ScientificScholar®
Knowledge is power
Publisher of Scientific Journals

www.surgicalneurologyint.com

Surgical Neurology International

Editor-in-Chief: Nancy E. Epstein, MD, Professor of Clinical Neurosurgery, School of Medicine, State U. of NY at Stony Brook.

SNI: Pediatric Neurosurgery

Editor
Frank Van Calenbergh, MD
University Hospitals; Leuven, Belgium

SNI
Open Access

Original Article

Increase of primary intracranial sarcoma in children: Clinical manifestations, diagnosis, and management

Jorge Zumaeta[1], Annel Murga[2], Noe Santiago Rea[1], Jose Daniel Flores-Sanchez[2], Manuel Lazon[2], Fernando Palacios Santos[2], Sandro Casavilca Zambrano[3], Immanuel Olarinde[1], Jose Valerio[1]

[1]Department of Neurosurgery Oncology, Latinoamerica Valerio Foundation, Weston, Florida, United States, [2]Vascular, Tumors and Functional Neurosurgery Service - Department of Neurosurgery, Guillermo Almenara Irigoyen National Hospital, Lima, [3]Chair of the Functional Unit of the National Tumor Bank, National Institute of Neoplastic Diseases, Lima, Peru.

E-mail: *Jorge Zumaeta - jorzusa87@gmail.com; Annel Murga - annelmurgav@gmail.com; Noe Santiago Rea - noe.santiago.rea@hotmail.com; Jose Daniel Flores-Sanchez - jdannister@gmail.com; Manuel Lazon - manuellazon@yahoo.com; Fernando Palacios Santos - fernando.palacios@essalud.gob.pe; Sandro Casavilca Zambrano - scasavilcazambrano@gmail.com; Immanuel Olarinde - olarindei@yahoo.com; Jose Valerio - jevalerio@jvaleriomd.com

***Corresponding author:**
Jorge Zumaeta,
Department of Neurosurgery Oncology, Latinoamerica Valerio Foundation, Weston, Florida, United States.

jorzusa87@gmail.com

Received: 19 March 2024
Accepted: 08 September 2024
Published: 22 November 2024

DOI
10.25259/SNI_202_2024

Quick Response Code:

ABSTRACT

Background: Primary intracranial sarcomas (PISs) are very rare malignant tumors, and there is paucity of data on it, exclusively in patients <18 years old. We report pediatric PIS at a tertiary hospital in Peru, where the incidence of PIS has increased in recent years.

Methods: We retrospectively analyzed data in children diagnosed with PIS based on clinical presentation, imaging studies, and histopathology between January 2020 and December 2023.

Results: Twenty-five cases were identified. The median age was 5 years. There is slight female predominance (56%). On presentation, 68% of patients had features of intracranial hypertension (ICH), others had convulsions or motor deficits. There was radiologic evidence of cerebral hemorrhage in 80% of those with features of ICH and convulsion. All but one case had a supratentorial tumor. Emergency craniotomy was done in 84% of cases, and gross total resection (GTR) was achieved in the first surgery in 72% of cases. We used an adjuvant chemotherapy-radiotherapy-chemotherapy (CTX-RT-CTX) regimen in 72% of cases, but 12% started this scheme 2 weeks after surgical resection. The cases followed up for more than a year that were managed with CTX-RT-CTX after GTR had a survival greater than a year, compared to the cases that received complementary treatment after 4 weeks.

Conclusion: PIS among children represents an infrequent pathology that, in the last years, its incidence has increased in Peru. The presence of intracerebral hemorrhage is a very suggestive finding of this diagnosis; therefore, emergent surgical management is an option before an irreversible ICH presents. Adjuvant treatment with the CTX-RT-CTX regimen started 2 weeks after GTR may improve survival in children with PIS.

Keywords: Cerebral hemorrhage, Children, Intracranial hypertension, Sarcoma, Neurosurgery

INTRODUCTION

Primary intracranial sarcomas (PISs) in children are rare and highly malignant. They are classified as mesenchymal non-meningothelial tumors.[11] Although their etiopathogenesis is still unclear, radiation exposure has been implicated. Its origin is thought to be the primitive mesenchymal pluripotential cells related to the meninges and their pial extensions in the brain. Perhaps due to its pluripotential origin, PIS displays vast heterogeneity in presentation and response to treatment modalities.[1]

The true prevalence of PIS is unclear but varies from 0.1% to 4.3%.[1] In addition to causing mass effects like other intracranial tumors, intracerebral hemorrhage is a common presentation due to high vascularity.[1,8,13] Radiographical features also vary significantly. Tumors may appear solid or cystic, occur in the cortex or meninges, and may exhibit hemorrhagic features.[1,2,13] Although there is no well-established consensus, management focuses on radical resection of the tumor followed by adjuvant chemotherapy (CTX) and radiotherapy (RT). Despite advances in treatment, the overall prognosis is still poor. The paucity of data to support consensus management guidelines, especially in children, contributes to the grim outcome of PIS.[1,2,8,13]

To the best of our knowledge, this manuscript is the second largest case series on pediatric PIS. Most published case series and case reports on PIS comprise only adults or a mixture of adults and children. There is a deficit of papers on PIS, exclusively in children.[1-3,8,13] Since it is an infrequent pathology, the increases in cases have sparked interest in understanding the clinical and radiological characteristics that allow for the diagnosis and proper management of patients. Thus, our work will fill the gap in our current understanding and management of pediatric PIS. To contribute to this effort, we share our experience managing 25 cases of pediatric PIS at a tertiary hospital in Peru, where the incidence of PIS skyrocketed from 2020 to 2023 [Figure 1].

MATERIALS AND METHODS

At a tertiary hospital in Peru, we retrospectively collected data of patients <18 years old with immunohistochemical diagnosis of PIS from January 1, 2020, to December 31, 2023. We employed Maher *et al*. definition of PIS as sarcoma that originated in the brain from non-neuronal, non-glial, and non-reticular elements, with no previous evidence of systemic sarcoma and no sarcomatous transformation of a previously known benign tumor.[13] We retrospectively analyzed prospectively collected data on demography, presentation, radiography, histopathology, surgical, and adjuvant management of each patient. The extent of surgical resection was determined from the operating report and contrast computerized tomography (CT) scan performed within 72 hours after the surgical procedure. We defined gross total resection (GTR) as the extirpation of >90% of the tumor, subtotal resection (STR) as removal of 50–90% of the tumor, and partial resection (PR) as removal of <50% of the tumor.[8] Surgical specimens were reviewed at two centers, and we performed immunohistochemical studies.

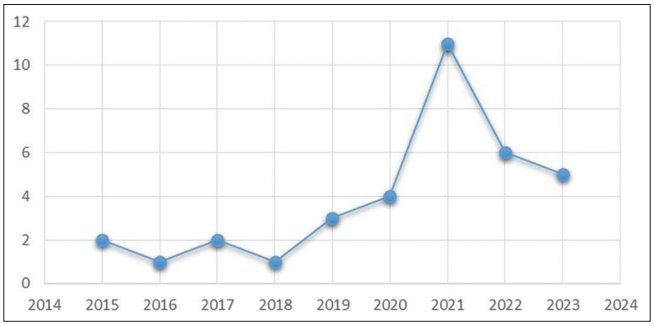

Figure 1: Incidence of primary intracranial sarcoma in children in a tertiary hospital in Peru from 2015 to 2023; the highest incidence peak was in 2021.

RESULTS

Table 1 summarizes the demography, presentation, and tumor location of all 25 patients.

Demography and presentation

None of the patients had any known risk factors. There were 14 females (56%) and 11 males (44%), from 2 to 17 years of age, with a median age of 5. Children under 10 years of age accounted for 84% of cases. On initial evaluation, most patients had signs and symptoms of intracranial hypertension (ICH) (68%), such as acute headache, nausea, and vomiting. Others presented with convulsions (20%) and motor deficits (12%). About 86% of all patients with ICH and convulsion had intracerebral hemorrhage, whereas only one in three patients with motor deficits had radiologic evidence of intracerebral hemorrhage.

Radiography

Preoperative CT scans showed all but one patient had supratentorial lesions. About 88% of the 24 supratentorial tumors were lobar, 8% were related to the falx cerebri in the midline, and 4% were in the basal ganglia. The tumors had a mixed pattern of contrast-enhancing solid portion accompanied by a cystic component. In all cases, the lesions were > 3 cm and compressing surrounding structures without evidence of leptomeningeal metastasis. In cases where brain magnetic resonance imaging (MRI) was performed, the lesions were hyperintense on T2, and fluid-attenuated inversion recovery showed flow voids and an irregular contrast enhancement. About 80% of cases had radiographic evidence of hemorrhage within the tumor and associated perilesional vasogenic edema. Three cases had radiographic evidence of intracerebral hemorrhage without a visible mass, followed by cerebral angiography, which was negative for arteriovenous malformation. Repeat scans, after neurologic deterioration, showed a tumor in the hemorrhagic zone, requiring emergency surgery.

Surgery

Most of the patients underwent emergency surgery for ICH and impaired consciousness. Almost half of the patients

Table 1: Demography, presentation, and tumor location of our cases.

Case	Age	Gender	Clinical manifestation	Location	Intracranial hemorrhage
1	10 y	F	ICH	Supratentorial Lobar (FP left)	Yes
2	7 y	M	Convulsion	Supratentorial Middle line (Falx cerebri)	Yes
3	9 y	F	ICH	Supratentorial Lobar (FP right)	Yes
4	5 y	M	ICH	Supratentorial Lobar (FP left)	Yes
5	6 y	M	Convulsion	Supratentorial Lobar (F left)	Yes
6	6 y	F	Convulsion	Supratentorial Lobar (P left)	No
7	5 y	M	Convulsion	Supratentorial Lobar (P right)	Yes
8	6 y	F	ICH	Supratentorial Lobar (T left)	No
9	3 y	M	ICH	Supratentorial Lobar (P left)	No
10	10 y	F	ICH	Supratentorial Lobar (T left)	Yes
11	10 y	F	ICH	Supratentorial Lobar (FP right)	Yes
12	3 y	M	ICH	Supratentorial Lobar (T right)	Yes
13	7 y	F	ICH	Supratentorial Lobar (P left)	Yes
14	6 y	M	ICH	Infratentorial Cerebellar left	Yes
15	2 y	F	ICH	Supratentorial Lobar (FTP left)	Yes
16	17 y	F	Motor deficit	Supratentorial middle line (Falx cerebri)	Yes
17	4 y	F	ICH	Supratentorial Lobar (F left)	Yes
18	4 y	F	ICH	Supratentorial (BG left)	Yes
19	5 y	F	Motor deficit	Supratentorial Lobar (F right)	No
20	5 y	M	ICH	Supratentorial Lobar (F left)	Yes
21	3 y	M	Convulsion	Supratentorial Lobar (F left)	Yes
22	2 y	M	ICH	Supratentorial Lobar (FP right)	Yes
23	8 y	F	Motor deficit	Supratentorial Lobar (FP right)	No
24	5 y	F	ICH	Supratentorial Lobar (F left)	Yes
25	5 y	M	ICH	Supratentorial Lobar (T left)	Yes

ICH: Intracranial hypertension (Headache, nausea, and/or vomiting), F: Frontal lobe, P: Parietal lobe, T: Temporal lobe, BG: Basal ganglia

(48%) entered the OR with a Glasgow coma scale (GCS) ≤12. Case 12 had the lowest GCS of 4 associated with rebleeding [Figure 2 and Table 2].

In 72% of the cases, a GTR was achieved in the first surgery. In 24% of cases, an STR was done in the first surgery, followed by a second GTR in three of those cases. In Case 10, PR was initially done due to profuse bleeding followed by GTR later [Figure 3].

In some cases, the use of fluorescence aided GTR. Grossly, the tumors are pearly or light brown, soft, friable, highly vascularized, necrotic, and hemorrhagic. We identified several friable vessels that are difficult to control. Most of the lesions in our series are infiltrating the cerebral parenchyma and the meninges. Only a few had a well-defined plane of dissection. The preferred surgical technique was circumferential dissection with devascularization followed by "en bloc" tumor removal. In addition, we resected infiltrated meningeal tissue (dura mater or the falx cerebri), followed by meningeal repair with periosteum or fascia lata.

Pathology

The pathology department reported two histologic features. Fusiform spindle cells with large hyperchromatic nuclei embedded in abundant pinkish stroma are described as fusocellular sarcoma and highly vascularized poorly differentiated pleomorphic cells consistent with high-grade sarcoma. No molecular diagnosis was done to determine specific subtypes. Figure 4 shows histologic characteristics of the lesion resected in Case 1.

Immunohistochemical studies in all patients were negative for glial fibrillary acidic protein (GFAP) but positive for vimentin and P53. Eighty percent had over 70% Ki-67 levels. Three cases initially diagnosed as giant cell glioblastoma, gliosarcoma, and hemangiopericytoma were changed to PIS based on immunohistochemical results.

In some of our cases, it was possible to identify focal chondroid differentiation, focal rhabdomyoblastic differentiation, and focal leiomyomatous differentiation, highlighting the rhabdomyoblastic type in the patients who presented intracerebral hemorrhage.

Adjuvant therapies

CTX before and after RT was administered to 68% of patients. The CTX regimen consisted of ifosphamide, cisplatin, and etoposide. About 60% of cases received CTX during the 1st month after surgery, while 12% received CTX 2 weeks after surgery. We treated only one case with radiosurgery and

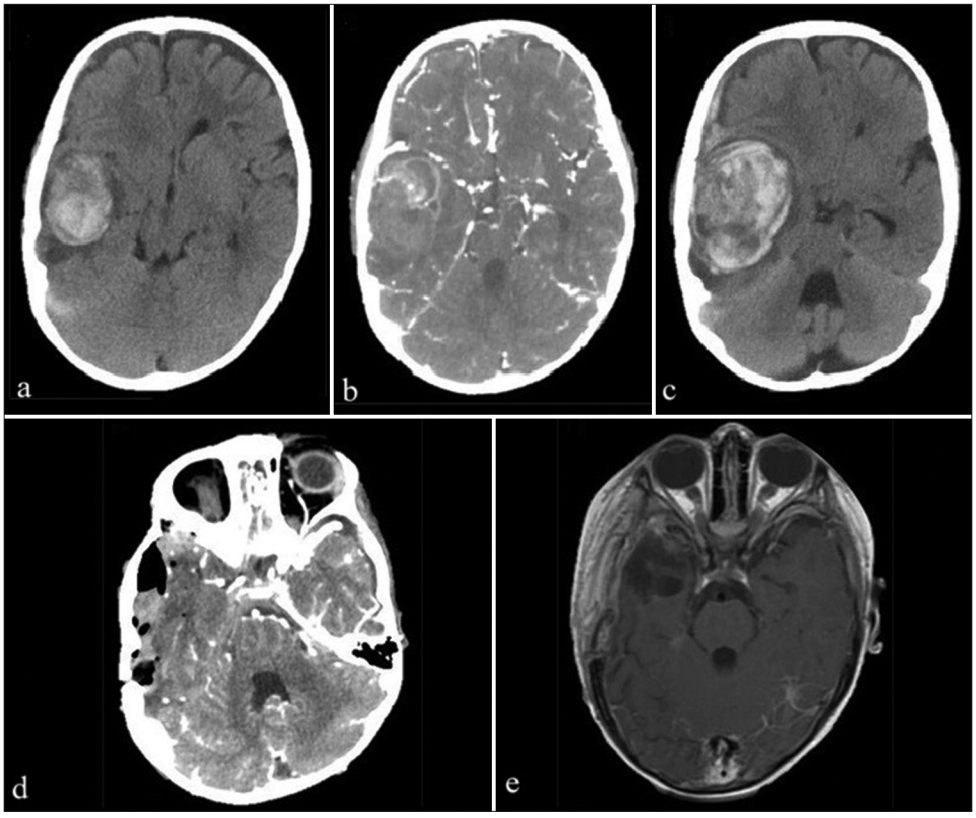

Figure 2: Brain scans of Case 12. (a and b) Initial computerized tomography (CT) scans show hemorrhagic brain tumor in the right temporal lobe; (c) repeat CT scan 3 days later shows expanding hemorrhage with midline shift, causing conscience deterioration (Glasgow comma scale of 4), warranting emergency surgery; (d) immediate postoperative CT scan confirms gross total resection and hemostasis; and (e) follow-up magnetic resonance imaging at 3 months shows no recurrence. The patient had an uneventful recovery for 2 years after surgery.

bevacizumab. The delay in adjuvant therapy could be attributed to late pathology reports, high patient volume, inconsistent follow-up, or poor accessibility to the hospital from rural areas.

Outcome

Eighteen patients were alive at the end of the study. Patients who did not receive CTX and RT on time had a greater recurrence rate and decreased overall survival [Table 2]. All patients given adjuvant therapy 2 weeks after surgery were alive in 1 year. In contrast, six out of 22 patients who did not get adjuvant therapies 2 weeks after surgery died in the 1st year of follow-up. Case 1, who is the longest survivor, also got adjuvant therapy 2 weeks after GTR [Figure 5].

Other representative Cases, 2 and 15, are shown in Figures 6 and 7, respectively.

DISCUSSION

The prevalence of PIS ranges from 0.1% to 4.3%.[1] Although many case reports and small case series have been reported in the literature,[1,2,8,13] large case series of PIS exclusively in children spanned several years and involved multiple centers [Table 3].[1-3]

We report 25 cases at a single hospital over 4 consecutive years (2020–2023), with a peak incidence of 11 cases in 2021. The incidence of primary sarcomas in children in Peru is very high compared to other countries.[3] The observed spike in the incidence of PIS during the study is similar to what was reported in other studies done around the same time.[12] Despite occurring at any age, PIS is likely more common in children than adults.[1,13] In our series, the oldest patient is 17 years old, the youngest is 2 years old, and the median age is 5 years, making our study the second youngest case series of PIS in children [Table 2]. Although the literature reports no significant differences in gender predilection [1-3,8,13], there were slightly more females than males in our series. The etiopathogenesis of PIS is not well established. Radiation is the most cited risk factor[1,16], but none of our patients was exposed in the past. We could not find an association with a predisposing genetic syndrome; however, one patient (Case 14) had Noonan syndrome, which is usually associated

Table 2: Histopathology, preoperative GCS, interventions, and survival time.

Case	Preop GCS	Surgery	Histopathology	Adjuvant therapy	CTX 2 weeks after surgery	Survival time*
1	14	1st GTR 2nd GTR (R)	Fusocellular sarcoma	CTX-RT-CTX (after 2nd Sx)	Yes	3 years
2	14	GTR	Fusocellular Sarcoma	CTX	No (>1 m)	5 months†
3	11	STR	High-Grade Sarcoma	No	No	1 day†
4	14	1st STR 2nd GTR (R) 3rd GTR	Fusocellular Sarcoma	CTX-RT-CTX (after 2nd Sx)	No (<1 m)	2 years†
5	14	GTR	Fusocellular Sarcoma	CTX	No (<1 m)	2 years
6	15	GTR	Fusocellular Sarcoma	Radiosurgery/CTX	-	2 years
7	10	GTR	High-Grade Sarcoma	CTX-RT-CTX	No (<1 m)	2 years
8	14	GTR	High-Grade Sarcoma	CTX-RT-CTX	No (<1 m)	2 years
9	12	GTR	High-Grade Sarcoma	CTX-RT-CTX	No (<1 m)	2 years
10	14	1st PR 2nd GTR 3rd GTR (R)	High-Grade Sarcoma	CTX-RT-CTX (after 2nd Sx)	Yes	2 years
11	14	1st GTR 2nd GTR (R)	High-Grade Sarcoma	CTX (after 1st Sx)	No (<1 m)	2 years
12	4	GTR	Fusocellular Sarcoma	CTX-RT-CTX	No (<1 m)	2 years
13	14	GTR	Fusocellular Sarcoma	CTX-RT-CTX	No (<1 m)	2 years
14	12	GTR	High-Grade Sarcoma	CTX-RT-CTX	No (>1 m)	2 years
15	11	STR	High-Grade Sarcoma	CTX-RT-CTX	No (<1 m)	2 years
16	8	GTR	High-Grade Sarcoma	RT	-	5 months†
17	12	1st STR 2nd GTR 3rd GTR	High-Grade Sarcoma	CTX-RT-CTX (after 2nd Sx)	Yes	1 year
18	7	STR	High-Grade Sarcoma	No	No	2 days†
19	13	1st GTR 2nd GTR	High-Grade Sarcoma	CTX-RT-CTX	No (<1 m)	1 year
20	10	1st STR 2nd GTR 3rd GTR	High-Grade Sarcoma	CTX-RT-CTX (after 2nd Sx)	No (>1 m)	1 year†
21	9	GTR	Fusocellular Sarcoma	CTX-RT-CTX	No (<1 m)	1 year
22	14	1st GTR 2nd STR	Fusocellular Sarcoma	CTX-RT-CTX (after 1st Sx)	No (>1 m)	7 months†
23	15	GTR	High-Grade Sarcoma	CTX-RT-CTX	No (<1 m)	1 year
24	14	GTR	High-Grade Sarcoma	CTX-RT-CTX	No (<1 m)	7 months
25	10	GTR	High-Grade Sarcoma	CTX-RT-CTX	No (<1 m)	3 months

GCS: Glasgow comma scale, GTR: Gross total resection, STR: Subtotal resection, PR: Partial resection, (R): Recurrence, CTX: Chemotherapy, RT: Radiotherapy, Sx: Surgery, †Deceased, *Follow-up until the end of the study.

Table 3: Large case series of PIS in children.

Study	Duration	Center	Cases	Median age (years)
Al-Gahtany M *et al.*[1]	1960–1999	Single	16	4.8
Benesch M *et al.*[2]	1988–2009	Multiple	19	9.7
Diaz Coronado RY *et al.*[3]	2005–2018	Multiple	70	6
Current study	2020–2023	Single	25	5

PIS: Primary intracranial sarcomas

with dysembryoplastic neuroepithelial tumor and low-grade astrocytoma but not aggressive sarcomas.[4,10,14] The initial clinical presentation was features of ICH (68%), seizure (20%), or motor deficit (12%) [Table 1]. About 80% of our patients with ICH or seizures had intracranial hemorrhage, similar to other studies.[1,2,8,9,13] This emphasizes prompt management with emergency craniotomy in patients with known or suspected PIS associated with intracranial hemorrhage. Given how rare PIS is, there is a danger of missing the diagnosis while pursuing other causes of intracranial hemorrhage. In our series, Case 3 had a small intracerebral hemorrhage, initially suspected to be due to an arteriovenous malformation, but angiography was negative; after a month, the patient returned to the hospital in a deteriorated state due to hemorrhagic PIS with a significant mass effect.

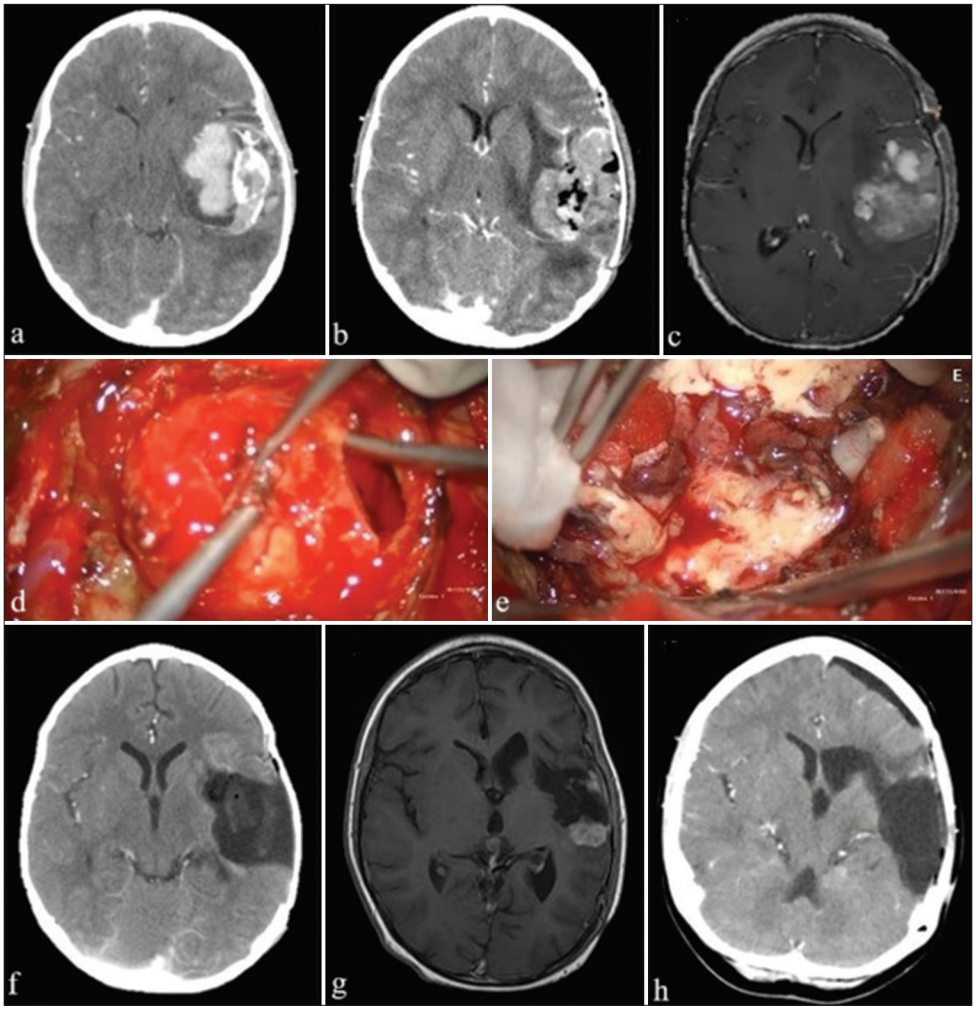

Figure 3: Case 10 brain scans and intraoperative images. (a) Hemorrhagic brain tumor in the left temporal and insular lobes on computerized tomography (CT) scan; (b) CT scan after emergency partial tumor resection and hemorrhage control; (c) preoperative magnetic resonance imaging (MRI) before second surgery; (d) exposed vascularized tumor during second surgery; (e) surgical bed after gross total resection (GTR) of tumor during second surgery; (f) postoperative CT scan confirms GTR; (g) MRI scan 18-months-after second surgery shows recurrent lesions; and (h) CT scan after GTR of recurrent lesions.

Nonspecific imaging features of PIS make diagnosis difficult. Most have a mixed solid-cystic appearance with perilesional edema and associated intracerebral hemorrhage. The solid component is enhanced by contrast due to hypervascularity, as also demonstrated in other studies.[1,2,8,13] MRI scans were like two recent studies on MRI characteristics of primary sarcomas of the central nervous system that found restriction on diffusion study of the solid component, hemorrhage at various stages, meningeal involvement, and necrosis.[9,15] The intracranial distribution of PIS is like other series [Table 4].[1-3]

In most of our cases, tumors were supratentorial and located proximal to the meninges, like other series.[1,2,8,9,12,13,15] For this reason, it is crucial to obtain images of the entire neuroaxis before and after surgery. However, in our case series, an MRI could not be performed since most of the patients underwent emergency craniotomy due to the deteriorating neurologic condition. In cases 2 and 16, the tumor involved the falx cerebri. Only one case evidenced an infratentorial lesion, which did not differ in imaging characteristics from supratentorial lesions. In our series, most lesions involve one or two cerebral lobes. However, the tumor in Case 18 involved three lobes, and Case 15 had a lesion in the basal ganglia. In our experience, tumor location influenced the type of incision, surgical approach, feasibility of GTR, and postsurgical outcome. Patients with superficial single lobe lesions had a better outcome, which is likely attributed to higher rates of GTR, than those with deeper or multi-lobe lesions.

Compared to adults, sarcomas in children tend to be either undifferentiated or differentiate into myocytes[1],

Table 4: Tumor location, intervention, and outcome of the largest case series on pediatric PIS.

Study	Cases	Location	Intervention	Outcome
Al-Gahtany M *et al.*[1]	16	14 had intracranial and 2 had intraspinal tumors 9 had supratentorial tumors 6 had CSF dissemination 1 had distant metastasis	9 achieved GTR 6 achieved PR 11 got RT The majority got multi-agent CTX	9 alive Median survival 4.6 years Survival range 1 month–16 years
Benesch M *et al.*[2]	19	17 had supratentorial tumors 0 had CSF dissemination or metastasis at diagnosis 1 had bone metastasis at recurrence	11 achieved GTR 5 achieved PR 1 got biopsied 11 got RT The majority got muti-agent CTX	10 alive Median follow-up 5.8 years 5-year OS and PFR 74% and 47%
Diaz Coronado RY *et al.*[3]	70	66 had supratentorial tumors 7 had metastasis	41 achieved GTR 27 achieved STR 55 got RT 48 got multi-agent CTX 18 got ICE before RT	Median follow-up 2.1 years 2-year PFS: 79% for ICE before RT 40% for local RT, then ICE 50% for local RT, then VAC 21% with RT only 67% with other CTX
Current study	25	24 had supratentorial tumors 1 had infratentorial tumor 0 had metastasis at diagnosis	18 achieved GTR 6 achieved STR 1 achieved PR 20 got RT 18 got CTX before RT 12% got adjuvant therapy 2 weeks after surgery	Still being monitored

PIS: Primary intracranial sarcomas, CSF: Cerebrospinal fluid, GTR: Gross total resection, PR: Partial resection, RT: Radiotherapy, CTX: Chemotherapy, OS: Overall survival, PFS: Progression-free survival, STR: Subtotal re-section, ICE: Ifosfamide, carboplatin, etoposide, VAC: Vincristine, actinomycin D, cyclophosphamide

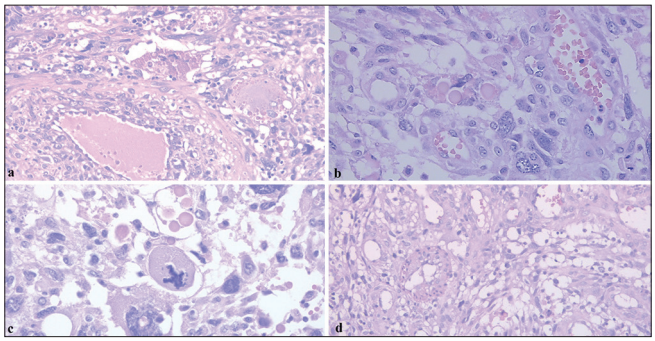

Figure 4: Histopathology of primary intracranial sarcoma in Case 1. (a) Intracranial sarcoma showing pleomorphic features and prominent vasculature. Hematoxylin and eosin (H&E) stain ×20 objective, 200 augments; (b) cytoplasmic hyaline globules in pleomorphic sarcoma. H&E stain ×40 objective, 400 augments; (c) atypical multipolar mitosis and marked nuclear anaplasia with the presence of cytoplasmic hyaline globules. H&E stain ×40 objective, 400 augments; and (d) intracranial sarcoma showing prominent vasculature and tumoral cells cytoplasmic vacuolization. H&E stain ×20 objective, 200 augments.

reflected by the histopathological diagnoses of high-grade undifferentiated sarcoma and spindle cell sarcoma in our series [Table 2]. Given the vast overlap of all the features of PIS with several conditions, immunohistochemical studies should be done for definitive diagnosis. Ki-67, a marker of proliferation, was > 70% in most cases, as seen in other series.[1,8,9,12,13,15,17] Furthermore, the lesions were negative for GFAP but stained strongly for vimentin and P53, consistent with the pattern in other studies.[1,2,8,9,12,13,15,17] PIS with focal rabdomyoblastic differentiation has been related to intracerebral hemorrhage,[8,18] similar to our case series. To specify PIS (DICER1), additional genetic study is required to confirm.[3,6,7,11,16,18] We did not determine sarcoma subtypes with molecular and genetic studies.

The mainstay of treatment is surgery, especially in patients with ICH. Most studies propose radical surgical resection [1-3,8,9,12,13,15,17] followed by adjuvant CTX and RT.[3,8,13] The most frequently used chemotherapeutic agents are ifosfamide, etoposide, carboplatin, vincristine, and cyclophosphamide. Combining ifosfamide, carboplatin, and etoposide with focal RT shows promise [Table 4].[8,13] The "sandwich" regimen, where CTX is used before and after focal RT, has had very good results.[2]

We achieved GTR in most cases, but only 12% received adjuvant therapies 2 weeks after surgery. We observed better disease control and lower recurrence rate in those who got adjuvant therapy

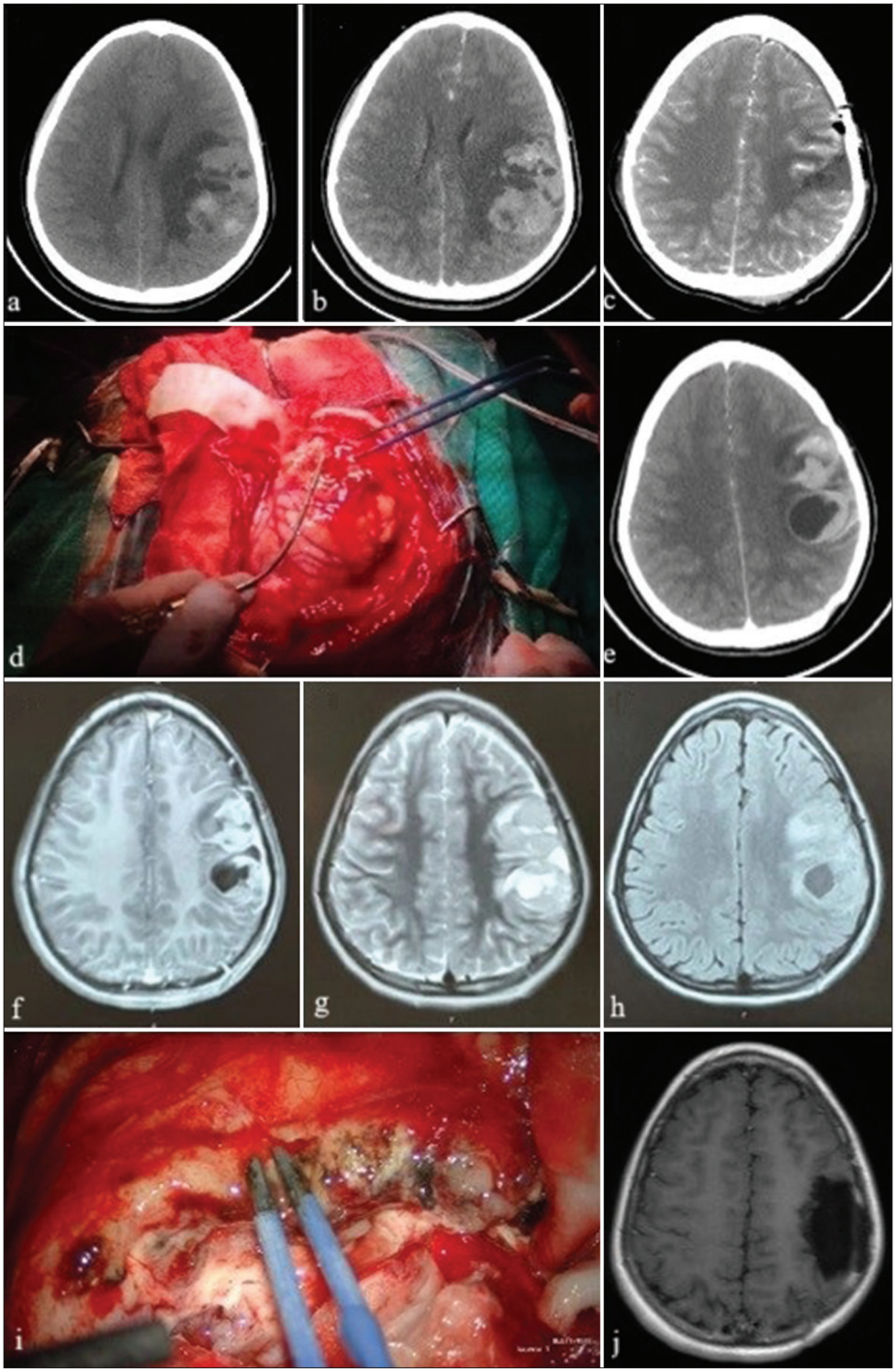

Figure 5: Brain scans and intraoperative images of Case 1. (a and b) Computerized tomography (CT) scans of left frontoparietal hemorrhagic tumor with mild midline shift; (c) postoperative CT scan confirms gross total resection; (d) exposed tumor during first surgery; (e) hyperintense lesions at site of initial surgery suggestive of recurrence 1 month after first surgery; (f-h) magnetic resonance imaging (MRI) scan of recurrent lesions at surgical site; (i) fluorescein-guided resection of recurrent lesions during second surgery; and (j) postoperative MRI confirms successful resection of recurrent lesions.

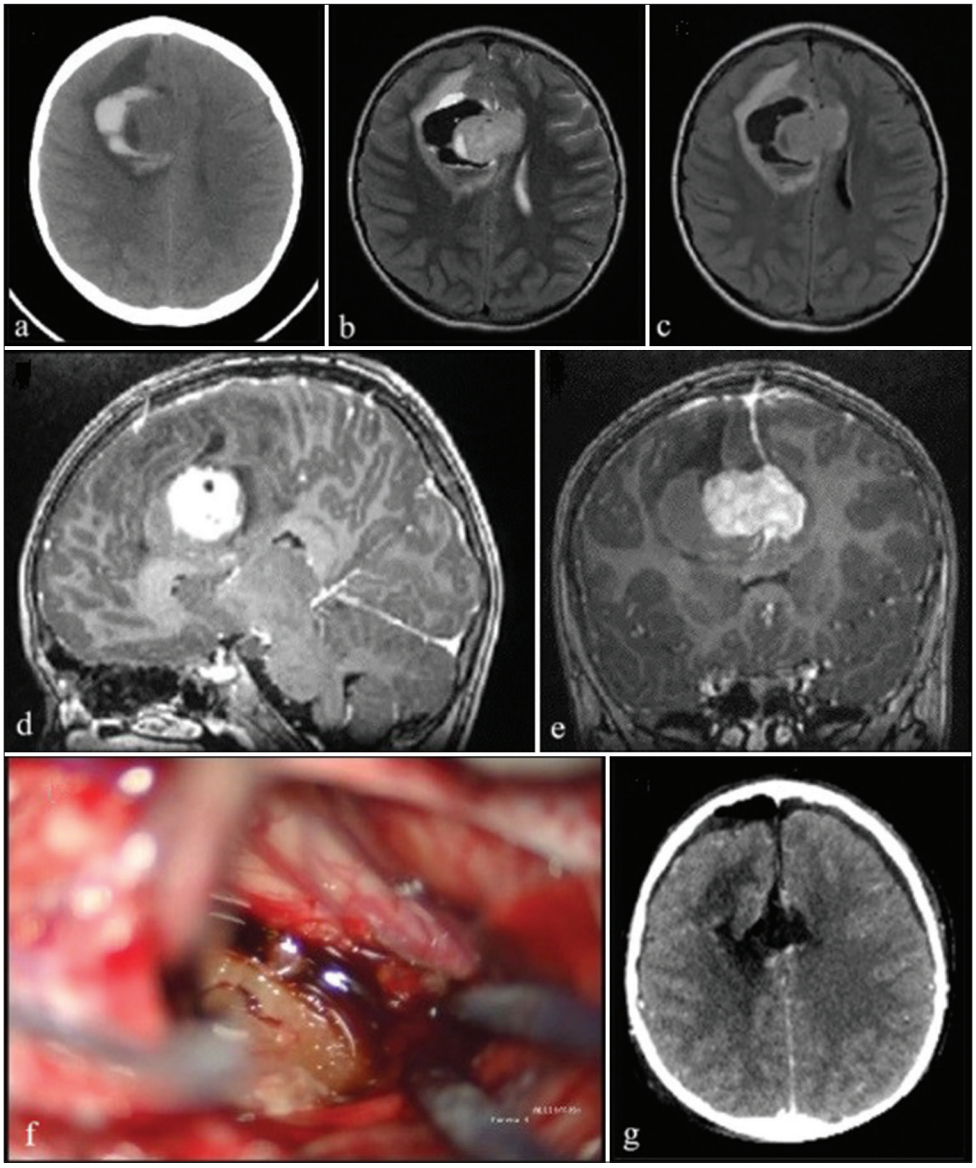

Figure 6: Scans and intraoperative image of Case 2. (a-c) Axial scans show hemorrhagic brain tumor with falx cerebri infiltration; (d and e) sagittal scans show midline hyperintense irregular mass attached to the falx cerebri; (f) intraoperative image of craniotomy and tumor resection through an interhemispheric approach; and (g) postoperative scan confirms successful gross total resection.

2 weeks after surgery compared to those who did not. In addition, all patients who got adjuvant therapy 2 weeks after surgery were alive for 1 year, emphasizing the importance of early adjuvant therapy. After surgery, Case 6 attained adequate disease control with radiosurgery and bevacizumab. The benefits of combination radiosurgery and bevacizumab require further investigation.[5,19]

Although the overall prognosis of PIS is poor, as observed in our study and corroborated by other papers, GTR followed by early CTX and RT might improve prognosis.[1-3,8,9,12,13,15,17] In case of recurrence, further surgery may be offered as long as resection remains safe. RT in patients under 3 years of age is controversial and is not indicated due to adverse effects.[1] Alternatives to RT in this age group are needed to prevent delay in starting adjuvant therapy. Improving access to health services will enhance overall survival in children with PIS.

Limitations and future directions

Despite the high incidence of PIS in children in Peru, this study should be cautiously generalized since it was carried out at a single center. Despite our case series being larger than other series, it is small to perform a quantitative statistical analysis. Therefore, we made a primarily descriptive analysis

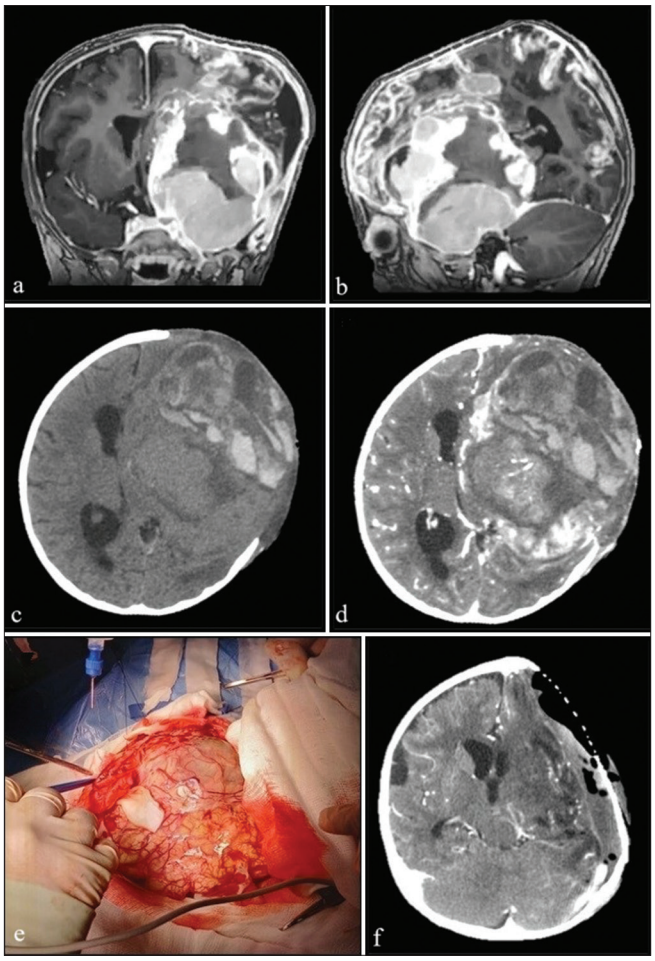

Figure 7: Scans and intraoperative image of Case 15. (a) Coronal cranial magnetic resonance imaging (MRI) after decompressive craniotomy for intracerebral hemorrhage show giant brain tumor in the left cerebral hemisphere; (b) sagittal cranial MRI shows a heterogenous mass with surrounding edema and diffuse intracerebral hemorrhage; (c and d) axial head computerized tomography (CT) scan without contrast and with contrast showing a mass in the left cerebral hemisphere, mild hemorrhage, and brain herniation through craniotomy; (e) intraoperative image during subtotal tumor resection, duraplasty with bovine pericardium, and coverage of cranial defect with titanium mesh; and (f) postoperative axial CT scan showing residual tumor with hemostatic control.

of the results. The number of surgical resections may modify or confound the true impact of early adjuvant therapy on patient survival. In addition, the short follow-up and study duration preclude concluding the long-term effects of treatment modalities on prognosis. Larger case series and prospective studies with genetic analysis are required to investigate the differences in survival among different therapeutic subgroups observed in this study.

CONCLUSION

Even though Peru is a country with a high prevalence of PIS in children, there was an increased incidence between 2020 and 2023 in tertiary hospitals for still unknown reasons. Patients often present with signs and symptoms of increased intracranial pressure due to intracerebral hemorrhage. Most are supratentorial cortical tumors located beneath the meninges. Imaging studies typically show intracerebral hemorrhage irregular contrast enhancement with perilesional edema. Immunohistochemical staining confirms the diagnosis. Although there is still no consensus and established protocol for the management of PIS, safe maximum resection followed by CTX and focal RT may offer the best long-term survival. Repeat surgery can be done for recurrent local disease. We devote more effort to fully understanding the genetics of PIS because molecular patterns could help personalize adjuvant therapy.

Acknowledgment

We would like our sincere thanks to the entire team at Vascular, Tumors and Functional Neurosurgery Service, Neurosurgery Department, Guillermo Almenara Irigoyen National Hospital, for their unwavering dedication and expertise in treating patient with brain tumors. Their collaborative efforts and exceptional care have greatly contributed to the presentation of this work.

We would also like to express our gratitude to the Latinoamerica Valerio Foundation, particularly to CFO Dr. Silvana Valerio, Director of research and innovation Dr. Andres Alvarez Pinzon, and Dr. Maria P. Fernandez for their valuable collaboration and support in the completion of this paper.

Ethical approval

The Institutional Review Board approval is taken, approval no is : NIT 753-2024-484 / Project 103-2024.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript, and no images were manipulated using AI.

REFERENCES

1. Al-Gahtany M, Shroff M, Bouffet E, Dirks P, Drake J, Humphreys R, *et al.* Primary central nervous system sarcomas in children: Clinical, radiological, and pathological features. Childs Nerv Syst 2003;19:808-17.
2. Benesch M, von Bueren AO, Dantonello T, von Hoff K, Pietsch T, Leuschner I, *et al.* Primary intracranial soft tissue sarcoma in children and adolescents: A cooperative analysis of the European CWS and HIT study groups. J Neurooncol 2013;111:337-45.
3. Diaz Coronado RY, Mynarek M, Koelsche C, Mora Alferez P, Casavilca Zambrano S, Wachtel Aptowitzer A, *et al.* Primary central nervous system sarcoma with DICER1 mutation-treatment results of a novel molecular entity in pediatric Peruvian patients. Cancer 2022;128:697-707.
4. El-Ayadi M, Ansari M, Kühnöl C, Bendel A, Sturm D, Pietsch T, *et al.* EPID-18. Noonan syndrome can be associated with high grade glioma, a report of two cases. Neuro Oncol 2017;19:vi72.
5. Flannery T, Kano H, Niranjan A, Monaco EA 3rd, Flickinger JC, Kofler J, *et al.* Gamma knife radiosurgery as a therapeutic strategy for intracranial sarcomatous metastases. Int J Radiat Oncol Biol Phys 2010;76:513-9.
6. Kamihara J, Paulson V, Breen MA, Laetsch TW, Rakheja D, Shulman DS, *et al.* DICER1-associated central nervous system sarcoma in children: Comprehensive clinicopathologic and genetic analysis of a newly described rare tumor. Mod Pathol 2020;33:1910-21.
7. Koelsche C, Mynarek M, Schrimpf D, Bertero L, Serrano J, Sahm F, *et al.* Primary intracranial spindle cell sarcoma with rhabdomyosarcoma-like features share a highly distinct methylation profile and DICER1 mutations. Acta Neuropathol 2018;136:327-37.
8. Lafay-Cousin L, Lindzon G, Taylor MD, Hader W, Hawkins C, Nordal R, *et al.* Successful treatment of primary intracranial sarcoma with the ICE chemotherapy regimen and focal radiation in children. J Neurosurg Pediatr 2016;17:298-302.
9. Lazarte-Rantes C, Pillaca-Cruzado O, Baca-Hinojosa N, Mamani W, Lee-Diaz J, Ugas-Charcape CF. MRI findings of primary intracranial sarcomas in children. Pediatr Radiol 2023;53:1698-703.
10. Lodi M, Boccuto L, Carai A, Cacchione A, Miele E, Colafati GS, *et al.* Low-grade gliomas in patients with noonan syndrome: Case-based review of the literature. Diagnostics (Basel) 2020;10:582.
11. Louis DN, Perry A, Wesseling P, Brat DJ, Cree IA, Figarella-Branger D, *et al.* The 2021 WHO classification of tumors of the central nervous system: A summary. Neuro Oncol 2021;23:1231-51.
12. Lovaton-Espadin R, Alaba-Garcia W. EPID-25. Six consecutive cases of primary intracranial sarcoma in children in two private institutions from lima during COVID-19 pandemic. Neuro Oncol 2023;25:v121.
13. Maher OM, Khatua S, Mukherjee D, Olar A, Lazar A, Luthra R, *et al.* Primary intracranial soft tissue sarcomas in children, adolescents, and young adults: Single institution experience and review of the literature. J Neurooncol 2016;127:155-63.
14. McWilliams GD, SantaCruz K, Hart B, Clericuzio C. Occurrence of DNET and other brain tumors in Noonan syndrome warrants caution with growth hormone therapy. Am J Med Genet A 2016;170A:195-201.
15. Melgar-Granados F, Segundo CH. Primary intracranial spindle cell sarcoma with features similar to rhabdomyosarcoma in pediatric patients: Cases series 2020-2021. Intercien Méd 2023;13:50-8.
16. Niwa J, Hashi K, Minase T. Radiation induced intracranial leiomyosarcoma: Its histopathological features. Acta Neurochir (Wien) 1996;138:1470-1.
17. Rueda-Franco F, López-Corella E. Sarcomas in the central nervous system of children. Pediatr Neurosurg 1995;22:49-56.
18. Sakaguchi M, Nakano Y, Honda-Kitahara M, Kinoshita M, Tanaka S, Oishi M, *et al.* Two cases of primary supratentorial intracranial rhabdomyosarcoma with DICER1 mutation which may belong to a "spindle cell sarcoma with rhabdomyosarcoma-like feature, DICER1 mutant". Brain Tumor Pathol 2019;36:174-82.
19. Yang G, Yuan Z, Ahmed K, Welsh EA, Fulp WJ, Gonzalez RJ, *et al.* Genomic identification of sarcoma radiosensitivity and the clinical implications for radiation dose personalization. Transl Oncol 2021;14:101165.

How to cite this article: Zumaeta J, Murga A, Santiago Rea N, Flores-Sanchez JD, Lazon M, Palacios Santos F, *et al.* Increase of primary intracranial sarcoma in children: Clinical manifestations, diagnosis, and management. Surg Neurol Int. 2024;15:426. doi: 10.25259/SNI_202_2024