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REVIEW PAPER

Desmoplastic astrocytoma: new insights into its clinical profile, diagnosis, and treatment

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Abstract
Background Desmoplastic astrocytoma (DA) is a rare intracranial tumor which usually affects pediatric patients. The aim of this study is to describe the clinical features and management of DA based on a joint analysis of the cases reported in the scientific literature.
Material and methods A thorough review was carried out, gathering those pathologically proven DAs reported since the first description of this entity. Two new own cases were included in order to illustrate this review. Epidemiological, clinical, radiological, therapeutic, and follow-up data were analyzed with the software SPSS version 20.
Results A total of 52 DAs were recorded. Most cases occurred in the first 2 years of life, although older patients were also reported. Patients mainly presented symptoms and signs of elevated intracranial pressure. According to their radiological features, we were able to classify DAs in four main groups, with distinct differential diagnosis and prognosis. After treatment, 14.2 % of patients presented persistent neurological impairment and the mortality rate was close to 10 %.
Conclusion DAs can be diagnosed at any age from birth to adolescence. These neoplasms can show up a wider range of radiological morphologies than previously thought. Surgery represents the treatment of choice for DAs, although chemotherapy can also be useful in the setting of recurrence or progression of the disease. Those DAs lacking classic radiological features, especially type 4 tumors, were linked with a poorer clinical outcome.

Keywords Desmoplastic astrocytoma · Infantile neuroepithelial tumors · Infancy

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Background

Desmoplastic astrocytomas (DAs) are uncommon tumors which usually involve the superficial cerebral cortex and meninges of the supratentorial compartment in pediatric patients. These neoplasms were first described in 1982 by Taratuto et al. [33] and are currently considered as a grade I neoplasm by the World Health Organization (WHO). Microscopically, DAs consist of three distinct elements [15, 33]. The desmoplastic leptomeningeal component contains a mixture of fibroblast-like spindle-shaped cells and pleomorphic neoplastic neuroepithelial cells with eosinophilic cytoplasm, both arranged in fascicles or in a storiform pattern and embedded in a prominent reticulin network [15, 33]. The immature component consists of poorly differentiated neuroepithelial cells [15, 33]. Most of the tumor remains in the subarachnoid space respecting the pial layer, but tongues of neoplastic tissue extend into the leptomeninges, Virchow-Robin spaces, and the adjacent cortex (cortical component), producing a vigorous reactive astrocytosis [15, 33].

Given the dearth of large series in the scientific literature, the diagnostic and therapeutic management of DAs have not

been well established and are mainly based on the limited knowledge obtained from the study of case reports. In this revision, we present two new patients diagnosed of DA and include a thorough review of similar cases reported on since the first description of this entity to date.

Material and methods

A systematic review of the literature was carried out in the Pubmed database using the terms *desmoplastic* and *astrocytoma*. A total of 106 references were obtained, and only those papers reporting cases of pathologically verified DAs were selected. Additional cases were gathered from the study of their references lists. Data concerning the epidemiology, clinical and radiological features, pathological findings, therapy, and follow-up of the patients were collected. Two new cases were identified among the oncological records of our institution and were included in order to illustrate this review. Descriptive and analytic statistics were accomplished by using the SPSS software (version 20).

Results

Demography

A total of 52 cases were gathered (Table 1). Their age ($n = 52$) ranged from newborn to 18 years old (mean 25.4 months, median 7 months) (Fig. 1). Males were 56.3 % ($n = 48$). The most common clinical symptoms ($n = 49$) occurred as a result of elevated intracranial pressure (42.9 %). Of patients, 16.3 % presented focal symptoms, including hemiparesis (13 cases), cranial nerve deficit (2 cases), visual field deficit (6 cases), nystagmus (3 cases), and paraparesis (2 cases). Seizures were recorded in 6.1 % of cases. About a third of the patients presented a variable combination of the three main categories of symptoms enumerated above. Only one case of DA was diagnosed incidentally, after suffering a cranial traumatism, but a visual field deficit was subsequently revealed [30]. The onset of clinical symptoms was either acute (up to 1 day) (11.4 %), subacute (up to 1 month) (50 %), or chronic (36.4 %). In one case, symptoms were present at delivery [33]. Association of DA with a congenital syndrome occurred only in one patient [16].

Diagnosis

Radiological diagnosis ($n = 49$) was based on CT (40.8 %), MRI (32.7 %), or both (24.5 %). One case was diagnosed by employing echography and MRI (case 52). On the basis of their neuroradiological features, we were able to classify DAs in four main categories as follows. Type 1 DAs (67.3 %) are predominantly cystic tumors with a superficial, mural, contrast-enhancing solid component. The cyst is characteristically deep-seated, multiloculated, and bigger than the nodular component. Its content displays a signal similar to cerebrospinal fluid. Enhancement of the cyst wall is extraordinarily rare [3, 5]. Type 2 includes those solid DAs with a hypodense (hypointense on T1-weighted MRI) center and ring enhancement (5.8 %). Solid DAs with homogeneous enhancement were classified as type 3 (15.4 %). These tumors often contained small cystic areas. Type 4 groups together those cases displaying multiple lesions in the central nervous system at the moment of diagnosis (11.5 %).

Tumors presenting as a unique lesion (types 1 to 3) ($n = 46$) were mostly located in the supratentorial compartment (95 %), with a similar distribution between hemispheres. The size of these lesions ($n = 39$) ranged from 2.5 to 13 cm (mean 8.4, median 8.25), so three quarters of these unique, supratentorial DAs involved at least two cerebral lobes, especially the frontal and parietal areas. Exceptionally, suprasellar [38] and spinal [25] single DAs were also reported.

Single tumors typically presented a close relationship with a dural surface, mostly at the convexity (29 cases) but also at the parasagittal area (6 cases), the falco-tentorial junction (2 cases), the tentorium (2 cases), or the central middle cranial base (1 case). Duramater and arachnoid thickening with enhancement was present in 40.6 % of these tumors ($n = 32$). Vasogenic edema ($n = 32$) could only be identified in 13 cases and was usually from mild to moderate. Significant mass effect with brain shift ($n = 38$) was evident in 94.7 % of single tumors and was especially associated with type 1 DAs (28 cases).

Six patients presented multiple neoplastic lesions (type 4). Four of them displayed high-sized lesions in the suprasellar area [1, 6, 8, 31]. One patient developed bilateral supratentorial lesions [29], and in one case, a mesial temporal mass extending to the interpeduncular cistern was described [37]. Additional tumoral lesions were mainly identified in the posterior fossa (five cases) [1, 8, 29, 31, 37] and along the spinal axis (three cases) [1, 28, 31]. Malignant cells were evidenced by cytological analysis of cerebrospinal fluid in one case [31].

Radiological signs of active hydrocephalus were present in 15 cases. An obstructive mechanism caused by severe midline displacement [3, 10, 12, 19, 20, 23, 26, 32, 33, 35, 38] or a large suprasellar mass [8] was implied in 12 of them. Communicant hydrocephalus was diagnosed in one patient [29], and a mixed mechanism was involved in two cases [6, 31]. Only four patients required a ventricular-peritoneal shunt.

Calcifications were described in five tumors [14, 21, 24, 29, 34, 37]. Involvement of the cranium was rarely present and consisted in cranial bossing [7, 10, 20, 32–34] or erosion [23, 28, 33].

Angiography was performed in six cases; DAs were mainly described as avascular masses [13, 18, 24, 33], although tumoral blush with vascularization from pial feeders was also described in two cases [5, 20].

Table 1 Cases of DA reported on in the literature

Case	Reference	Sex/age	Symptoms	Location	Morphology	Size (cm)	Treatment	Malignancy	Recidive/ progression	Follow-up	Outcome
1	Taratuto et al. [33]	F/6m	HICP	FP/L	Type 1	11	STR + Rt	Absent	No	5.5y	ND
2		F/6m	HICP	F/R	Type 1	13	STR + Rt	Absent	No	3.5y	ND
3		M/6m	HICP	FP/R	Type 1	10	STR + Rt + Cht	Absent	No	3.5y	ND
4		M/1.5m	HICP + F	FP/R	Type 1	12	PR	Absent	No		Death
5		M/7m	HICP	FP/L	Type 1	12	STR + VPS + Rt	Absent	No	1.5y	ND
6		F/9m	HICP	FP/L	Type 1	10	CP + GTR	Absent	No	11m	ND
7	VandenBerg et al. [39]	F/2m	NA	PTO/L	Type 1	NA	GTR + Rt	Absent	No	3.5y	ND
8		M/3m	NA	FP/L	Type 1	NA	GTR	Absent	No	1.5y	ND
9	de Chadarévian et al. [9]	F/6.5m	HICP + F + S	FP/L	Type 1	10	GTR	Absent	No	14m	ND
10	Louis et al. [19]	F/5.5m	HICP	PT/R	Type 1	7	GTR	Absent	No	1.5y	ND
11		M/14m	S	P/R	Type 2	3	GTR	Absent	No	1y	ND
12	Paulus et al. [23]	F/6m	HICP	PTO/L	Type 1	8.5	GTR + Cht	Absent	No	3y	ND
13		M/6m	F	PT/L	Type 1	7	GTR	Absent	No	12.5y	ND
14	Rushing et al. [28]	M/5m	HICP	PT/L	Type 1	8	GTR + Cht	Absent	No	12y	ND
15		M/10m	S	F/R	Type 1	NA	GTR	Absent	No	4.2y	ND
16		M/9m	HICP + S	PT/R	Type 3	NA	STR + Cht	Absent	No	4y	ND
17	Aydin et al [4]	F/7.5m	HICP	FP/R	Type 1	5 cm	CP + GTR	Absent	No	1y	ND
18	Chacko et al. [7]	F/7y	F + S	PT/L	Type 1	NA	PR	Absent	No	2y	ND
19	Serra et al. [30]	F/6m	I + F	PO/L	Type 1	5 cm	STR	Absent	No	NA	NA
20	Al-Sarraj et al. [3]	F/8m	HICP	P/L	Type 1	8 cm	STR + Cht	Present	No	3y	ND
21	Setty et al. [31]	M/4m	HICP + F	M	Type 4		B + Cht	Absent	No	3.1y	SND
22	Vajtai et al. [38]	M/2y	HICP	SS	Type 3	4 cm	PR	Absent	NA	NA	NA
23	Park et al. [22]	M/9m	F	FPT/R	Type 1	9 cm	PR	Present	2y/GTR	4y	ND
24	Olas et al. [21]	M/7m	HICP + F	FT/L	Type 1	11 cm	GTR + VPS	Absent	NA	NA	NA
25	Kurose et al. [18]	M/9y	HICP + S	T/R	Type 3	6 cm	GTR	Absent	No	6m	SND
26	Malucci et al. [20]	NA/3m	HICP + F	NA	Type 1	9.5 cm	GTR	Absent	No	4.2y	ND
27		M/5m	HICP	FPT/L	Type 3	11 cm	B + Cht	Absent	1y/GTR	1y	Death
28		NA/10m	HICP + F	NA	Type 1	10 cm	GTR	Absent	No	4.2y	ND
29		NA/3.5y	F	NA	Type 1	13 cm	GTR	Absent	No	4.2y	ND
30	Kandalkar et al. [11]	NA/6m	HICP	FP/NA	Type 1	7 cm	CP + GTR	Absent	No	3m	ND
31	Kopniczky et al. [16]	F/10y	S + NSS	F/R	Type 3	2.5 cm	GTR + Rt	Present	No	6m	ND
32	Kros et al. [17]	M/10m	NA	FP/L	Type 1	8 cm	GTR	Absent	No	3y	ND
33	Bock et al. [6]	M/4m	HICP + F	M	Type 4		B + Cht	Absent	Yes/Cht	5m	Death
34	Rodriquez Morales et al. [26]	M/4m	HICP	FPT/R	Type 1	13 cm	GTR	Absent	No	NA	ND
35	Sugiyama et al. [32]	F/3m	HICP	FPT/L	Type 1	12 cm	CP + GTR	Absent	No	4.2y	ND
36	Kato et al. [13]	M/9y	F	FP/L	Type 2	4 cm	GTR	Absent	No	1y	ND
37	Trehan et al. [34]	F/2.5m	HICP	FPT/NA	Type 1	NA	GTR	Absent	No	2y	ND
38		F/4y	HICP + F	FPO/NA	Type 3	NA	PR + Rt + Cht	Present	Yes	13m	Death
39	Darwish et al. [8]	M/4m	HICP + F	M	Type 4		PR + VPS	Absent	Yes	2m	Death
40	Ulu et al. [36]	F/4y	F	PTO/R	Type 3	8 cm	GTR	Absent	No	11m	ND
41	Beppu et al. [5]	M/12m	HICP	F/L	Type 1	8 cm	CP + GTR	Absent	No	NA	ND
42	Tsuji et al. [35]	M/3m	HICP + F	PO/L	Type 1	8 cm	PR	Present	Involution	24m	ND
43	Santhosh et al. [29]	M/11y	HICP + F	M	Type 4		CP + STR + VPS	Absent	No	NA	SND

Table 1 (continued)

Case	Reference	Sex/age	Symptoms	Location	Morphology	Size (cm)	Treatment	Malignancy	Recidive/ progression	Follow-up	Outcome
44	Uro-coste et al. [37]	M/5y	F + S	M	Type 4		GTR (P-fossa) + Cht	Absent	No	1y	SND
45	Gu et al. [10]	M/1m	HICP	PO/R	Type 1	11 cm	CP + GTR	Absent	No	1.5y	ND
46	Phi et al. [24]	F/22m	F	FPT/R	Type 1	8 cm	GTR	Absent	8y/GTR + Rt + Cht	9y	MND
47	Rasalkar et al. [25]	F/18y	F	S	Type 3	3 cm	STR	Absent	No	4y	SND
48	Al-Kharazi [2]	F/1.5m	HICP	FT/R	Type 1	12 cm	GTR + VPS	Present	3m/Cht	9m	SND
49	Karabagli et al. [12]	M/6y	HICP	T/R	Type 2	4.5 cm	TV + B/(4m)GTR	Absent	9m/GTR + Rt + Cht	16m	ND
50	Abuharbid et al. [1]	F/11m	F	M	Type 4		GTR (P-fossa)	Absent	Enlargement/ regression	16m	ND
51	Our cases	M/5m	HICP	FP/L	Type 1	9 cm	STR	Absent	No	48m	ND
52		F/9m	HICP + F	FP/R	Type 1	10 cm	GTR	Absent	No	54m	ND

Size: major diameter in centimeters. Malignancy: microscopic signs of aggressiveness

NA not available; Sex: *F* female, *M* male; Age: *y* years, *m* months; Symptoms: *HICP* high intracranial pressure, *F* focal symptoms, *S* seizures; Location: *F* frontal, *T* temporal, *P* parietal, *O* occipital, *L* left hemisphere, *R* right hemisphere, *M* multiple lesions; Treatment: *GTR* gross total resection, *STR* subtotal resection, *PR* partial resection, *B* biopsy, *Cht* chemotherapy, *Rt* radiotherapy, *VPS* ventricular-peritoneal shunt, *TV* third ventriculostomy, *P-fossa* posterior fossa; Outcome: *ND* normal development, *MND* mild neurological deficit, *SND* severe neurological deficit

Surgical treatment

Surgical features of DAs were thoroughly described in 42 cases. Most common findings among type 1 DAs (26 cases) included a solid, superficial, firm rubbery component that could be grayish, ivory-colored, or purplish. It was typically avascular and presented tight adhesions to the duramater, occasionally eroding the bone [28], and finger-like projections that seemed to blend with the adjacent cortex. In one case, this solid component displayed a deeper location and was attached to an intracystic septum [24]. The deep-seated cystic component always contained clear or xanthocromic fluid, but in one DA, the presence of dark fluid was attributed to hemorrhage [3].

Surgical findings in type 2 ($n = 2$) and 3 ($n = 6$) tumors resembled those of the solid component of type 1 DAs, with one report describing signs of old and recent intratumoral hemorrhage [13].

Removal degree of single lesions (types 1–3) was described as total in 65.2 %, subtotal in 19.6 %, and partial in 13 % of cases. Only one tumor was biopsied [20]. Among the causes precluding a complete resection, the following were listed: tight adhesion to a major venous sinus (four cases), absence of plane of dissection with the surrounding brain (four cases), massive blood loss (two cases), eloquent parenchyma involvement (one case), and avoidance of brain collapse putting bridging veins under excessive tension (one case) [35].

Multiple lesions (type 4 DAs) were managed by biopsy (two cases) or complete resection of the most accessible or symptomatic mass (two cases). Setty et al. [31] performed a biopsy of a suprasellar lesion and observed opacification and thickening of the leptomeninges of the basal cisterns, which were attributed to leptomeningeal spread of the tumor. Darwish et al. [8] attempted to remove a giant suprasellar mass, but it was precluded by encasement of the internal carotid artery. Finally, Santosh et al. [29] performed a palliative procedure with resection of a right frontal mass and punction of a contralateral cystic lesion.

Puncture of the cyst was also carried out in six single DAs. This procedure was performed through the anterior fontanelle or a burr hole to alleviate acute intracranial hypertension [10, 11] or during elective surgery in order to relax the underlying brain [4, 5, 32].

Eight patients developed surgical complications ($n = 52$), which included respiratory failure [33], massive blood loss [20, 34], arterial infarction [2], subdural higroma (case 52) [2], worsening of neurological deficit [37], and hydrocephalus [2].

Pathology

All tumors fulfilled the WHO criteria described above for the diagnosis of DA. Nevertheless, six tumors presented aggressive focal signs such as an increased mitotic rate, necrosis, or both (Table 1). A detailed microscopical analysis of the cyst wall in

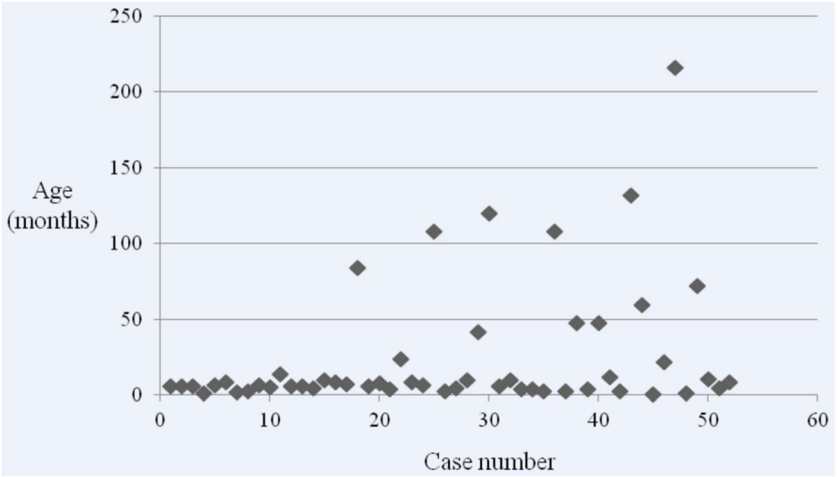

Fig. 1 Graph illustrating dispersion of the variable *age*, measured in months, among the 52 cases of DA

type 1 DAs showed cerebral atrophy with normal layered architecture, with intense gliosis in the outer layers and interstitial edema in the innermost part of the cyst wall [11]. There were no records of tumor invasion of the cyst wall, even in those cases which displayed contrast enhancement [5].

Adjuvant treatment

Fourteen patients received adjuvant treatment including chemotherapy (Cht), radiotherapy (Rt), or both (Table 1). Cht drug regimens were variable and included combinations of vincristine, carboplatin, methotrexate, and cisplatin [3]; carboplatin, ifosfamide, etoposide, and vincristine [31]; vincristine, cyclophosphamide, methotrexate, carboplatin, and etoposide [6]; and vincristine and carboplatin [37]. An aggressive Cht regimen was the cause of severe neurological impairment in one patient [31].

Details of Rt were not provided in most cases. Taratuto et al. [33] treated their patients with conventional Rt including 3500 to 5000 rad, and 30 cycles of 1.8 Gy were applied by Kopniczky et al. [16] to the tumoral bed in their case. Rt and Cht were also employed in the setting of progression or recurrence of the disease as described below.

Outcome

Follow-up was reported in 45 cases and ranged from 2 to 150 months (mean 34.6). Local recurrence of the tumor after gross total resection was detected in three patients [2, 12, 24], and progression of the disease was reported in five cases [6, 8, 20, 22, 34]. Progression and recurrence were treated as described in Table 1. The case published by Abuharbid et al. [1] experienced progression of some lesions, while others spontaneously regressed. Tumoral regression was also reported in a case of type 1 DA treated by subtotal resection [35].

The final clinical status of the patients was described in 49 cases. Most of them (75.5 %) progressed normally, but 14.2 % presented a neurological deficit, which was considered as disabling in six patients at last follow-up examination. Five patients (10.2 %) died as a consequence of surgical complications [20, 33] or progression of the disease [6, 8, 34]. Mortality rates affected especially those patients diagnosed of type 4 (33.3 %) and type 3 (28.6 %) DAs. An analysis of the outcome, comparing those patients who followed a good clinical course (normal development or mild neurological deficit) with those who experienced a poorer one (severe neurological deficit or death), demonstrated a statistical significant difference between type 1 and the remaining DA types (Fisher's exact test, $p = 0.001$). A poor prognosis was also associated with the presence of recurrence or progression of the neoplasm ($p = 0.009$), but there was no relationship with the diagnosis of microscopic aggressive signs ($p = 0.605$).

Illustrative cases

Case 1

A 5-month-old male presented facial asymmetry and progressive pathological enlargement of the occipitofrontal circumference. Brain MRI demonstrated a left fronto-parietal mass (Fig. 2a–c). A subtotal resection of the tumor was carried out (Fig. 2d–e), except for a small portion of 1 cm tightly adherent to the superior sagital sinus. The fluid drained from the cystic component was acellular, and the pathological findings were consistent with the diagnosis of DA. The patient remains asymptomatic 4 years after the surgical procedure, and last follow-up MRI showed stability of the small tumoral remnant (Fig. 2f).

Case 2

A 9-month-old female was admitted to our department with acute refractory vomiting. She had a history of progressive

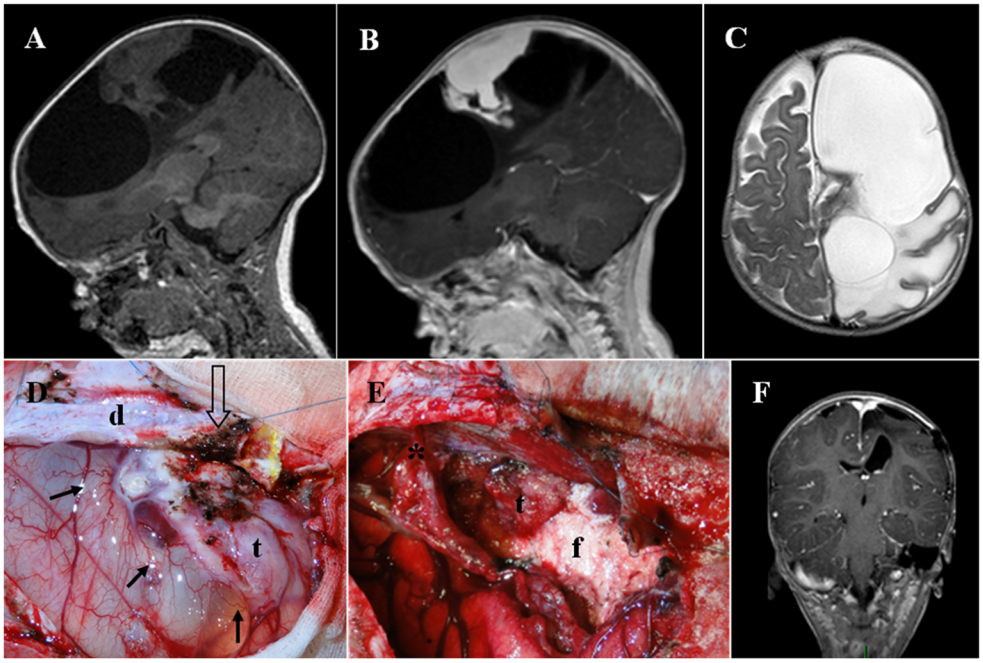

Fig. 2 Preoperative brain MRI corresponding to case 1 (**a**–**c**). **a** T1WI, sagittal slice showing a 9 × 6 × 5.5 cm solid cystic tumor in the left frontal and parietal lobes. The solid portion displays an isointense signal, while that corresponding to the cyst contents is hypointense. **b** Strong, homogeneous enhancement of the solid component after administration of gadolinium. **c** T2-weighted MRI, axial slice showing the isointense signal of the solid component and hyperintense signal in the cyst. The tumor associates with moderate vasogenic edema. **d** Intraoperative findings consisting in tight adherence of the solid component of the tumor (*t*) to the convexity duramater (*d*), that was dissected with bipolar coagulation (*transparent arrow*). This solid component seemed to blend with the adjacent brain (*small arrows*) and becomes translucent, insinuating the underlying cyst. A plane of consistence was used for dissection. **e** Final stages of the surgical procedure, showing the falx cerebri (*f*) and a portion of the tumor tightly adhered to the lateral wall of the sagittal sinus. Observe the collapse of the brain, which puts the bridging veins under tension (asterisk). **f** Postoperative T1-weighted, gadolinium-enhanced MRI, coronal slice showing a small remnant of the tumor in close relationship with the sagittal sinus

weakness of the left limbs and cranial enlargement during the last 2 months. Transfontanelar ultrasonography showed a giant multiloculated cystic lesion. Brain MRI demonstrated a mixed solid cystic lesion of 10 × 7 × 7 cm located in the right frontoparietal area. The solid region showed homogeneous enhancement after gadolinium administration. The tumor was completely removed through a right frontoparietal approach. She progressively recovered a normal motor function but presented a right frontal hygroma which resolved spontaneously over several months. Microscopical analysis of the lesion showed the typical features of DA (Fig. 3). Last follow-up MRI, performed 54 months after surgical treatment, showed no signs of recurrence of the tumor.

Discussion

DAs must be considered rare neoplasms, with only 52 cases described to date. These tumors represented 1.25 % of all intracranial neoplasms of infancy and childhood in the series of Taratuto et al. [33], which included 483 patients over a 12-year period. In our experience, DAs comprised 2.9 % of brain tumors diagnosed in pediatric patients.

Most DAs were diagnosed in children aged less than 2 years old (Fig. 1), as were our own cases described above, suggesting a congenital development of the neoplasm. The large size of the tumors at diagnosis and the high frequency of acute and subacute clinical symptoms at presentation could traduce a relatively high rate of tumoral enlargement. However, DAs have also been described in older individuals, including the period of adolescence. Noteworthy, none of those patients diagnosed after the first 2 years of life was diagnosed of a type 1 DA. Some of this older patients presented neurological symptoms early after birth, but the cause was not investigated or was misdiagnosed [7, 18, 20], which led to severe neurological deficits as a consequence of progression of the disease [18]. Nevertheless, most of these older patients did not present previous medical records, suggesting that DAs can also develop during childhood [13, 16, 34, 36, 37] or adolescence [25].

The most common clinical symptoms in children aged less than 2 years old consisted of elevated intracranial pressure, including increased occipitofrontal circumference, feeding problems, bulging fontanelles, “sunset” eyes, vomiting, and impaired consciousness in severe cases. Older patients tended to present seizures and focal symptoms. DAs were not systematically associated with any congenital syndrome [16].

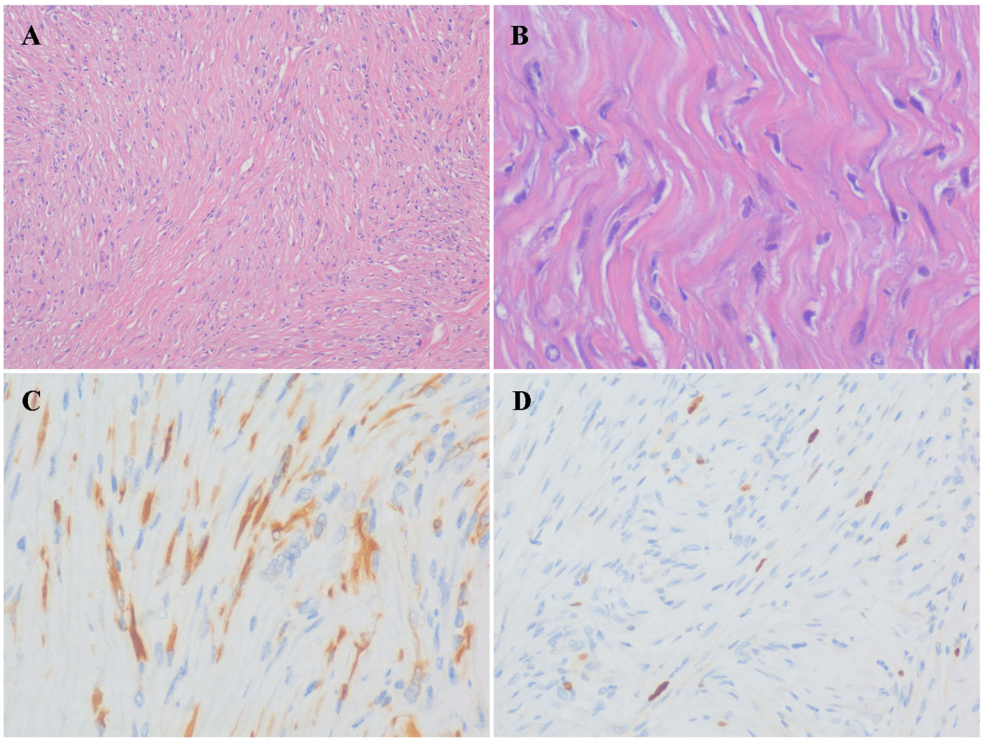

Fig. 3 Microscopic pathological findings corresponding to case 2. **a**–**b** H-E x. Microscopically, the lesion consisted in astrocyte proliferation with intense desmoplasia, fascicular pattern of collagen, and reticulin fibers, with no evidence of necrosis, mitosis, or ganglion cells (**a** HE ×25 and **b** HE ×100). Tumoral cells were positive for GFAP immunostaining (**c**) (×100). Low positivity rate for Ki-67 (1 %) (**d**)

The term DA seems to encompass a more heterogeneous group of neoplasms than thought before. On the basis of their radiological appearance, we were able to classify these tumors in four main groups. Single lesions comprise types 1 to 3. Type 1, which should also be named as *classic* or *typical* DA, is characterized by the morphology described by Taratuto et al. [33] in their pioneering publication. The radiological differential diagnosis includes dysembryoplastic neuroepithelial tumor, pleomorphic xanthoastrocytoma, supratentorial ependymoma, ganglioglioma, and teratoma. The radiological differential diagnosis becomes more difficult in the absence of typical signs, so that type 2 tumors can be misdiagnosed as other more common ring-enhancing lesions. Type 3 DAs must be radiologically distinguished from other solid, contrast-enhancing lesions such as meningiomas and gliofibromas.

The treatment of choice of single DAs is complete tumor resection. But, these tumors often represent a surgical challenge as a consequence of their large size at diagnosis and their macroscopic morphology, which shares characteristics of both extra- and intra-axial tumors. The presence of tight attachments to extra-cerebral structures represents a special surgical issue to be addressed. Complete removal of the tumor becomes especially hazardous in those tumors intimately adhered to bridging veins, a dural sinus (Fig. 2d–e) or, more rarely, to major vessels and cranial nerves from the cranial base [2, 20, 34, 37]. As a matter of fact, the only fatal case reported among type 1 DAs was the consequence of a hypovolemic shock, which also occurred in one patient diagnosed of a type 3 neoplasm [20, 33]. Leaving a small remnant of the tumor adhered to these structures should be considered a valid strategy, given the generally benign biological behavior of these neoplasms.

Difficulties may also arise in those DAs located near eloquent cortex, as the tumoral mass presents extensions within the surrounding brain tissue (Fig. 2d). Nevertheless, a plane of consistence between the tumor and brain parenchyma, which coincides with the microscopic margin of the neoplasm, can usually be found and followed during dissection [32].

The brain tends to collapse after resection of these generally voluminous masses, putting the bridging veins under excessive tension and predisposing to the development of subdural effusions [10, 35]. These postoperative subdural hygromas must not be treated in the absence of clinical symptoms, as they tend to disappear over time, as occurred in one of our patients [10].

The cyst wall in type 1 DAs does not represent a true neoplastic component, so it should not be included in the resection plan [10, 11]. Moreover, the presence of a cyst is a clear advantage in the management of younger patients, allowing an initial diagnostic approach with transfontanellar ultrasound. This technique can guide a percutaneous or fontanellar puncture of the cyst, which becomes particularly useful in the setting of acute increased intracranial pressure [10, 11, 33]. This procedure can be repeated as needed to stabilize the patient during the diagnostic checkup [10]. During elective surgery, the cyst can also be evacuated before opening the duramater in order to avoid extensive brain herniation [4, 5, 32].

Needle biopsy should be avoided in those cases in which a radiological diagnosis of single DA has been performed. However, if biopsy is peremptory, it should be assured that a representative sample of the lesion is obtained. The results must also be interpreted with caution, as the mitotic activity is increased in the immature neoplastic component when compared to the desmoplastic one [20, 33], and a higher grade neoplasm may erroneously be diagnosed [20, 32].

Given their benign biological behavior, adjuvant therapy should not be systematically applied in single DAs. Even subtotal resections have been linked with a good prognosis, and spontaneous involution of tumoral remnants has also been reported [1, 35]. That said, all patients should be followed closely for early detection in case that local recurrence or progression of the tumor occur. These must be considered rare events, with only six cases described to date [2, 12, 20, 22, 24, 34], so we were not able to find an association with any variable, including the radiological type of single DA, the presence of microscopic aggressive features, and the degree of surgical removal of the neoplasm. In this context, most authors performed a second surgical procedure aimed at complete resection or cytoreduction, followed by chemotherapy and radiotherapy. Progression of the disease finally caused the death of one patient diagnosed of a type 3 DA [34].

Type 4 DAs deserve special consideration [27]. Most patients presented a large-sized solid tumor closely related to the basal cisterns and additional tumoral lesions along the neuraxis, suggesting a leptomeningeal dissemination of the disease [1, 6, 8, 31, 37]. This mechanism of spread was confirmed in one patient by cytological analysis of CSF [31] and was radiologically suspected in an additional case [6]. As an exception, the patient described by Santosh et al. developed multiple solid cystic lesions in the supratentorial compartment along several months, which could be attributed to metachronous disease. However, the presence of a reabsortive HCP in their patient can be interpreted as an indirect sign of leptomeningeal involvement [29].

Surgical management of type 4 DAs becomes restricted to biopsy or removal of an accessible and/or symptomatic lesion. Surgery was followed by chemotherapy in three cases [6, 31, 37], and control of the disease was achieved in two of them [31, 37]. All those patients who were not treated with chemotherapy experienced progression of the disease [1, 8], which finally caused one fatality [8]. Despite the obvious limitations of this series, it could be suggested that chemotherapy could play an important role in the management of multiple DAs, although this must be the object of future investigations [27].

Conclusions

1. DAs can be diagnosed in a wider range of age and appear with more variable radiological features than previously thought.
2. Our classification of DAs in four subgroups facilitates the radiological differential diagnosis and associates a prognostic value.
3. Gross total surgical resection is the treatment of choice of single DAs (types 1–3). This aim can be hampered by the specific macroscopic morphological features and location of the tumor.
4. Multiple lesions in DA type 4 seem to develop as a consequence of leptomeningeal dissemination. This type associates with a worse prognosis and subsequently requires a more aggressive therapeutic strategy.
5. Tumor recurrence must be considered a rare, unpredictable phenomenon, so close follow-up should be recommended in all patients. Recurrence should be treated by surgery and individualizing the decision of instauration of adjuvant treatment.

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Compliance with ethical standards

Conflict of interest The authors declare no conflicts of interests.

References

1. Abuharbid G, Esmaeilzadeh M, Hartmann C, Hermann EJ, Krauss JK (2015) Desmoplastic infantile astrocytoma with multiple intracranial and intraspinal localizations at presentation. Childs Nerv Syst 31:959–964
2. Al-Kharazi K, Gillis C, Steinbok P, Dunham C (2013) Malignant desmoplastic infantile astrocytoma? A case report and review of the literature. Clin Neuropathol 32:100–106
3. Al-Sarraj ST, Bridges LR (1996) Desmoplastic cerebral glioblastoma of infancy. Br J Neurosurg 10:215–219
4. Aydin F, Ghatak NR, Salvant J, Muizelaar P (1993) Desmoplastic cerebral astrocytoma of infancy. A case report with immunohistochemical, ultrastructural and proliferation studies. Acta Neuropathol 86:666–670
5. Beppu T, Sato Y, Uesugi N, Kuzu Y, Ogasawara K, Ogawa A (2008) Desmoplastic infantile astrocytoma and characteristics of the accompanying cyst. Case report. J Neurosurg Pediatr 1:148–151
6. Bock D, Rümmele P, Friedrich M, Wolff JE (2002) Multifocal desmoplastic astrocytoma, frontal lobe dysplasia, and simian crease. J Pediatr 141:445
7. Chacko G, Chandi SM, Chandy MJ (1995) Desmoplastic low grade astrocytoma a case report and review of literature. Clin Neurol Neurosurg 97:32–35
8. Darwish B, Arbuckle S, Kellie S, Besser M, Chaseling R (2007) Desmoplastic infantile ganglioglioma/astrocytoma with cerebrospinal metastasis. J Clin Neurosci 14:498–501
9. de Chadarévian JP, Pattisapu JV, Faerber EN (1990) Desmoplastic cerebral astrocytoma of infancy. Light microscopy, immunocytochemistry, and ultrastructure. Cancer 66:173–179

10. Gu S, Bao N, Yin MZ (2010) Combined fontanelle puncture and surgical operation in treatment of desmoplastic infantile astrocytoma: case report and a review of the literature. J Child Neurol 25:216–221
11. Kandalkar B, Shah V, Shet T (2001) Desmoplastic astrocytoma of infancy—a case report. Indian J Pathol Microbiol 44:329–332
12. Karabagli P, Karabagli H, Kose D, Kocak N, Etus V, Koksal Y (2014) Desmoplastic non-infantile astrocytic tumor with BRAF V600E mutation. Brain Tumor Pathol 31:282–288
13. Kato M, Yano H, Okumura A, Shinoda J, Sakai N, Shimokawa K (2004) A non-infantile case of desmoplastic infantile astrocytoma. Childs Nerv Syst 20:499–501
14. Kim JH, Kim IO, Kim WS, Kim KH, Park CM, Yeon KM (2003) MR findings of desmoplastic cerebral astrocytoma of infancy. Acta Radiol 44:688–690
15. Kleihues P, Burger PC, Scheithauer BW (1993) The new WHO classification of brain tumours. Brain Pathol 3:255–268
16. Kopniczky R, Kóbor J, Maráz A, Vajtai I (2001) Desmoplastic neuroepithelial tumor of infancy in the nevus sebaceus syndrome. Pathol Res Pract 197:279–284
17. Kros JM, Delwel EJ, de Jong TH, Tanghe HL, van Run PR, Vissers K, Alers JC (2002) Desmoplastic infantile astrocytoma and ganglioglioma: a search for genomic characteristics. Acta Neuropathol 104:144–148
18. Kurose A, Beppu T, Miura Y, Suzuki M, Ogawa A, Arai H, Kubo Y, Sugawara A, Sawai T (2000) Desmoplastic cerebral astrocytoma of infancy intermingling with atypical glial cells. Pathol Int 50:744–749
19. Louis DN, von Deimling A, Dickersin GR, Dooling EC, Seizinger BR (1992) Desmoplastic cerebral astrocytomas of infancy: a histopathologic, immunohistochemical, ultrastructural, and molecular genetic study. Hum Pathol 23:1402–1409
20. Mallucci C, Lellouch-Tubiana A, Salazar C, Cinalli G, Renier D, Sainte-Rose C, Pierre-Kahn A, Zerah M (2000) The management of desmoplastic neuroepithelial tumours in childhood. Childs Nerv Syst 16:8–14
21. Olas E, Kordek R, Biernat W, Liberski PP, Zakrzewski K, Alwasiak J, Polis L (1998) Desmoplastic cerebral astrocytoma of infancy: a case report. Folia Neuropathol 36:45–51
22. Park K, Yoo J, Cho H, Cho W, Park S (1998) Desmoplastic cerebral astrocytoma of infancy: a case report. J Korean Med Sci 13:440–444
23. Paulus W, Schlote W, Perentes E, Jacobi G, Warmuth-Metz M, Roggendorf W (1992) Desmoplastic supratentorial neuroepithelial tumors of infancy. Histopathology 21:43–49
24. Phi JH, Koh EJ, Kim SK, Park SH, Cho BK, Wang KC (2011) Desmoplastic infantile astrocytoma: recurrence with malignant transformation into glioblastoma: a case report. Childs Nerv Syst 27:2177–2181
25. Rasalkar DD, Paunipagar BK, Ng A (2012) Primary spinal cord desmoplastic astrocytoma in an adolescent: a rare tumour at rare site and rare age. Hong Kong Med J 18:253–255
26. Rodriguez-Morales EL, Correa Rivas MS, Colon CE (2002) Desmoplastic astrocytoma of infancy: a case report with histopathologic and immunohistochemistry profile. P R Health Sci J 21:129–132
27. Rojas-Medina LM, Moro RC (2015) Multiple desmoplastic astrocytoma: a benign neoplasm? Childs Nerv Syst 31:2007–2008
28. Rushing EJ, Rorke LB, Sutton L (1993) Problems in the nosology of desmoplastic tumors of childhood. Pediatr Neurosurg 19:57–62
29. Santhosh K, Kesavadas C, Radhakrishnan VV, Abraham M, Gupta AK (2008) Multifocal desmoplastic noninfantile astrocytoma. J Neuroradiol 35:286–291
30. Serra A, Strain J, Ruyle S (1996) Desmoplastic cerebral astrocytoma of infancy: report and review of the imaging characteristics. AJR Am J Roentgenol 166:1459–1461
31. Setty SN, Miller DC, Camras L, Charbel F, Schmidt ML (1997) Desmoplastic infantile astrocytoma with metastases at presentation. Mod Pathol 10:945–951
32. Sugiyama K, Arita K, Shima T, Nakaoka M, Matsuoka T, Taniguchi E, Okamura T, Yamasaki H, Kajiwara Y, Kurisu K (2002) Good clinical course in infants with desmoplastic cerebral neuroepithelial tumor treated by surgery alone. J Neurooncol 59:63–69
33. Taratuto AL, Monges J, Lylyk P, Leiguarda R (1984) Superficial cerebral astrocytoma attached to dura. Report of six cases in infants. Cancer 54:2505–2512
34. Trehan G, Bruge H, Vinchon M, Khalil C, Ruchoux MM, Dhellemmes P, Ares GS (2004) MR imaging in the diagnosis of desmoplastic infantile tumor: retrospective study of six cases. AJNR Am J Neuroradiol 25:1028–1033
35. Tsuji K, Nakasu S, Tsuji A, Fukami T, Nozaki K (2008) Postoperative regression of desmoplastic infantile astrocytoma. No Shinkei Geka 36:1035–1039
36. Ulu MO, Tanriöver N, Biçeroğlu H, Oz B, Canbaz B (2008) A case report: a noninfantile desmoplastic astrocytoma. Turk Neurosurg 18:42–46
37. Uro-Coste E, Ssi-Yan-Kai G, Guilbeau-Frugier C, Boetto S, Bertozzi AI, Sevely A, Lolmede K, Delisle MB (2010) Desmoplastic infantile astrocytoma with benign histological phenotype and multiple intracranial localizations at presentation. J Neurooncol 98:143–149
38. Vajtai I (1997) Desmoplastic cerebral astrocytoma in intraventricular location: simplifying histogenesis by broadening the spectrum of desmoplastic neuroepithelial tumors of infancy? AJR Am J Roentgenol 168:1385
39. VandenBerg SR, May EE, Rubinstein LJ, Herman MM, Perentes E, Vinores SA, Collins VP, Park TS (1987) Desmoplastic supratentorial neuroepithelial tumors of infancy with divergent differentiation potential ("desmoplastic infantile gangliogliomas"). Report on 11 cases of a distinctive embryonal tumor with favorable prognosis. J Neurosurg 66:58–71