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The role of screening spinal MRI in children with solitary posterior fossa low-grade glial tumors

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OBJECTIVE Solitary posterior fossa low-grade glial tumors (SPFLGT) in children are rarely associated with leptomeningeal dissemination (LMD). To date, there are no clear guidelines regarding the role of screening and surveillance spinal MRI (sMRI) in children with SPFLGT, at diagnosis or during follow-up periods. The current study reviews a cohort of children with SPFLGT, focusing on sMRI findings.

METHODS In this binational retrospective study, the authors analyzed 229 patients with SPFLGT treated and followed over 13 years. One hundred twelve children had at least 1 total sMRI screening or surveillance examination. One hundred seventeen had no sMRI, but did not present with clinical spinal signs or symptoms. Collected data included demographics, disease characteristics, radiology, pathology, and clinical follow-up data.

RESULTS For the 112 children with at least 1 sMRI, the mean duration from diagnosis to first sMRI was 11.73 ± 28.66 months (range 0–165 months). All sMRI scans were conducted as screening examinations, with no spinal-related symptoms. One patient was found to have a sacral intradural lesion concurrent to the brain tumor diagnosis. Over the course of 180 radiological and 533 clinical follow-up years for the 112 patients with sMRI, and 582 clinical follow-up years for the 117 patients with no sMRI, there were no additional cases with spinal tumor spread.

CONCLUSIONS The yield of screening sMRI in the absence of cranial metastasis, or spinal symptoms, is extremely low. Because preoperative sMRI is recommended for medulloblastomas and ependymomas, it may be logical to acquire. During the follow-up period the authors recommend limiting sMRI in patients without symptoms suggesting a spinal lesion, in patients without known cranial metastases, or recurrence or residual SPFLGT.

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KEYWORDS low-grade glioma; leptomeningeal dissemination; posterior fossa; spine MRI; screening; oncology

Low-grade gliomas (LGGs) are the most frequent CNS tumors among children, and pilocytic astrocytoma (PA) is the most prevalent LGG in children (19% of all brain tumors up to 14 years of age, 15% between the ages of 15 and 19 years).[14] More than 60% of PAs are found in the posterior fossa, mainly in the cerebellar hemispheres or brainstem.

Leptomeningeal dissemination (LMD) is estimated to occur in 3%–12% of cases of PA.[1] However, most of the primary sites include chiasmatic-hypothalamic tumors; the number of cases in which the primary tumor was located in the posterior fossa is small. Although rare, LMD has been reported in children with diffuse astrocytoma, oligodendroglioma, or ganglioglioma, as well as in patients with chiasmatic-hypothalamic tumors.[2,3,16] Spinal MRI (sMRI) is recommended based on symptoms or signs suggestive of possible LMD such as back pain, radicular sensorimotor symptoms or signs, loss of bladder and bowel function, as well as signs of LMD on brain imaging.[5–8,10,12] Rarely, spinal LMD may occur in the absence of cranial LMD, even many years following removal of a solitary posterior fossa low-grade glial tumor (SPFLGT).[4,9] However, sMRI is not

ABBREVIATIONS EOR = extent of resection; LGG = low-grade glioma; LMD = leptomeningeal dissemination; PA = pilocytic astrocytoma; sMRI = spinal MRI; SPFLGT = solitary posterior fossa low-grade glial tumor.

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regularly performed as part of the diagnostic or follow-up protocols in the absence of cranial LMD, or symptoms or signs suggesting spinal LMD.

The role of the current study was to evaluate the value of screening and surveillance sMRI in children with solitary posterior fossa LGG, in the absence of cranial LMD, and other symptoms or signs suggesting spinal LMD.

Methods

Study Population

Following IRB approval, a retrospective data collection was performed. Inclusion criteria were patients diagnosed with an SPFLGT who underwent an operation on or before the age of 18 years. Exclusion criteria involved signs and/or symptoms that suggested spinal LMD during diagnosis (i.e., back pain, neurological findings suggestive of a spinal cord compression or radicular compression, and urinary/fecal incontinence). Patients with additional brain lesions, or with predisposing genetic disorders (such as neurofibromatosis type 1 or 2, tuberous sclerosis, etc.) or prior oncological disease were also excluded. A database was compiled of all relevant patients operated on at Dana Children's Hospital, Tel-Aviv Medical Center, in Tel-Aviv, Israel, and St. Louis Children's Hospital in St. Louis, Missouri, between the years 2004 and 2017. Patient and parental consent was waived.

Data Collection

Data collected included the following: demographics; presenting signs and/or symptoms, including their timing and duration; duration of follow-up; and brain imaging at diagnosis and follow-up. We also focused on tumor characteristics, such as: was it exophytic; did it abut the CSF pathways; extent of resection (EOR); and the histopathology. Spinal data included the time to first sMRI; accumulated spinal, clinical, and radiographic follow-up; and whether or not a positive spinal LMD was present at any point. Spinal LMD was diagnosed based on radiological findings suggestive of intradural extramedullary lesions, regardless of whether they enhanced, or leptomeningeal enhancement of the spinal cord, nerve roots, or cul-de-sac. Tissue histological confirmation was not necessary for such a diagnosis.

We divided patients into three subgroups according to the time at which the sMRI was performed relative to the surgical procedure for the posterior fossa tumor. These subgroups were "perioperative" (1 month prior–6 months after surgery), "within first year" (7–12 months after surgery), and "after first year."

Spinal follow-up was evaluated radiologically and clinically. Radiological follow-up was calculated as time from diagnosis to last sMRI. Clinical follow-up was calculated from diagnosis of posterior fossa tumor to last clinical follow-up. The endpoints of our study were diagnosis of positive LMD in the brain or spine, radiotherapy or chemotherapy, or death.

Statistical Analysis

Data was collected using FileMaker Pro software (version 12). Data was exported and analyzed using a Microsoft Excel spreadsheet (Microsoft Corp.). Data analysis was based on descriptive analysis. Numerical data are presented as range and average ± standard deviation.

TABLE 1. Demographics

Variable	sMRI	No sMRI	Entire Group
No. of patients	112	117	229
Age at diagnosis of SPFLGT, yrs			
Mean	7.55	7.8	7.7
Median (range)	6 (1–17)	7 (0.1–17)	7 (0.1–17)
Males/females	52:60	61:56	113:116

Results

We identified 229 patients with SPFLGT from both centers (100 from St. Louis and 129 from Tel-Aviv). One hundred twelve patients had at least 1 complete sMRI scan performed. An additional 117 patients with SPFLGT did not have sMRI, but had clinical follow-up. Table 1 summarizes basic demographics of the 112 patients with sMRI and the 117 with no sMRI. Primary tumor characteristics, as well as EOR in each group, are summarized in Table 2. There was no cranial LMD diagnosed at any stage for any of the 229 patients.

Spinal MRI Group

Most patients underwent their first sMRI examination within 6 months of surgery for the posterior fossa tumor (n = 85, 75.9%). Fifty-five patients (49.1%) had sMRI concurrently with the cranial MRI. Nine patients (8%) had the first sMRI 7–12 months after surgery, and 18 patients (16.1%) had the first sMRI performed more than 1 year after surgery. The mean time from diagnosis to first sMRI was 11.73 ± 28.66 months (range 0–165 months). Forty-four patients had sMRI (the first, or as a follow-up scan) performed more than 6 months since diagnosis. Twenty-two patients had more than 1 sMRI performed, with a time span of 42.09 ± 37.81 months (range 6–138 months) between scans. Data regarding sMRI timing is summarized in Fig. 1.

One patient (with a posterior fossa PA) had a spinal lesion suspected of being an LMD concurrent with the diagnosis of the SPFLGT. No additional lesions suspected of being an LMD were diagnosed in this patient over an 8-year follow-up course, and she was never operated on for the spinal lesion. None of the other sMRI scans showed spinal LMD.

The mean time from diagnosis to last sMRI was 19.32 ± 34.67 months (range 0–165 months). Overall, the spinal radiological follow-up included 180.33 years for the 112 patients, with at least 1 sMRI.

Clinical Follow-Up

The mean clinical spinal follow-up duration for the sMRI group was 57.15 ± 44.03 months (range 0–214 months), 59.68 ± 54.87 months (range 0–224 months) for the non-sMRI group, and 58.44 ± 49.77 months (range 0–224 months) for the entire study group. Patient clini-

TABLE 2. Posterior fossa lesion location, pathology, and EOR

Posterior Fossa Lesion	sMRI (n = 112) No.	%	No sMRI (n = 117) No.	%	Total No.	%
Location						
Cerebellar hemisphere	61	54.5	61	52.1	122	53.3
Cerebellar peduncle	28	25	24	20.5	52	22.7
Vermis	27	24.1	14	12	41	17.9
Midbrain	1	0.9	10	8.5	11	4.8
Medulla	3	2.7	12	10.2	15	6.5
Pons	18	16.1	12	10.2	30	13.1
Fourth ventricle	26	23.2	22	18.8	48	21
Exophytic						
Yes	20	17.9	85	72.6	105	45.9
No	92	82.1	32	27.4	124	54.1
Abutting the CSF						
Yes	81	72.3	66	56.4	147	64.2
No	31	27.7	51	43.6	82	35.8
Pathology						
PA	101	90.2	103	88	204	89.1
Ganglioglioma (grade 1)	2	1.8	6	5.1	8	3.5
Other LGG	9	8	8	6.8	17	7.4
EOR						
Gross-total	82	73.2	90	76.9	172	75.1
Subtotal	24	21.4	22	18.8	46	20.1
Biopsy	6	5.4	5	4.3	11	4.8

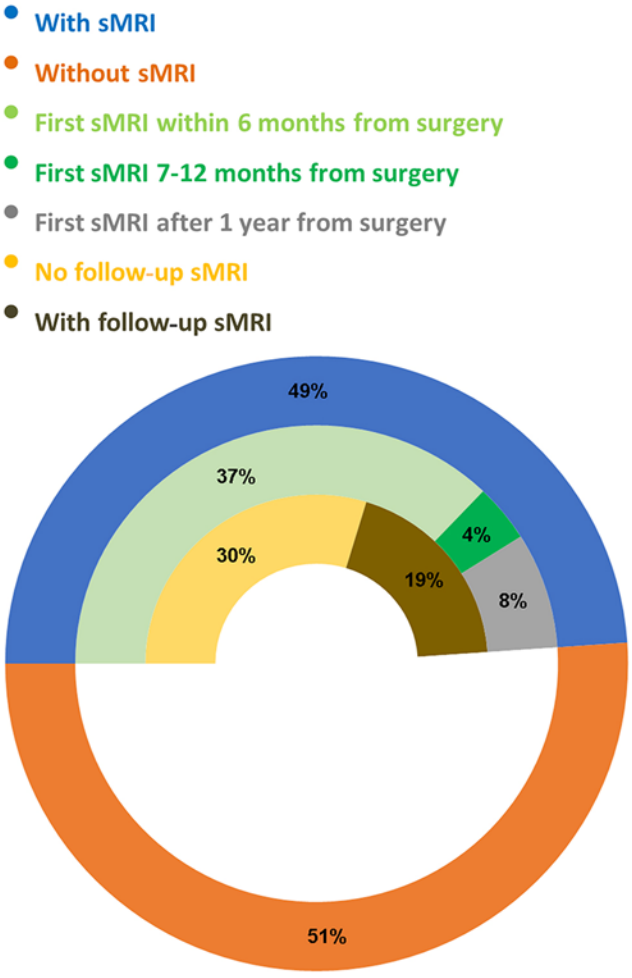

FIG. 1. Spinal imaging data showing an overview of sMRI timing. Figure is available in color online only.

cal follow-up years added up to 1115.32 years for all 229 patients, 533.41 years for the 112 patients with at least 1 sMRI and 581.91 years for the 117 patients without any sMRI. During follow-up, none of the patients (besides the patient diagnosed with spinal LMD at diagnosis) developed signs or symptoms suggestive of spinal LMD.

Discussion

This is the first study to systematically evaluate the role of screening sMRI in children with solitary LGG (the majority being PA), in the absence of cranial metastasis, and no spinal symptoms or signs. Two major conclusions may be deduced from our study: 1) the yield of screening sMRI in SPFLGT is very low, and 2) if a screening sMRI has been performed (and is negative), the yield of additional sMRI in the absence of cranial LMD or symptoms suggesting spinal LMD is very low. The implication of these conclusions is important, potentially decreasing the number of MRI scans performed, reducing costs, anxiety, and anesthesia time in young children.

Metastatic PA is uncommon, occurring in 3%–12% of all cranial PAs. In a study by Bian et al.,[1] 59 patients had disseminated PA, most of whom were drawn from a summary of the literature, including 14 cerebellar tumors, although it was not stated how many were initially diagnosed with PFSLGT. In these 59 patients, 88% had LMD, while others had spread via subependymal and white matter tracts, as well as secondary to shunts.[1] It is worth mentioning that 36% already had a concurrent dissemination at presentation; however, total craniospinal imaging was obtained only after patients had shown signs or symptoms suggestive of dissemination, and not as a screening tool. Follow-up data from 50 patients were available, of whom 17 died (the mean time from dissemination to death was 23 months). Possible risk factors for dissemination were proposed, including young age, subtotal resection, and adjacency of the primary tumor to CSF pathways. Several other cases have identified spinal LMD following local tumor recurrence after resection of solitary posterior fossa PA, or subtotal resection, even several years later.[4,11,15,18] It is important to stress that the low yield of screening sMRI as presented in the current study is not in contradiction to the above-referred statistics. Our study focused on a very selected (but common) scenario of an SPFLGT with no spinal symptoms. Our conclusions are that for this selected group, the rate of asymptomatic spinal spread (with no cranial tumor) is minimal.

In a study by Mazloom et al., the authors discuss the outcome of patients with PA and LMD.[13] This literature review study included children and adults with a range of

tumor locations (16 were located in the cerebellum and 57% were chiasmatic-hypothalamic tumors); however, it was not stated if any of these patients presented with SPFLGT. They report 66.5% and 34.6% 5-year survival and progression-free survival rates, respectively. This study also divided the patients into two groups, depending on the timing of the LMD in relation to the primary tumor (synchronous vs metachronous); 48.9% of the patients presented with a synchronous disease. For the metachronous disease group (51.1%), the average duration from primary diagnosis to LMD diagnosis was 3 years, 6 months. The outcome of the synchronous group was better (5-year survival of 42.2%, as opposed to 22.5%) but the difference was not statistically significant. Moreover, no outcome difference was found between primary tumor locations or different therapy regimes. However, it was found that PA with LMD has a better prognosis than LMD that originates from other LGGs.[13]

Despite the low yield of screening sMRI, our results should also be evaluated in a practical manner. Young children presenting with new-onset symptoms of a possible brain tumor often undergo diagnostic brain MRI under sedation. Additionally, radiological differentiation between a low-grade glial tumor may overlap that of higher-grade tumors such as medulloblastomas and ependymomas. Because a baseline MR image is needed in medulloblastomas and ependymomas for staging purposes, it is recommended to perform a total CNS examination including an sMRI prior to surgery, to avoid postoperative artifacts.[17] Thus, we recommend that for cases undergoing initial diagnostic MRI under general anesthesia, a screening sMRI should be performed concurrently to the brain MRI if a cranial tumor is diagnosed, especially for posterior fossa tumors. Additionally, for older children with brain MRI that may suggest a higher-grade tumor, such as fourth ventricle tumors or tumors with restriction on diffusion, a screening sMRI should be conducted prior to surgery. On the other hand, patients presenting for treatment who already have cranial MRI with what appears to be an SPFLGT (such as an exophytic brainstem tumor or a hemispheric cystic lesion with no restriction on diffusion-weighted imaging) may be spared the need for baseline sMRI. Another subgroup that may be at risk for spinal LMD is patients with recurrent local disease, as well as patients with residual tumor. For these children, we also recommend performing a screening sMRI once every few years, even in the absence of cranial LMD or spinal symptoms.

Limitations

Although the number of patients with sMRI in this study is high (112), most underwent the MRI during the first 6 months from diagnosis, thus not necessarily reflecting long-term outcome. This is important, because for PA, most LMD does not occur at the time of diagnosis, but rather after several years. Clinical follow-up was negative for spinal symptoms and signs; however, patients may have had clinically occult spinal LMD. Despite a relatively large number of patients compared to current studies in the literature, the study group is small, and heterogeneous in regard to age, tumor location, and time from diagnosis. Diagnosis of spinal LMD was based primarily on radiological interpretations. There was no central review of the images; images were obtained on various MRI systems, and using various nonunified protocols.

Conclusions

The yield of screening sMRI in the absence of cranial metastasis, or spinal symptoms, is extremely low. Therefore, we recommend limiting sMRI screenings to patients with signs or symptoms suggesting a spinal lesion (such as back pain, lower-limb sensorimotor deficits, and loss of bladder and bowel function), or patients with known cranial metastases (at diagnosis, or while performing follow-up cranial imaging). We do recommend performing baseline sMRI in children undergoing the primary diagnostic cranial MRI under sedation, if a cranial tumor is diagnosed. Children with recurrent (after prior resection of SPFLGT) or residual tumor are also recommended to undergo sMRI as a screening tool. This may prove beneficial to better utilize the resources available, as well as sparing patients from unnecessary and sometimes costly examinations.

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Disclosures

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Author Contributions

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

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