patients experience stabilization of their lesions. For some patients without symptoms until 30 years old, lifelong drug treatment with mTOR inhibitors may be required.

Endoscopy

The prevalence of tumor growth inside the ventricular system has rendered SEGAs attractive for endoscopic management since the late 1990s. As for other kind of ventricular tumors, in the early era tumors growing into an enlarged lateral ventricle were favoured for endoscopic treatment, with size limits set at 2 cm. Larger lesions were documented to require operating times longer than the ones of microsurgery, hence not justifying the procedure. Even the use of a double port endoscopic removal that was advised for larger than 2 cm lesions by some authors [41, 42] was critically viewed because it

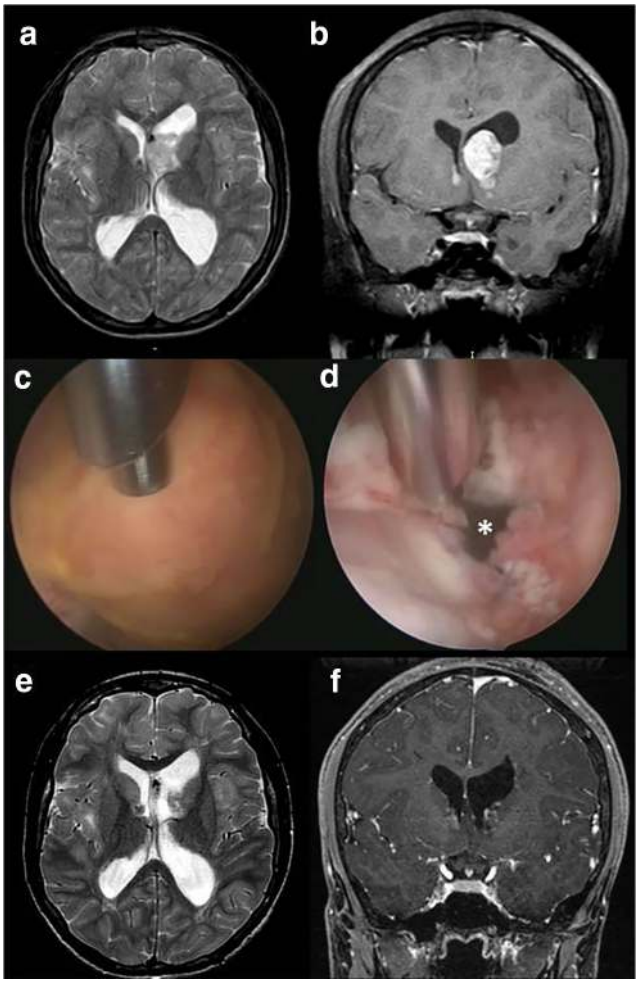

Fig. 1 16-year-old boy with left SEGA and progressive ventricular dilation (**a**, **b**). Tumor was resected by endoscopic approach with the aid of endoscopic ultrasonic aspirator (Sonoca®, Söring GmbH, Germany) (**c**), thus freeing the foramen of Monro (**d**, asterisk). Postoperative axial T2-weighted and coronal T1-weighted after contrast administration MR images confirming the total removal of the tumor (**e** and **f**, respectively)

rendered, in fact, endoscopic management more invasive than microsurgery [43].

Major technological advances have led to a more extensive use of endoscopy in the management of SEGAs as well as of other solid intraventricular tumors in children. These are represented by the development and rapid diffusion of magnetic neuronavigation in the early 2000s [44, 45], the application of new tools such as the endoscopic ultrasonic aspirator (Fig. 1), the contact laser coagulation and, more recently, the side cutting/aspirating devices [46–48]. As a result, size of the tumor has gained a lower relevance compared with the past. In fact, cases of endoscopically resected tumor as large as 3 cm (maximum diameter) have been successfully reported [17, 45]. A broad-based attachment of the tumor to the caudate nucleus, the presence of significant calcifications and vascularity, and the trajectory inside the ventricular system actually represent the main limits of the endoscopic management of these tumors [45, 46]. The trajectory is included among the main limits because most of the modern tools are designed and can be used with rigid endoscopes, thus warranting fixed trajectories. Having this in mind, an endoscopic approach is much less favourable if the trajectory of the endoscope can be tangential, rather than perpendicular to the main axis of tumor development [45].

Recently, various techniques combining microsurgery and endoscopy have been described. In this context, no significant difference has been reported in terms of invasiveness with respect to the surrounding brain structures for endoscopic-assisted microsurgery, compared with microsurgical tumor removal [49]. Extra-endoscopic minimally invasive

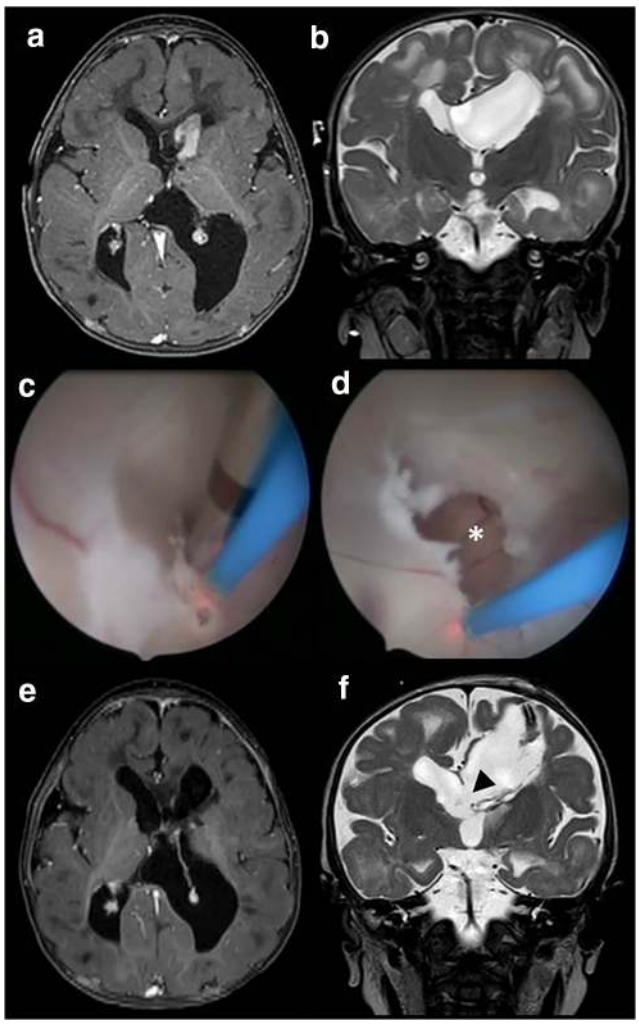

Fig. 2 1-year-old girl with progression of left residual SEGA (**a**) and trapped lateral ventricle (**b**). Tumor was resected endoscopically with the aid of NICO Myriad® (NICO Corporation, Indianapolis, IN) and thulium laser (RevoLix™, LISA laser products OHG, Germany) (**c**); septostomy was also performed (**d**, asterisk). Postoperative axial T1-weighted after contrast administration MR image confirming the total removal of the tumor (**e**) and coronal T2-weighted MR image documenting the patency of the septostomy (**f**, arrowhead)

neurosurgical procedures may represent an alternative and, in fact, have acquired increasing popularity. The difference with endoscope-assisted microsurgery is represented by the fact that in the extra-endoscopic procedures, only a keyhole or minimal craniotomy is needed. Surgery is performed with the use of microsurgical instruments under the vision of the endoscope, which is positioned much closer to the surgical field than any microscope and is able to enlighten it through smaller surgical corridors [50]. Engh et al. reported GTR or near total resection in 80% of the cases operated with an extra-endoscopic technique, surgical resection having been performed via an 11.5-mm transparent conduit (Neuroendoport) positioned with stereotactic guidance under endoscopic vision [51]. A drawback is represented by the reduced space of manoeuvre compared with microsurgical tumor resections, instruments actually being part of a traditional microsurgical armamentarium.

Neuronavigation is considered an essential tool by the majority of authors dealing with endoscopic removal of intraventricular tumors. This rule is confirmed in the case of SEGAs. It allows not only to consider endoscopy in cases with normal or small size ventricles but also to correctly plan the burr hole placement and the best trajectory according to the tumor extension inside the ventricular system [44, 45]. The general rule that is followed in most centres is to access lesions through the larger lateral ventricle, if the lateral ventricles are asymmetrically dilated. In the case of eccentric third ventricular lesions and symmetric enlargement of the lateral ventricles, an approach to the lateral ventricle contralateral to the tumor attachment might be considered in order to first devascularize the lesion [17, 45]. Reduction of vision as a consequence of tumor haemorrhage is however an expected occurrence. Whenever there is no clearing and stopping of the bleeding with rinsing and coagulation, the advice which is more and more agreed is to substitute CSF with air, a manoeuvre which allows to rapidly improve the possibility to visually detect the bleeding site [45].

Among the other advantages of the endoscopic management for SEGAs, there is the possibility to add septostomy to tumor removal. This gesture has to be considered in all cases, since it represents a safety measure for the possible occurrence of scarring at the level of the Monro foramen, and consequent unilateral hydrocephalus [17] (Fig. 2).

Laser interstitial thermal therapy

Further to earlier indications in paediatric neurosurgery, most in the field of epilepsy surgery and deep-seated tumors, laser interstitial thermal therapy (LITT) has been proposed as an alternative modality, also for the treatment of SEGAs.

Few cases have been reported so far. Tumor shrinkage up to 80% has been described in more than 80% of the cases, but the duration of the follow-up (6–12 months) is too short to draw definitive conclusions [52]. It should also be remembered that, as tumor edema occurs soon after laser heating of the tumor tissue, this methodology should be cautiously considered in case of an already partial obstruction of the Monro foramen, due to the risk of an acute hydrocephalus in the immediate postoperative period. Some authors have for this reason suggested to implant in selective cases a ventricular catheter at the time of surgery as a safety tool or to perform a septostomy under stereotactic guidance in case of an asymmetric ventricular dilation [53]. A further suggestion to limit postoperative edema is the use of lower powers (60% instead of 70% of 15 W) for longer periods (15 min instead of 6 min with 980 nm lasers), in order to distribute more extensively in time the energy to the tumor tissue [52, 53].

Conclusions

The results of the present review of the literature allow us to conclude that thanks to the reduction of the invasiveness of open surgical approaches and to the acquisition of new tools available for endoscopic tumor removal, surgical treatment of SEGAs stays with a renewed extension of interest in the paediatric neurosurgical community. Medical treatment has a definite role and should be proposed as an alternative to families of children with SEGAs, clearly explaining the possible need to interrupt the therapy in case of secondary effects of this treatment and the risk of tumor recurrence at the time of discontinuation. LITT represents a more recent option and preliminary results are promising, although no data exist on the long-term follow-up.

Compliance with ethical standards

Conflict of interest The authors declare that are no conflict of interest to disclose.

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