Absence of expression of *SMARCB1/INI1* in malignant rhabdoid tumors of the central nervous system, kidneys and soft tissue: an immunohistochemical study with implications for diagnosis

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Malignant rhabdoid tumors are high-grade neoplasms of the central nervous system (CNS), kidneys and soft tissue that usually occur in children. The histologic diagnosis of malignant rhabdoid tumor depends on identification of characteristic rhabdoid cells—large cells with eccentrically located nuclei and abundant, eosinophilic cytoplasm—and immunohistochemistry with antibodies to vimentin, keratin and epithelial membrane antigen. In most malignant rhabdoid tumors, the *SMARCB1/INI1* gene, located in chromosome band 22q11.2, is inactivated by deletions and/or mutations, so genetic diagnosis is often possible. However, tissue may not be available for genetic analysis or studies not confirmatory. We assessed *SMARCB1/INI1* expression in 17 rhabdoid tumors and 57 other tumors of the CNS, kidney or soft tissue using immunohistochemistry. In total, 12 brain, three renal and two soft tissue rhabdoid tumors were examined along with four glioblastomas, four pilocytic astrocytomas, four oligodendrogliomas, two ependymomas, two choroid plexus papillomas, five pituitary adenomas, four germinomas, four renal carcinomas with Xp11.2 translocations, two clear cell sarcomas, two Wilms' tumors, one renal medullary carcinoma, two desmoplastic small round cell tumors, two alveolar rhabdomyosarcomas, two embryonal rhabdomyosarcomas, one low-grade chondrosarcoma, two extraskeletal myxoid chondrosarcomas, one mesenchymal chondrosarcoma, four malignant peripheral nerve sheath tumors, five metastatic carcinomas and four epithelioid sarcomas, two primary and two metastatic. The neoplastic cells of all rhabdoid tumors, the four epithelioid sarcomas and the renal medullary carcinoma did not express *SMARCB1/INI1* by immunohistochemistry; neoplastic cells of all other tumors expressed *SMARCB1/INI1*. Immunohistochemistry to assess expression of *SMARCB1/INI1* may be useful in the diagnosis of rhabdoid tumors of the CNS, kidneys and soft tissue.

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Malignant rhabdoid tumors are highly aggressive neoplasms that usually occur in the central nervous system (CNS), kidneys and soft tissue of children.¹ The histologic diagnosis of malignant rhabdoid tumor is based on the observation of medium-sized

to relatively large cells with eccentrically located nuclei and abundant cytoplasm, often with paranuclear filamentous inclusions, and a polyphenotypic immunoprofile with frequent expression of vimentin, keratin and epithelial membrane antigen. In most malignant rhabdoid tumors, the *SMARCB1/INI1* gene, located in chromosome band 22q11.2, is inactivated by deletions and/or mutations, so genetic diagnosis is often possible.^{2–8} Sometimes, though tissue is not available for genetic analysis or studies are not confirmatory.⁸

We used immunohistochemistry to assess *SMARCB1/INI1* expression in malignant rhabdoid tumors of the kidney and soft tissue and atypical

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teratoid/rhabdoid tumors, the analogous CNS tumors. We also examined expression of *SMARCB1/INI1* in a variety of pediatric kidney tumors and adult and pediatric brain and soft tissue tumors to assess the role of *SMARCB1/INI1* immunohistochemistry in diagnosis.

Materials and methods

Seventy-four tumors—12 brain, three renal and two soft tissue rhabdoid tumors, four glioblastomas, four pilocytic astrocytomas, four oligodendrogliomas, one WHO grade II and three WHO grade III, two ependymomas, two choroid plexus papillomas, five pituitary adenomas, four germinomas, four renal carcinomas with Xp11.2 translocations, two clear cell sarcomas, two Wilms' tumors, one renal medullary carcinoma, two desmoplastic small round cell tumors, two alveolar rhabdomyosarcomas, two embryonal rhabdomyosarcomas, one low-grade chondrosarcoma, two extraskeletal myxoid chondrosarcomas, one mesenchymal chondrosarcoma, four malignant peripheral nerve sheath tumors, five metastatic carcinomas and four epithelioid sarcomas, two primary and two metastatic, one of each in two patients—were selected from the surgical pathology files of the Departments of Pathology of Children's Medical Center and the University of Texas Southwestern Medical Center. The tumors were chosen to provide an indication of the specificity of expression of *SMARCB1/INI1* among CNS, kidney and soft tissue neoplasms and individual cases selected if enough tissue was available for confirmation of the diagnosis and additional immunohistochemical stains. In addition, equivocal, focal or unexpected staining of some tumors reported by Judkins *et al*⁹ prompted inclusion of several examples of oligodendrogliomas and pituitary adenomas. The diagnoses were based on assessment of clinical data and examination of hematoxylin and eosin-stained sections, usually other immunohistochemically stained sections and, in some cases, other ancillary studies. Specifically, for CNS glial tumors, immunohistochemistry was used in selected cases to identify expression of glial fibrillary acidic protein, microtubule-associated protein 2, prealbumin and Ki-67. For germinomas, immunohistochemistry was used to identify placental alkaline phosphatase and, for pituitary adenomas, chromogranin and/or synaptophysin and some or all anterior pituitary hormones. For case 28, an anaplastic oligodendroglioma, genetic analysis revealed 1p/19q loss of heterozygosity. For the renal carcinomas, cytogenetic analysis identified t(X;1) or t(X;17) translocations. For soft tissue tumors and carcinomas, immunohistochemical stains included those to identify muscle antigens, S100 and keratin.

All staining was performed using a BioTek Solutions TechMateTM 500 system (Ventana Medical Systems, Tucson, AZ, USA) using the ultra-strepta-

vidin biotin system with horseradish peroxidase and diaminobenzidine (DAB) as chromogen (Signet Laboratories, Dedham, MA, USA). RevealTM (BioCare Medical, Walnut Creek, CA, USA) was used for heat-induced epitope retrieval. Optimum primary antibody dilutions were predetermined using known positive control tissues. A microarray that included sections of normal cerebellum, small cell carcinoma of the lung and colonic adenocarcinoma was included in each staining run. Moreover, in tumor sections, non-neoplastic cells—eg, lymphocytes, fibroblasts, endothelial cells, fat cells, cells of renal tubules and glomeruli, pneumocytes and neurons and glial cells—served as internal positive controls. Not all non-neoplastic cells of a given tissue stained.

Paraffin sections were cut at 3 μ m on a rotary microtome, mounted on positively charged glass slides (POP 100 capillary gap slides, Ventana Medical Systems, Tucson, AZ, USA) and air-dried overnight. The sections were deparaffinized in xylene and ethanol, quenched with fresh 3% hydrogen peroxide for 10 min and rinsed with deionized water. For heat-induced epitope retrieval, sections were placed in 200 ml RevealTM citrate buffer, boiled in a circulating waterbath for 15 min at 100°C then cooled in buffer for 20 min and rinsed in deionized water then buffer. Then, the sections were incubated in unlabeled blocking serum for 15 min (to block nonspecific binding of the secondary antibody), then incubated overnight at 4°C with either BAF47, an antibody to the *SMARCB1/INI1* gene product (1:40, BD Biosciences, Chicago, IL, USA) or buffer alone (as a negative reagent control). Following washing in buffer, the sections were incubated for 25 min with a biotinylated polyvalent secondary antibody solution (containing goat antibodies to rabbit and mouse immunoglobulins). Following another buffer wash, the sections were incubated in horseradish peroxidase-conjugated streptavidin-biotin complex for 15 min, washed in buffer, incubated with two changes, 5 min each, of a freshly prepared mixture of DAB and H₂O₂ in buffer, then washed in buffer, and then in water. Finally, the sections were counterstained with hematoxylin, dehydrated in a graded series of ethanols, then xylene and coverslipped.

Results

Clinical data and results of *SMARCB1/INI1* immunohistochemistry are shown in Tables 1–3. Table 1 shows the staining results for 37 primary intracranial tumors. The 12 patients with atypical teratoid/rhabdoid tumors ranged in age from 3 months to 5 years 3 months with a median age of approximately 1 year 5 months. Male to female ratio was 0.83 to 1. Six of 11 tumors occurred in the posterior fossa, three occurred in the cerebral hemispheres and one in the hypothalamus. Expression of *SMARCB1/INI1* was not detected by immunohistochemistry in

Table 1 Brain tumors

Patient	Age (years)	Sex	Site	Histology	SMARCB1/INI1 IHC
1	2	F	Brain, NOS	AT/RT	No staining
2	3 months	F	SCP	AT/RT	No staining
3	1 year 5 months	F	Posterior fossa	AT/RT	No staining
4	2	M	Temporal lobe	AT/RT	No staining
5	4 months	M	Hypothalamus	AT/RT	No staining
6	1 year 5 months	M	Posterior fossa	AT/RT	No staining
7	4 months	F	Posterior fossa	AT/RT	No staining
8	1 year 2 months	M	CPA	AT/RT	No staining
9	11 months	F	Temporoparietal	AT/RT	No staining
10	1 year 9 months	F	Posterior fossa	AT/RT	No staining
11	5	M	Frontal lobe	AT/RT	No staining
12	5 months	M	Frontal lobe	AT/RT	No staining
13	10	M	Thalamus	Germinoma	Nuclear staining
14	6	F	Suprasellar	Germinoma	Nuclear staining
15	6	F	Third ventricle	Germinoma	Nuclear staining
16	12	M	Pineal region	Germinoma	Nuclear staining
17	4	M	Optic nerve	Pilocytic astrocytoma	Nuclear staining
18	4	F	Temporal lobe	Pilocytic astrocytoma	Nuclear staining
19	2	F	Posterior fossa	Pilocytic astrocytoma	Nuclear staining
20	12	F	Cerebellum	Pilocytic astrocytoma	Nuclear staining
21	51	M	Frontal lobe	Glioblastoma	Nuclear staining
22	48	M	Intraventricular	Glioblastoma	Nuclear staining
23	54	M	Temporal lobe	Glioblastoma	Nuclear staining
24	42	M	Frontal lobe	Glioblastoma	Nuclear staining
25	36	M	Frontal lobe	Oligodendroglioma II	Nuclear staining
26	49	F	Frontal lobe	Oligodendroglioma III	Nuclear staining
27	54	M	Temporal lobe	Oligodendroglioma III	Nuclear staining
28	31	F	Frontal lobe	Oligodendroglioma III	Nuclear staining
29	56	F	Spinal cord	Ependymoma	Nuclear staining
30	58	F	Spinal cord	Ependymoma	Nuclear staining
31	31	F	Pituitary	Adenoma	Nuclear staining
32	37	F	Pituitary	Adenoma	Nuclear staining
33	61	F	Pituitary	Adenoma	Nuclear staining
34	40	M	Sella	Adenoma	Nuclear staining
35	43	M	Pituitary	Adenoma	Nuclear staining
36	45	M	Lateral ventricle	CPP	Nuclear staining
37	35	F	Brain, NOS	CPP	Nuclear staining

SCP, superior cerebellar peduncle; CPA, cerebellopontine angle; AT/RT, atypical teratoid/rhabdoid tumor; CPP, choroid plexus papilloma; IHC, immunohistochemistry.

Table 2 Renal tumors

Patient	Age (years)	Sex	Histology	SMARCB1/INI1 IHC
38	1 year 6 months	M	MRT	No staining
39	8 months	M	MRT	No staining
40	3	F	MRT	No staining
41	1 year 1 months	M	Clear cell sarcoma	Nuclear staining
42	3	F	Clear cell sarcoma	Nuclear staining
43	3	F	Wilms' tumor	Nuclear staining
44	3	M	Wilms' tumor	Nuclear staining
45	10	F	RC/t(X;17)	Nuclear staining
46	11	M	RC/t(X;17)	Nuclear staining
47	1 year 5 months	M	RC/t(X;17)	Nuclear staining
48	15	M	RC/t(X;1)	Nuclear staining
49	19	M	Medullary carcinoma	No staining

MRT, malignant rhabdoid tumor; RC, renal carcinoma; IHC, immunohistochemistry.

neoplastic cells in the 12 tumors. All or the vast preponderance of neoplastic nuclei were unstained in all cases (Figure 1).

The age range for the other 25 brain tumors was 2–61 years. Nine occurred in the cerebral hemispheres,

six in the sella or suprasellar region, two in the posterior fossa, two in the spinal cord and one each in the thalamus, optic nerve, pineal region and 3rd and lateral ventricles. There was expression of *SMARCB1/INI1* by neoplastic cells in all tumors.

Table 3 Soft tissue rhabdoid tumors and other soft tissue or metastatic tumors

Patient	Age (years)	Sex	Site	Histology	<i>SMARCB1/INI1</i> IHC
50	16 days	M	Neck	MRT	No staining
51	4 months	F	Orbit	MRT	No staining
52	14	M	Abdomen	DSRCT	Nuclear staining
53	13	M	Omentum	DSRCT	Nuclear staining
54	17	F	Chest wall	Alveolar RMS	Nuclear staining
55	10	F	Nose	Alveolar RMS	Nuclear staining
56	3	M	Ear	Embryonal RMS	Nuclear staining
57	8	M	Retroperitoneum	Embryonal RMS	Nuclear staining
58	17	F	Hip	Chondrosarcoma I	Nuclear staining
59	7	M	Chest wall	Myxoid CHS	Nuclear staining
60	35	M	Paraspinal	Myxoid CHS	Nuclear staining
61	4	M	Vertebra	Mesenchymal CHS	Nuclear staining
62	55	F	CPA	MPNST	Nuclear staining
63	20	F	Frontal lobe	MPNST	Nuclear staining
64	43	M	Spinal cord	MPNST	Nuclear staining
65	39	F	Posterior fossa	MPNST	Nuclear staining
66	70	F	Temporal lobe	Metastatic carcinoma	Nuclear staining
67	38	F	Parietal lobe	Metastatic carcinoma	Nuclear staining
68	67	F	Frontal lobe	Metastatic carcinoma	Nuclear staining
69	61	M	Cerebellum	Metastatic carcinoma	Nuclear staining
70	44	M	Occipital lobe	Metastatic carcinoma	Nuclear staining
71	26	M	Wrist	Epithelioid sarcoma	No staining
72	26	M	Lymph node	Metastatic ES	No staining
73	15	M	Hand	Epithelioid sarcoma	No staining
74	15	M	Lung	Metastatic ES	No staining

CPA, cerebellopontine angle; MRT, malignant rhabdoid tumor; DSRCT, desmoplastic small round cell tumor; RMS, rhabdomyosarcoma; CHS, chondrosarcoma; MPNST, malignant peripheral nerve sheath tumor; ES, epithelioid sarcoma; IHC, immunohistochemistry.

The vast preponderance of neoplastic nuclei were stained in all cases (Figure 2).

Table 2 shows the staining results for 12 childhood kidney tumors. Three patients, two male and one female, ages 8 months, 1 year 6 months and 3 years 7 months had malignant rhabdoid tumors. The age range for the other kidney tumors was 1 year 1 month to 19 years 6 months. There were four renal carcinomas, three with t(X;17) and one with t(X;1), two clear cell sarcomas, two Wilms' tumors and one renal medullary carcinoma. Expression of *SMARCB1/INI1* was not detected by immunohistochemistry in neoplastic cells in the rhabdoid tumors or the medullary carcinoma. All or the vast preponderance of neoplastic nuclei were unstained (Figure 3). There was nuclear expression of *SMARCB1/INI1* by neoplastic cells in all renal carcinomas and both clear cell sarcomas and Wilms' tumors (Figure 4). In general, the vast preponderance of neoplastic nuclei were stained. In case 45, a renal carcinoma t(X;17), stained nuclei were diffuse, but the percentage was not as great as in the other cases.

Table 3 shows the results for two soft tissue malignant rhabdoid tumors and 23 other soft tissue or metastatic tumors of types in the differential diagnosis of extrarenal rhabdoid tumors. Neoplastic cells of both soft tissue malignant rhabdoid tumors and all four epithelioid sarcomas did not express *SMARCB1/INI1* by immunohistochemistry. In all of these cases, all or the vast preponderance of neoplastic nuclei were unstained (Figure 5). There

was nuclear expression of *SMARCB1/INI1* in neoplastic cells in both desmoplastic small round cell tumors and all rhabdomyosarcomas, chondrosarcomas, carcinomas and malignant peripheral nerve sheath tumors (Figure 5). The vast preponderance of neoplastic nuclei were stained in all cases except the low-grade chondrosarcoma (case 58) and one of the malignant peripheral nerve sheath tumors (case 63). In these cases, like the renal carcinoma (case 45), stained nuclei were diffuse, but the percentage was not as great as in the other cases.

Discussion

The *SMARCB1/INI1* gene, that maps to chromosome 22q11.2, is part of the SWI/SNF chromatin remodeling complex that plays a role in transcriptional regulation.¹⁰ *SMARCB1/INI1* is inactivated homozygously in the majority of malignant rhabdoid tumors by deletions and/or mutations; up to 20% of tumors show no alterations at either the DNA or RNA levels.²⁻⁸ Thus, when informative, genetic analysis is useful for confirmation of the histologic diagnosis of malignant rhabdoid tumor. However, the genetic findings also suggest that immunohistochemistry can be used to identify inactivation of *SMARCB1/INI1* and thereby support the morphologic diagnosis of malignant rhabdoid tumor. Absence of expression of *SMARCB1/INI1* by immunohistochemistry in tumors of other morphologic types would lessen diagnostic usefulness but raise the

Figure 1 An atypical teratoid/rhabdoid tumor (a) (case 4) with absence of nuclear expression of *SMARCB1/INI1* (b). Note the expression by endothelial and inflammatory cells (b).

Figure 2 An anaplastic oligodendroglioma (a) (case 27) with nuclear expression of *SMARCB1/INI1* (b).

possibility of inactivation of the gene in those tumors.

In all, 12 (of 12) tumors that were clinically and morphologically atypical teratoid/rhabdoid tumors showed no nuclear staining by immunohistochemistry with the BAF47 antibody; 25 (of 25) other brain tumors of various types showed nuclear staining. With regard to specificity, we sought (1) to examine expression in tumors that are often considered in the differential diagnosis of cerebral, cerebellar and sellar region tumors in children and adults and (2) to complement Judkins *et al*⁹ study. Most CNS tumors in childhood, including atypical teratoid/rhabdoid tumors, occur in the posterior fossa¹¹ and the most common types are neuroglial: astrocytoma (usually pilocytic astrocytoma) primitive neuroectodermal tumor (PNET) and ependymoma. Tumors often considered in the differential diagnosis of atypical teratoid/rhabdoid tumor are PNET, germ cell tumors, choroid plexus carcinoma and ependymoma. The neoplastic cells of all four

pilocytic astrocytomas and both ependymomas expressed *SMARCB1/INI1* by immunohistochemistry. We also found expression of *SMARCB1/INI1* by the neoplastic cells of two choroid plexus papillomas. Judkins *et al*⁹ found nuclear expression of *SMARCB1/INI1* in 10 (of 10) PNETs. The second most common site for atypical teratoid/rhabdoid tumors in childhood is supratentorial/suprasellar. Pilocytic astrocytomas, craniopharyngiomas and germ cell tumors are among the most common sellar region tumors in children. In addition to the observed expression in pilocytic astrocytomas, the neoplastic cells of all four germinomas expressed *SMARCB1/INI1*. Judkins *et al*⁹ found nuclear staining in two (of two) craniopharyngiomas.

Most CNS tumors in adults occur in or in relation to the cerebral hemispheres and the majority of atypical teratoid/rhabdoid tumors in adults occur in the cerebral hemispheres or sellar region.¹² We found nuclear expression of *SMARCB1/INI1* in all glioblastomas (four of four) and oligodendrogliomas

Figure 3 A renal malignant rhabdoid tumor (a) (case 38) and medullary carcinoma (c) (case 49) with absence of nuclear expression of *SMARCB1/INI1* (b, d, respectively). Note the expression by entrapped renal tubule cells (b).

(four of four), two common types of infiltrating gliomas that occur most frequently in the cerebrum. Judkins *et al*⁹ found loss of *SMARCB1/INI1* expression by immunohistochemistry in an oligodendroglioma and focal expression in an anaplastic oligoastrocytoma. Their fluorescence *in situ* hybridization study of the oligodendroglioma showed no chromosome 22 deletion. Although more oligodendrogliomas should be studied, our findings suggest that *SMARCB1/INI1* is expressed in these gliomas.

Raisanen *et al*¹² called attention to the relative frequency of atypical teratoid/rhabdoid tumors in the sellar region of adults. The differential diagnosis of sellar region tumors in adults includes pituitary adenoma, five (of five) examples of which showed nuclear expression of *SMARCB1/INI1*. Judkins *et al*⁹ found faint nuclear staining (immunohistochemistry with BAF47) of cells in a single pituitary adenoma. Our findings indicate that *SMARCB1/INI1* is expressed in pituitary adenomas.

Altogether, the findings suggest that immunohistochemistry with an antibody to the *SMARCB1/INI1* gene product is a sensitive and specific means of identifying atypical teratoid/rhabdoid tumors.

We also studied *SMARCB1/INI1* expression in rhabdoid tumors of the kidney with a view toward differential diagnosis. The most common pediatric kidney tumor is Wilms' tumor (nephroblastoma).¹³ Other kidney tumors that occur in children are mesoblastic nephroma, clear cell sarcoma, rhabdoid tumor, renal medullary carcinoma and renal carcinomas associated with Xp11.2 translocations. All four Wilms' tumors, all four renal carcinomas and both clear cell sarcomas expressed nuclear *SMARCB1/INI1* by immunohistochemistry. There was no expression of *SMARCB1/INI1* by neoplastic cells of the three malignant rhabdoid tumors. In their study of renal and pediatric soft tissue tumors, Hoot *et al*⁶ reported no expression of *SMARCB1/INI1* by immunohistochemistry in neoplastic cells of

Figure 4 A Wilms' tumor (a) (case 43) with nuclear expression of SMARCB1/INI1 (b).

19 renal malignant rhabdoid tumors. Four (of four) cellular congenital mesoblastic nephromas, four (of four) clear cell sarcomas and six (of six) Wilms' tumors expressed SMARCB1/INI1. With regard to childhood kidney tumors, our findings support those of Hoot *et al* and suggest that absence of SMARCB1/INI1 expression by immunohistochemistry distinguishes malignant rhabdoid tumors from most common pediatric kidney tumors, including renal carcinomas associated with Xp11.2 translocations.

The tumor cells of a single case of renal medullary carcinoma did not express SMARCB1/INI1 by immunohistochemistry. Renal medullary carcinoma is a comparatively rare kidney tumor that usually occurs in patients 10–40 years old with sickle cell trait.¹⁴ The neoplastic cells are poorly differentiated with clear nuclei and prominent nucleoli and sometimes have rhabdoid morphology.¹⁴ There are few reports describing the cytogenetics of renal medullary carcinomas.^{14–16} Swartz *et al*¹⁴ reported a

case with loss of chromosome 22 and Stahlschmidt *et al*¹⁶ a case with a near tetraploid clone with all four 22 chromosomes with an abnormality of 22q11. Although only one case of medullary carcinoma was examined, the finding of loss of expression of SMARCB1/INI1 by immunohistochemistry raises the possibility of inactivation of the SMARCB1/INI1 gene in at least some of these tumors. More studies of SMARCB1/INI1 in renal medullary carcinomas are warranted.

The rhabdoid cells in two soft tissue malignant rhabdoid tumors did not express SMARCB1/INI1 by immunohistochemistry. A total of 19 other tumors of types in the differential diagnosis of extrarenal rhabdoid tumor expressed the protein—both desmoplastic small round cell tumors and all rhabdomyosarcomas, chondrosarcomas, carcinomas and malignant peripheral nerve sheath tumors. Hoot *et al*⁶ reported no expression of SMARCB1/INI1 by immunohistochemistry in neoplastic cells of eight (of eight) extrarenal malignant rhabdoid tumors; neoplastic cells of 13 (of 13) Ewing's sarcomas, five (of five) desmoplastic small round cell tumors, five (of five) rhabdomyosarcomas and two (of two) epithelioid sarcomas expressed SMARCB1/INI1. Perry *et al*¹⁷ found nuclear expression of SMARCB1/INI1 by immunohistochemistry in neoplastic cells of three (of three) melanomas.

Thus, as in the CNS and kidneys, absence of expression of SMARCB1/INI1 by immunohistochemistry helps to identify soft tissue malignant rhabdoid tumors.

In Hoot *et al* study⁶ of two epithelioid sarcomas, nuclear staining was diffuse and strong in one, but focal and variable in the other. We found absence of expression of SMARCB1/INI1 by immunohistochemistry in both primary and metastatic epithelioid sarcomas in two patients. The absence of expression of SMARCB1/INI1 is interesting in light of recent cytogenetic and molecular genetic studies by Modena *et al*¹⁸ that identified deletions of SMARCB1/INI1 in 5 of 11 so-called 'proximal type' epithelioid sarcomas. All five cases and one additional conventional or 'distal type' (six of 11) demonstrated inactivation at the protein level.¹⁸ So, in regard to differential diagnosis, absence of expression of the SMARCB1/INI1 protein may not help to distinguish malignant rhabdoid tumors from epithelioid sarcomas.

Since malignant rhabdoid tumors and epithelioid sarcomas are related by similar morphology and immunophenotype, the finding of inactivation of the SMARCB1/INI1 tumor suppressor gene in some cases of each type raises the possibility that they are entities in a spectrum.

The diagnoses of atypical teratoid/rhabdoid tumor and malignant rhabdoid tumor may be difficult because of the rarity of the tumors, diverse histology and polyphenotypic immunoprofiles with antigen expression that is usually multifocal. Immunohistochemical identification of absence of expression of

Figure 5 A malignant rhabdoid tumor (a) (case 51) of the orbit with absence of nuclear expression of *SMARCB1/INI1* (b) and a desmoplastic small round cell tumor (c) (case 53) of the omentum with expression of *SMARCB1/INI1* (d).

SMARCB1/INI1 may help to distinguish atypical teratoid/rhabdoid tumors from other intracranial tumors and malignant rhabdoid tumors from other common pediatric kidney tumors and adult and pediatric soft tissue tumors.

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