The Impact of Surgical Resection and Adjuvant Therapy on Survival in Pediatric Patients with Atypical Teratoid/Rhabdoid Tumor: Systematic Review and Pooled Survival Analysis

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Key words
- Atypical teratoid/rhabdoid tumor
- BRG1
- INI1
- Pediatric
- Survival

Abbreviations and Acronyms
ATRT: Atypical teratoid/rhabdoid tumor
BRG1: Brahma-related gene-1
CNS: Central nervous system
CSI: Craniospinal irradiation
GTR: Gross total resection
INI1: Integrase interactor 1
IRS-III: Third Intergroup Rhabdomyosarcoma Study
OS: Overall survival
PR: Partial resection
RT: Radiotherapy
STR: Subtotal resection
WHO: World Health Organization

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BACKGROUND: **Atypical teratoid/rhabdoid tumor (ATRT) is a rare malignant neoplasm in the pediatric population. ATRT is characterized by rhabdoid cells combined with the loss of either the INI1 (integrase interactor 1) or BRG1 (Brahma-related gene-1) protein.**

OBJECTIVE: **To systematically review and analyze patient and tumor characteristics, prognosis, and impact of treatment on survival in pediatric patients with ATRT confirmed by alterations in INI1 or BRG1. This systematic review is the first to include only pediatric cases of ATRT confirmed with either INI1 or BRG1 alterations.**

METHODS: **MEDLINE was searched using the terms "atypical teratoid/rhabdoid tumor" AND "paediatric/pediatric." Cases were included if confirmed by loss of INI1 or BRG1. The extracted dataset was analyzed using descriptive statistics, log-rank test, and Kaplan-Meier survival analysis via SPSS.**

RESULTS: **A total of 38 articles were included in this study. The average age at diagnosis was 3 years. The most common locations reported are the supratentorial region and cerebral hemispheres. Ninety-three patients were reported to show evidence of dissemination. The average overall survival was 29 months. A significant difference in survival was noted between the tumor location groups, particularly worse outcomes for patients with spinal ATRT ($P < 0.001$). Extent of resection and adjuvant therapy were significant for survival ($\chi^2 = 10.107$, $P = 0.018$ and $\chi^2 = 20.38$, $P < 0.0001$, respectively).**

CONCLUSIONS: **ATRT of the central nervous system in pediatric populations is a rare neoplasm associated with a poor prognosis in most patients. Future studies should be directed to find a standardized treatment protocol.**

INTRODUCTION

Central nervous system (CNS) atypical teratoid/rhabdoid tumor (ATRT) is a rare and clinically aggressive tumor that most often affects children aged 3 years and younger but can occur in older children and adults.[1,2] CNS ATRT is a histologically heterogeneous neoplasm characterized by scattered rhabdoid cells and large epithelioid cells accompanied by primitive neuroectodermal cells and mesenchymal and/or glial cells.[1] ATRT is part of a more prominent family of rhabdoid tumors. In this review, the term ATRT refers to CNS tumors only, and the term rhabdoid tumor reflects the possibility of both CNS and non-CNS tumors. Unless expressly noted in the text, this systematic exclusively refers to CNS ATRT.

In pediatric patients, approximately one half of ATRTs arise in the posterior cranial fossa.[3] ATRT is associated with somatic and germline of SMARCB1 (SWI/SNF-related, matrix-associated, actin-dependent regulator of chromatin, subfamily B, member 1) and SMARCA4 (SWI/SNF-related, matrix-associated, actin-dependent regulator of chromatin, subfamily A, member 4), which are tumor suppressor genes that code for the proteins INI1 (integrase interactor 1) and BRG1 (Brahma-related gene 1), respectively.[4] Thus, the 2021 World Health Organization (WHO) classification of CNS tumors highlights that a neuropathologic examination is not sufficient for diagnosis, and a genetic examination is mandatory for confirmation. There is no standard treatment for pediatric patients with ATRT. Multimodality treatment consisting of surgery, chemotherapy, and radiation therapy is under evaluation by clinical trials. Recent data from the AT/RT registry suggests that up to 30% of patients present with disseminated disease.[5-7] Dissemination likely occurs through the leptomeningeal pathway, affecting various locations of the CNS and even extra-CNS organs. Therefore, it is not surprising that almost 35% are prone to synchronous and multifocal tumors.[8-11]

The prognostic factors affecting the survival of patients with ATRT remain unclear. Most published data on outcomes of patients with ATRT are from small series and are retrospective. Initial retrospective studies reported an average survival from diagnosis of only about 12 months.[12-16] In a retrospective report, 2-year overall survival (OS) was better for patients who underwent a gross total resection (GTR) than for those who had a subtotal resection (STR). However, in this study, the effect of radiation therapy on survival was less clear.[15] There are reports of long-term survivors.[17] Improved survival has been reported for those who received intensive multimodality therapy.[6,10]

Given the limited number and dispersal of ATRT cases in multiple case reports and case series, patient and tumor characteristics, overall prognosis, and impact of extent of resection and adjuvant therapy remain unclear. In addition, previously published systematic reviews and meta-analyses have included tumors without a genetic confirmation with INI1 or BRG1 alterations, resulting in an analysis of a heterogeneous population who may contain tumors that are not molecularly defined as ATRT. This systematic review analyzed patient and tumor characteristics, prognosis, and impact of treatment on prognosis in pediatric patients with ATRT. The primary objective of this study was a pool-analysis of all pediatric cases of ATRT confirmed by alterations in INI1 or BRG1. This review is the first to include only pediatric cases of ATRT confirmed with either INI1 or BRG1 alterations. The secondary objective of our study was to examine predictive factors for survival. Our primary hypothesis was that the extent of survival would be influenced by age, gender, the extent of surgical resection, adjuvant therapy, and tumor location.

METHODS

This systematic review is reported per the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Our protocol was developed, registered, and published via the international prospective register of systematic reviews (PROSPERO) (registration number CRD42022300996).[18]

Research Question

In patients with genetically confirmed ATRT, what are the patient and tumor characteristics and how does age, gender, tumor location, the extent of resection, and adjuvant therapy affect survival outcomes?

Inclusion Criteria

Articles that included pediatric ATRT cases were included if the diagnosis was confirmed by alterations of either SMARCB1/SMARCA4 or INI1/BRG1. Studies reported before the new update of the WHO 2021 Classification CNS tumors were included if they confirmed their diagnosis with the criteria.

Search Strategy

We conducted a systematic review using MEDLINE (Ovid). We filtered results to studies published in English exclusively. We reviewed all articles published before December 2021. Search terms included "Atypical teratoid rhabdoid tumour" and "paediatric." References of relevant articles were used to supplement the scope of our search. The search strategy is shown in **Supplementary Table 1**.

Study Selection

All the articles were exported into Rayyan, a professional research software widely used by collaborators for ease of study selection decisions.[19] First, a minimum of 2 reviewers independently screened the titles and abstracts of the identified articles against the population, intervention, comparison, outcome, setting, and study design (PICOS) criteria defined in the protocol. Any disagreement between the reviewers' decisions prompted further discussion. If a disagreement persisted, a third reviewer resolved the conflict. The full texts of the remaining articles were also retrieved and screened independently by a minimum of 2 reviewers.

Data Extraction

Data extraction was performed in 2 stages: a pilot stage and a proper stage. The pilot stage consisted of having multiple authors, each going through the same 10 selected articles to extract data. This strategy was adopted to ensure that all participant authors could extract data accurately to ensure homogeneity in the data reporting and ensure that the data collection sheet captured all relevant and essential information from the included studies.

Studies that met our inclusion criteria were read in full text, and the following data were extracted, summarized, and tabulated in an Excel proforma sheet: title, year of publication, name of the first author, study design, study location, population size, participants' characteristics (including sex, mean age, and age range), neuropathologic diagnosis, intervention, and outcomes of care including follow-up durations, numbers of deaths reported, and survival outcomes.

Data Analysis

We collected patient demographics, tumor characteristics, survival, and treatment data. The data were analyzed using SPSS version 26 (IBM Corp., Armonk, New York, USA) for descriptive statistics and to deploy a log-rank test, assessing for differences in outcomes among GTR, STR, partial resection (PR), and biopsy. A log-rank test was also used to assess for differences in outcomes among those who received radiotherapy (RT), chemotherapy, immunotherapy, RT and chemotherapy, chemotherapy and proton therapy, and chemotherapy and immunotherapy. Kaplan-Meier curves were used to estimate the survival function.

A multivariate linear regression was performed to assess and predict survival (months) from the explanatory variables: tumor location, dissemination, extent of resection, and adjuvant therapy. Linearity was assessed by partial regression plots and a plot of studentized residuals against the predicted values. Independence of residuals was assessed by a Durbin-Watson statistic. Homoscedasticity was assessed by visual inspection of a plot of studentized residuals versus unstandardized predicted values. Multicollinearity was assessed by tolerance values >0.1. Studentized deleted residuals were assed for values $>\pm 3$ standard deviations, or leverage values >0.2, and values for Cook distance >1. The assumption of normality was assessed by a Q-Q plot. Regression coefficients and standard errors were tabulated. A P value ≤ 0.05 was considered statistically significant. Patients with

missing data for the variables were excluded from the analysis.

RESULTS

A total of 237 results were found from the MEDLINE search (Figure 1). Of the 237 results, 184 articles were deemed irrelevant to this study during the title/abstract screening stage. Thirty-eight articles were deemed eligible after matching our eligibility criteria. Articles were exuded during full-text screening for reasons including adult populations, wrong outcomes, or articles that included ATRT cases with no confirmed diagnosis per the new WHO definition.

Our systematic review found 165 pediatric patients diagnosed with ATRT from the 39 articles included in this study (Table 1). Supplementary Table 2 includes all the patients included in the pooled analysis (1, 2, 4–9, 11–42). Of the 165 patients, the average age was 2.49 (±2.94) years, ranging from 0.01 to 15.54 years. Of the 165 patients, 70 (40.7%) were female, 75 (43.6%) were male, and 27 (15.7%) were not identified.

Only 9 (6%) of the tumors were in the spinal cord, whereas the remaining 156 (94%) were split between supratentorial and infratentorial locations. The most common location was the infratentorial region ($n = 84$, 48.8%), followed by supratentorial region ($n = 72$, 41.9%). Only 7 patients did not have their tumor location reported ($n = 7$, 4.1%) (Figure 2). Over the entire course of the disease, 16 patients (9.3%) were known to have experienced disseminated ATRT.

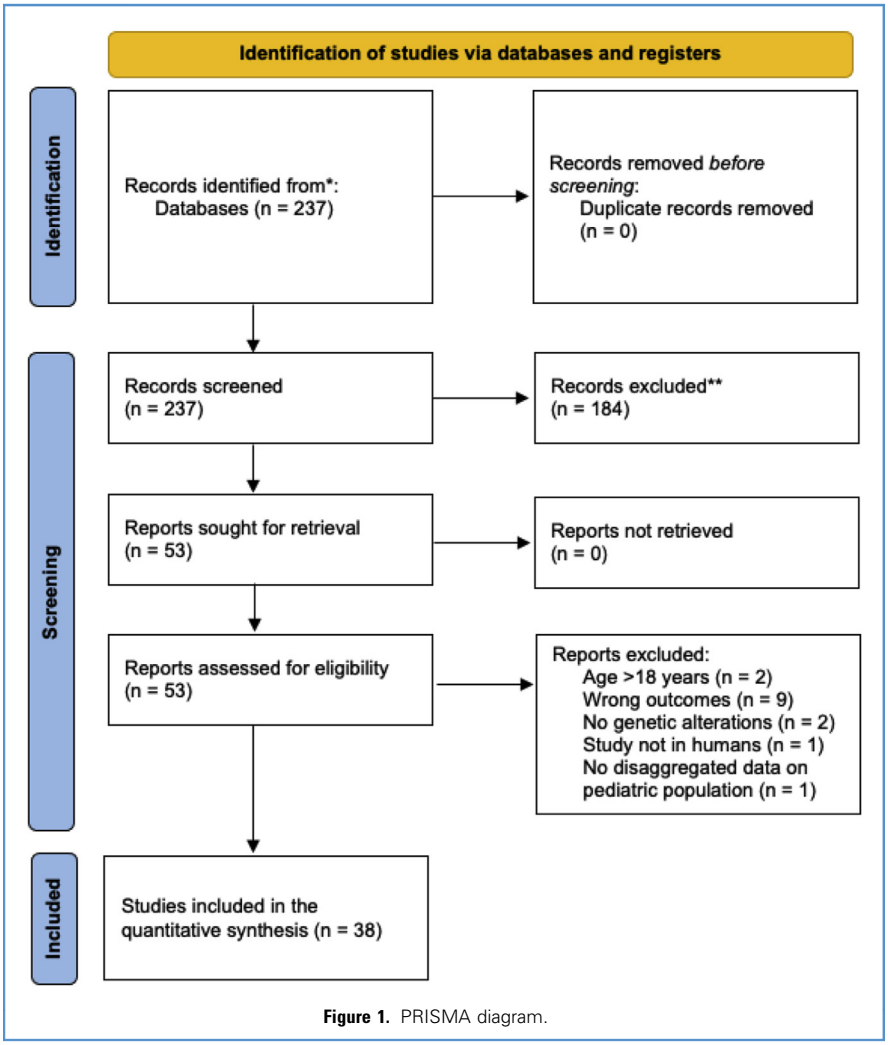

Figure 1. PRISMA diagram.

Tumor location was a statistically significant factor on the log-rank test ($\chi^2 = 9.471$; $P = 0.009$), showing significantly low survival for spinal tumors, compared with supratentorial and infratentorial tumors. The Kaplan-Meier curve is shown in Figure 3.

Of the 165 patients, 71 (24%) had GTR, 47 (42%) had STR, 5 (2.9%) had PR, and 8 (4.7%) had a biopsy. The extent of resection was not reported in 16 cases, and 25 patients did not have any surgical interventions. This situation is a consequence of metastatic/disseminated disease in which the intracranial/spinal tumors were inoperable. GTR was defined as 100% tumor resection with a concurrent absence of any visible residual tumor in the immediate postoperative magnetic resonance imaging or computed tomography. Most studies defined STR as >90% tumor resection. PR was defined as <50% tumor resection.

Regarding adjuvant therapy, 72 (41.9%) received combined RT and chemotherapy, 2 (1.2%) received RT only, 29 (16.9%) received chemotherapy only, 3 (1.7%) received immunotherapy only, 3 (1.7%) received combined chemotherapy and immunotherapy, and 1 (0.6%) received combined RT and immunotherapy. Forty patients (23%) did not receive adjuvant therapy, and in 7 cases, it was unknown if any adjuvant therapy was administered.

Of the 165 patients, 93 (54.1%) had died of their disease, with an average time to death of 0.85 ± 1.26 years (range, 0.01–8.84 years). Seventy-two patients (41.9%) were alive at last follow-up, with a mean follow-up of 3.74 ± 3.5 years (range, 0.08–15.54 years). Two patients experienced recurrent disease, after 1 month ($n = 1$) and 1 year ($n = 1$). Sixty-five patients had no recurrence at follow-up, with follow-up ranging from 0.005 to 15.54 years.

Of the 71 patients who had GTR, 35 (21.2%) had died, with an average time to death of 1.12 years after surgery. Forty-seven patients (42%) had STR, and 12 (57%) had died, with time to death ranging from postoperative to 2.5 years after surgery. The 1 patient who had a biopsy died 2.1 years after diagnosis. When comparing those who received GTR, STR, PR, biopsy, and no surgical intervention, there was a significant difference on the log-rank test ($\chi^2 = 10.107$; $P = 0.018$), showing a significant survival

Table 1. Patient and Tumor Characteristics from the Included Studies

Characteristics	Values
Patient	
Age at diagnosis (years), mean (SD)	2.49 (2.94)
Female gender	70 (40.7)
Tumor	
Location	
Supratentorial	72 (41.9)
Infratentorial	84 (48.8)
Spine	9 (6)
Unspecified	7 (4.1)
Dissemination	16 (9.3)
Treatment	
Surgery	
Gross total resection	71 (24)
Subtotal resection	47 (42)
Partial resection	5 (2.9)
Biopsy	8 (4.7)
No surgical intervention	25 (14.5)
Unspecified	16 (9.3)
Adjuvant therapy	
Chemotherapy, proton therapy	15 (8.7)
Chemotherapy only	29 (16.9)
Chemotherapy, RT	72 (41.9)
Chemotherapy, immunotherapy	3 (1.7)
Immunotherapy only	3 (1.7)
RT, immunotherapy	1 (0.6)
RT	2 (1.2)
No adjuvant therapy	40 (23.3)
Unspecified	7 (4.1)
Prognosis	
Alive at follow-up	72 (41.9)
Follow-up (years), mean (SD, range)	3.74 (3.5, 0.08 −15.54)
Death	93 (54.1)
Time to death (years), mean (SD, range)	0.85 (1.26, 0.01 −8.84)
Unspecified	7 (4.1)

Values are number (%) except where indicated otherwise.
SD, standard deviation; RT, radiotherapy.

advantage with GTR compared with other extents of resection. The Kaplan-Meier curve is shown in Figure 4.

Of the 28 patients who received combined RT and chemotherapy, 15 were alive at follow-up, ranging from 6 months to 17 years. Time to death for the remaining 13 of these 28 ranged from 3 months to 3 years after diagnosis. There were no patients alive at follow-up in the RT only, chemotherapy only, stereotactic radiosurgery only, and no adjuvant therapy groups. The 8 patients treated with RT died 2 weeks to 14 years after diagnosis. The 1 patient who received chemotherapy died 10 years after diagnosis. The 2 patients treated with stereotactic radiosurgery died 23 and 27 months after diagnosis. Of the 4 patients who did not receive adjuvant therapy, time to death ranged from the immediate postoperative period to 3 months after surgery. When comparing those who received RT and chemotherapy, RT only, and no adjuvant therapy, there was a significant difference in survival ($\chi^2 = 20.38$; $P < 0.0001$). Patients who received RT and chemotherapy had a significant increase in survival compared with patients who received RT alone ($\chi^2 = 11.42$; $P = 0.0007$) and patients who did not receive adjuvant therapy ($\chi^2 = 25.71$; $P < 0.0001$). There was no significant difference between the Kaplan-Meier curve, as shown in Figure 5. Gender was a statistically insignificant factor for survival ($\chi^2 = 2.378$; $P = 0.305$). The different chemotherapy and RT used in the eligible study are collated in Table 2.

A multiple regression was run to predict survival from tumor location, dissemination, extent of surgical resection, and adjuvant therapy. The multiple regression model statistically significantly predicted survival (months), $F_{4,29} = 3.539$; $P < 0.018$; adjusted $R^2 = 0.235$. Dissemination and adjuvant therapy weighed the most statistical significance to the prediction ($P < 0.05$). Regression coefficients and standard errors can be found in Table 3.

Quality Assessment: Risk of Bias and Critical Appraisal

The studies included in this systematic review were case reports and case series. The risk of bias could not be assessed using the Cochrane Collaboration's tool for assessing the risk of bias. The JBI Critical Appraisal Checklist for Case Reports appraised the included case reports and case series. No concerns were noted over the quality of the included case reports and case series, although limitations to our conclusions are noted. On analysis, case reports and case series on pediatric ATRT were prime examples of the importance of this type of study to derive hypothesis-generating research.

DISCUSSION

Summary of the Main Findings

Following the 2021 WHO Classification of Tumors of the CNS, and with a particular focus on ATRT, we included only patients with a confirmed neuropathologic diagnosis with loss of function mutations of either INI1 or BRG1. Our systematic review has shown that the OS of pediatric ATRT was 29 months. In addition, factors such as supratentorial location, GTR, dissemination, and chemoradiotherapy are statistically significant to improve survival.

Tumor Location and Dissemination

A study conducted by Rao et al.[40] found the most common location for the tumor in the infratentorial region (61.8%), similar to our review, which found 48.8% of the reviewed cases in the infratentorial region. Pediatric ATRTs have been found in males predominantly,[40-42] in contrast to the prevalence of ATRTs in adults, who have reported higher rates in females.[43] Although our study did find a slightly higher prevalence in males (43.6%) compared with females (40.7%), there was a significant number of patients (15.7%) who were unidentifiable. Recently gene-expression profiles and DNA methylation divided ATRT into 3 epigenetic subgroups (ATRT-MYC, ATRT-SHH, and ATRT-TYR), each with distinct clinical features.[44] A study[45] found that the subgroup ATRT-TYR was more common in the infratentorial region, whereas ATRT-MYC mainly occurred in the supratentorial region, with ATRT-SHH occurring equally in both regions. However, no study has been conducted on how the various subgroups affect the mortality in either adult or pediatric patients.

ATRT is known to spread through the subarachnoid space and can disseminate to various regions.[46] In our study, 16 patients were reported to show signs of

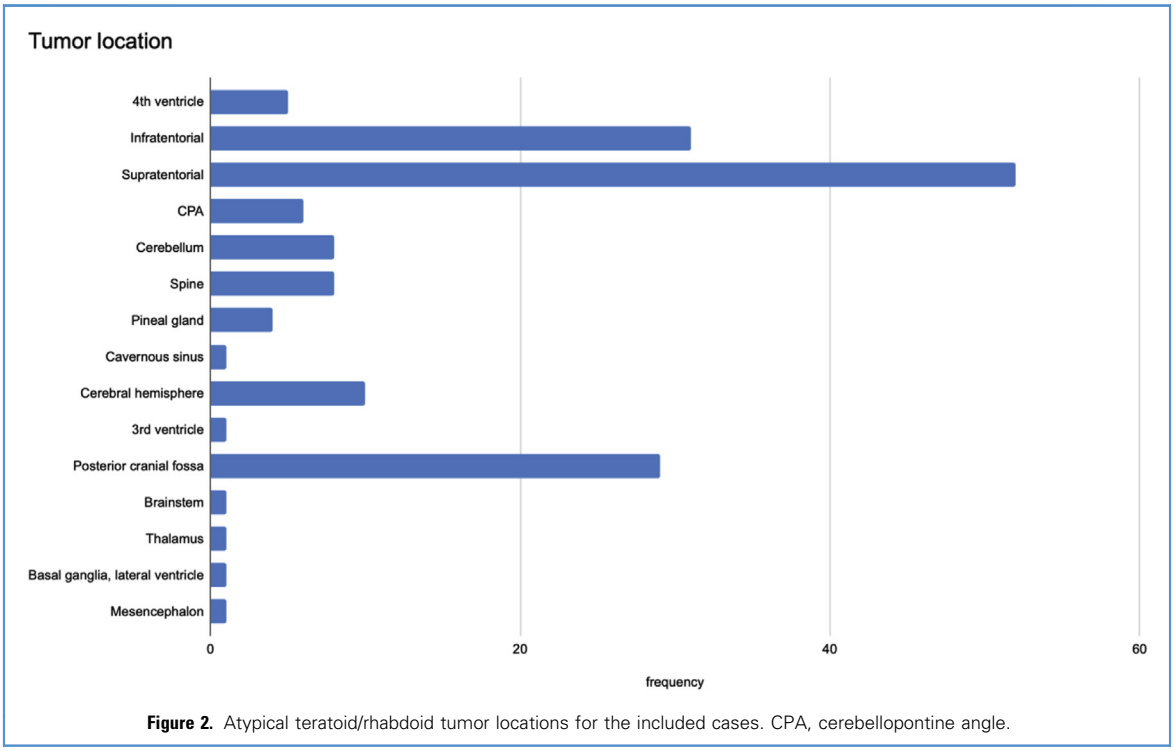

Figure 2. Atypical teratoid/rhabdoid tumor locations for the included cases. CPA, cerebellopontine angle.

dissemination; however, this number could be low because a variety of studies did not investigate dissemination. Dissemination seemed to occur in children 3 years or younger; 14 of the 16 patients with dissemination were younger than 3 years; this finding is similar to a study conducted by Tekautz et al. (2005).[39] Although dissemination usually occurs in the CNS, a study in adult patients has found distant metastasis to the lungs.[47]

The Impact of Extent of Surgical Resection

Treatment options vary, with surgery being the primary treatment option. Surgery involves patients undergoing surgical resection of the primary lesion and can be classified into 3 groups based on the percentage of tumor removed; GTR (no tumor), STR (>90% of tumor removed), and PR (<50% of tumor removed).[35] Our study found a considerable difference in the survival of patients depending on the extent of surgical resection, with patients who underwent GTR having a median survival of 4.167 years compared with only 0.9 years for STR and 0.639 years for PR, which aligns with the results from other studies that found a significant difference in survival between GTR and STR and only a slight difference between STR and PR.[6,21,48]

The Impact of Adjuvant Therapy

There are a variety of adjuvant therapies given to treat ATRT. From our analysis, the combination of chemotherapy and RT is the most common (41.9%), followed by only chemotherapy (16.9%), and chemotherapy and proton therapy (8.7%). A combination of chemotherapy and RT seemed to have helped the patients the greatest, with a median survival of 8.842 years, followed by a combination of chemotherapy and proton therapy, with a median survival of 4.942 years. Patients who solely received chemotherapy had the lowest median survival (0.833 years).

Given the rarity of ATRTs and the wide range of therapy regimens used, no standard therapeutic strategy has been developed. Patients treated with multiple diverse chemotherapeutic protocols are frequently included in case studies, making therapy standardization challenging. **Table 2** summarizes the included studies and chemotherapeutic regimens. Intrathecal chemotherapy as an adjunct to systemic chemotherapy is gaining lots of traction as evident by our included studies. Athale et al.[16] found that even without GTR, patients who received multiagent chemotherapy survived better, although this impact was especially noticeable in those <3 years old who did not receive RT. Without radiation, intrathecal chemotherapy improved OS (10.5 months vs. 6.5 months; $P = 0.011$).[16] Modified Third Intergroup Rhabdomyosarcoma Study (IRS-III) therapies include intrathecal chemotherapy as well as multiagent chemotherapy and focal radiation in patients who have nonmetastatic disease. Although the numbers in all reports are modest, there seems to be better survival for patients treated with IRS-III–based de novo treatment and high-dose alkylating agent compared with other chemotherapeutic regimens.[16] However, it is difficult to pinpoint the impact of the IRS-III regimen alterations. As previously indicated, intrathecal ATRT treatment and directional chemotherapy have been linked to better survival in patients who did not undergo radiation.[16]

Delaying radiation in patients with ATRT <3 years old was associated with a significantly bad prognosis, and several clinical trials use targeted radiation in

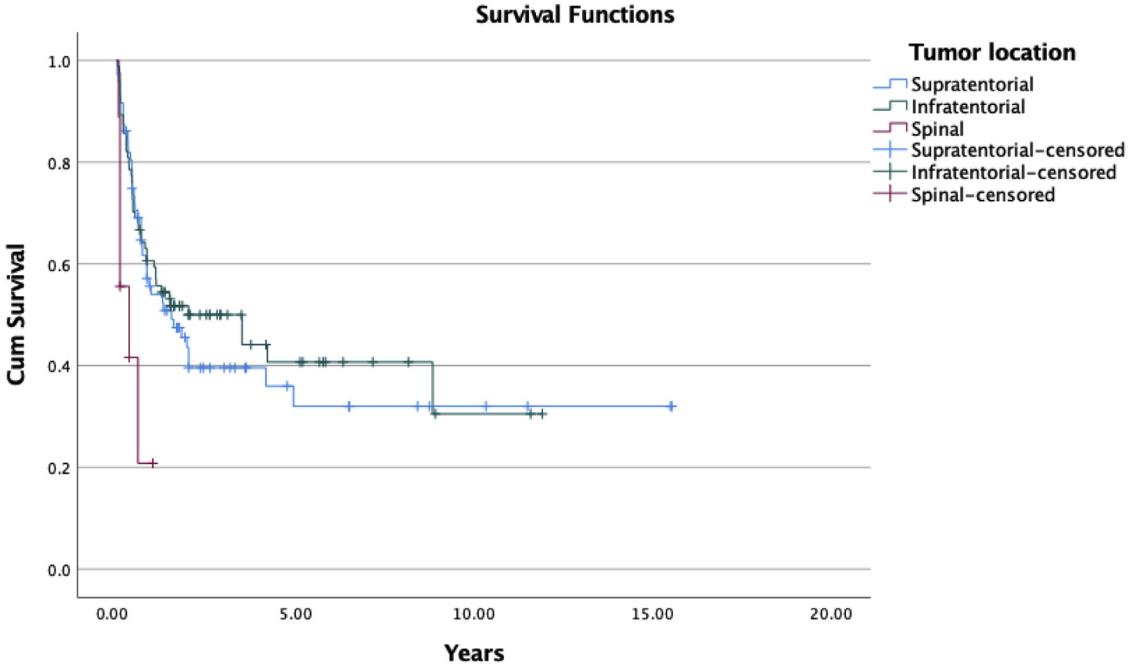

Figure 3. Kaplan-Meier curve for the tumor location. Cum, cumulative.

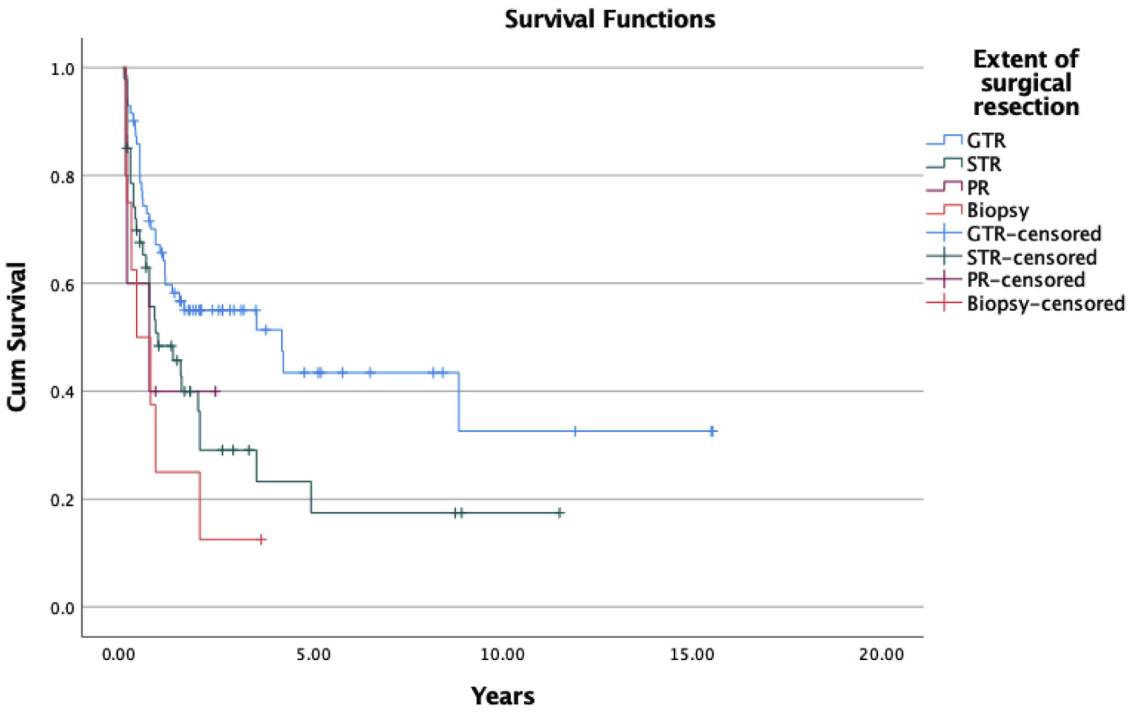

Figure 4. Kaplan-Meier curve for the extent of resection. Cum, cumulative; GTR, gross total resection; STR, subtotal resection; PR, partial resection.

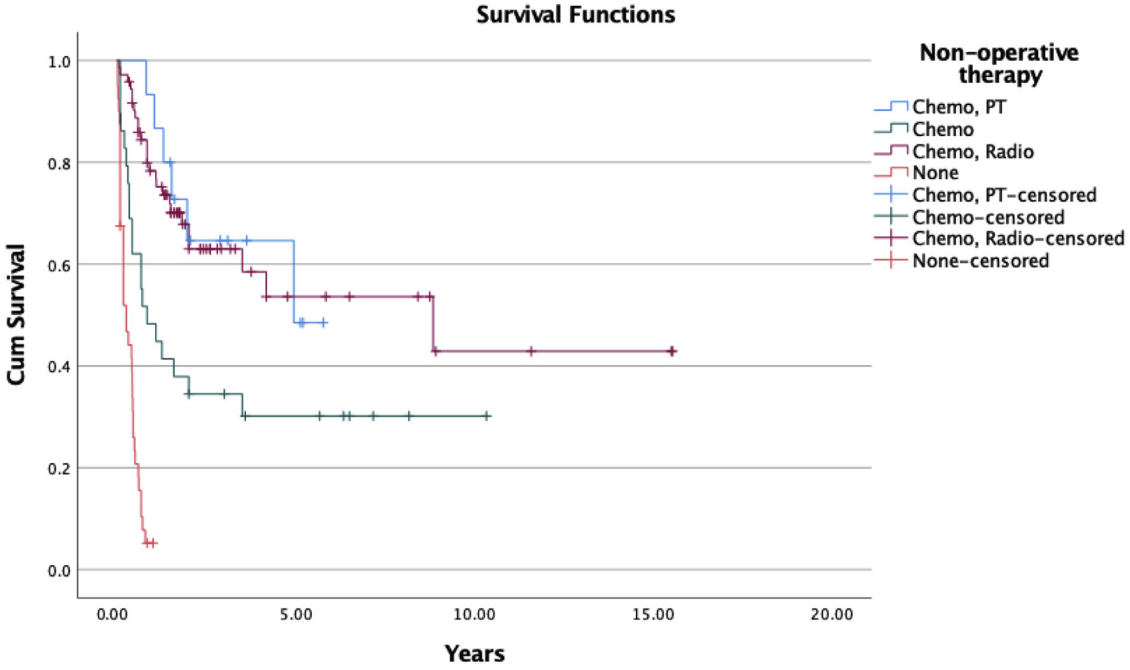

Figure 5. Kaplan-Meier curve for adjuvant therapy. Predicting survival through multivariate regression analysis. Chemo, PT, chemotherapy and proton therapy; Chemo, chemotherapy; Chemo, Radio, chemotherapy and radiotherapy; Cum, cumulative.

younger individuals than was previously believed appropriate.[39] Radiation has been linked to better survival in patients with ATRT, particularly those who receive craniospinal radiation with a focused boost to the tumor bed. Tekautz et al.[39] examined 31 patients with ATRT treated from 1987 to 2007 to assess failure patterns and local control with radiation. Patients' chemotherapy regimens and extent of resection varied, but all were treated with focused radiation alone or in combination with craniospinal irradiation (CSI). At a median follow-up of 48 months, the PFS was 32.2% ± 10% and the OS was 53.5% ± 10%. Using a Cox regression model, Tekautz et al.[39] discovered that patients with a GTR and stable illness before RT were less likely to have an adverse event, but patients with delayed RT were more likely to have an adverse event. Delayed RT was defined as occurring 1 month after surgery. In that study, only disease progression before RT affected OS. The presence of metastatic disease at the time of presentation had no effect on PFS or OS. At 4 years, individuals with less than GTR had a local failure rate of 53.3% ± 14%, whereas those with GTR had a local failure rate of 17.9% ± 10%. Local failure occurred in 29% (2/7) of individuals who had immediate postoperative CSI versus 58% (7/12) of those who received delayed postoperative CSI. The 6 patients younger than 3 years who were alive at the time of the final follow-up before publication all had focused RT.

Comparing Pediatric and Adult ATRT

There are various clinical differences and similarities between adult and pediatric patients. As mentioned, most pediatric patients were male compared with a majority of female adult patients diagnosed with ATRT. From our analysis, the most common tumor location was in the infratentorial location compared with sellar and hemispheric locations in adults.[43] ATRT has a poor prognosis in both the pediatric and adult populations. Our study reported an average survival of 10.2 months. These survival data are comparable to a reported median survival of 12–13.5 months in other studies,[15,49] similar to the reported median survival in adults of 11.1–14.3 months.[50,51]

Radiological Findings of ATRT

Radiologic findings were also similar between adult and pediatric patients. A study conducted by Warmuth-Metz et al.[52] of pediatric ATRT found 100% hyperattenuation on computed tomography, 44% were hypointense on T1 imaging, 73% were hypointense on T2 imaging, 63% had substantial enhancement, and 73% of patients showed possible necrotic areas or possible cysts. These findings are similar to other studies conducted on children[53,54] and adult patients.[55-58]

Our analysis shows that the extent of resection and the form of adjuvant therapy affects survival, although our study did find that patients who received a combination of RT and chemotherapy or who received GTR did have increased survival. However, survival may be influenced by confound factors, and most patients analyzed had surgery with a combination of adjuvant therapy,

Table 2. Chemotherapy and Radiotherapy Regimens, Doses, and Respective Survival Outcomes as Reported by the Eligible Studies

Reference	Type of Study	n	Median Age (months)	Chemotherapy (Route)	Radiotherapy	Survival Outcomes
Weber et al., 2015[20]	Retrospective study	15	18.9	Pilot Protocol ATRT EU-RHAB Protocol 2007 or 2010 (Intraventricular and intravenous) American DFC ATRT Protocol	Pencil beam scanning proton therapy	2-year OS and PFS was 64.6% and 66.0%
DiPatri Jr. et al., 2015[21]	Retrospective study	8	5.5	Modified Baby-POG: VCR, CDDP, cytoxan, and MTX Modified IRS-III—VCR, dactinomycin, CTX, CDDP, doxorubicin, TMZ and MTX, cytarabine, and hydrocortisone ACNS0333 regimen with VCR, MTX, VP, CTX, and CDDP Intravenous (intrathecal—MTX only)	Focal radiation therapy using intensity-modulated delivery Dose: 5400 cGy fractions	Median OS 5 months (range, 1—107 months)
Inoue et al., 2014[22]	Case report	1	18	IRS-III protocol—anthracycline-based chemotherapy (intrathecal)	Cranial radiographic irradiation. 54 Gy in 1.8-Gy fractions using intensity-modified delivery	Alive with disease at 29 months
Bush et al., 2014[23]	Case report	1	13	VCR, CTX, CDDP, VP, and high-dose MTX, followed by consolidation with high-dose CARBO/THIO and autologous stem cell rescue	On completion of chemotherapy, the residual disease was not amenable to surgical resection and the child proceeded to cranial-spinal proton beam radiation.	DOD after 10 months
Han et al., 2012[24]	Case report	1	108	CDDP and CTX	Whole brain by IMRT. Dose: 43 Gy/24 Fx+12.5 Gy/5 Fx. Spine by IMRT. Dose: 18 Gy/10 Fx+18 Gy/10 Fx	DOD after 12 months
Park et al., 2012[25]	Clinical trial—phase I/II	6	11.5	Pre-HDCT: Alternating cisplatin, etoposide, cyclophosphamide, vincristine and carboplatin, etoposide, ifosfamide, vincristine ×6 cycles HDCT: CARBO/THIO/VP then CTX/MELPH	Salvage after relapse/progression—radiotherapy. CSI/boost after HDCT	5 patients alive 16—70 months. 1 patient DOD 15 months
Bruggers et al., 2012[26]	Retrospective review	20	8.9	Induction A (n = 16) VCR/CDDP/CTX/VP. Induction B (n = 12) VCR/CDDP/IFOS/VP. Maintenance VCR/CDDP/CTX/VP. 6× maintenance chemotherapy CTX/CDDP/VCR)	Radiation therapy doses and field designs varied among patients, depending on the age of the patient at the time of diagnosis, tumor site, specific study, and curative versus palliative intent	Median survival 8 months
Heuer et al., 2010[27]	Case report	1	84	Boston ATRT CNS clinical trial guidelines. intrathecal chemotherapy as well as systemic courses of VCR/doxorubicin and AD/CTX and additional courses of TMZ and AD. (intrathecal and intravenous)	2 months after surgery, the patient received involved-field radiation over a 6-week period. 5400 Gy	DOD after 42 months
Nicolaides et al., 2010[28]	Retrospective study	6	24	Pre-HDCT: MTX, CTX, VP, CDDP, VCR (HSII) HDCT: MTX, CTX, VP, CDDP, VCR (HSII), or triple intrathecal chemotherapy, CDDP, VP, VCR, AD, IFOS, CTX, or MTX, CTX, VP, CDDP, VCR, intrathecal cytosine arabinoside	Focal or none	PFS and OS 10 months (range, 1—98 months)
Chi et al., 2009[29]	Clinical trial—phase II	20	26	Modified IRS-III—anthracycline-based induction chemotherapy regimen (intraventricular)	54 Gy focal (n = 11) 36 Gy CSI + boost (n = 4) —	2-year PFS 53% ± 13% 2-year OS 70% ± 10%

ATRT, atypical teratoid/rhabdoid tumor; EU-RHAB, European Rhabdoid Registry; DFC, Docetaxel, Cisplatin and Fluorouracil; OS, overall survival; PFS, progression-free survival; POG, Pediatric Oncology Group; VCR, vincristine; CDDP, cisplatin; MTX, methotrexate; IRS-III, Third Intergroup Rhabdomyosarcoma Study; TMZ, temozolomide; VP, etoposide; CARBO, carboplatin; THIO, thiotepa; DOD, died of disease; IMRT, intensity-modulated radiation therapy; Fx, fractions; HDCT, high-dose chemotherapy; CSI, craniospinal radiation; IFOS, ifosfamide; AD, actinomycin; CR, complete response; CTX, cyclophosphamide; MELPH, melphalan; ICE, ifosfamide, carboplatin, etoposide; EFS, event-free survival; HSII, MTX methotrexate, CX cyclophosphamide, VP VP16, CPLT cisplatin, VCR vincristine; DFS, Disease-Free Survival.

Continues

Table 2. Continued

Reference	Type of Study	n	Median Age (months)	Chemotherapy (Route)	Radiotherapy	Survival Outcomes
Fidani et al., 2009[30]	Clinical trial	8	39	Pre-HDCT: ICE ×2, cyclophosphamide, etoposide, carboplatin, thiotepa ×2 HDCT: VP/THIO/CTX	Received whole-brain radiotherapy treatment 9—10 months after diagnosis Initial dose of 45 Gy with a boost to 55—60 Gy	Median OS 10 months
Gidwani et al., 2008[31]	Case report	1	4	Received 5 cycles of chemotherapy including CDDP, VCR, CTX, VP, and high-dose MTX as per Headstart II protocol	Not received because of age and tumor location and volume —	DFS 24 months
Janson et al., 2006[32]	Case series	2	20	4 preradiation cycles of VCR, dexrazoxane, doxorubicin, CTX, VP, and CDDP (intrathecal)	Upfront 11 Gy Gamma Knife boost to a 2.6 cm^3 residual radiographic mass in the right cerebellar peduncle 54 Gy/30 fractions/47 days posterior fossa radiotherapy	PFS 42 months for patient 1 and DOD at 5 months for patient 2
Abu Arja et al., 2018[33]	Case report	1	0.25	Consisted of 8, 21-day cycles incorporating VCR, CDDP, doxorubicin, CTX, and triple intrathecal chemotherapy (MTX, hydrocortisone, and cytarabine) (intraventricular and/or triple intrathecal)	Focal radiotherapy	PFS 17
Johann et al., 2017[34]	Observational study	10	20	CDDP, VP, CTX and VCR followed by 3 cycles of high-dose chemotherapy: CARBO, THIO	54 Gy	OS 53
Lee et al., 2017[35]	Observational study	9	32	High-dose chemotherapy	Radiotherapy	2-year OS: 62.2% 2-year EFS: 46.7%
Byers et al., 2017[36]	Case report	1	12	Induction of 2 cycles: VCR, MTX, VP, CTX, and CDDP	Adjunct proton beam radiation 45.92 Gy/28 fractions/30 days	OS 18 months
Wang et al., 2016[37]	Observational study	22	24	VCR/bevacizumab; TMZ; ifosfamide/bevacizumab/docetaxel	Radiation therapy 30.6—39.6 Gy CSI/18—54 Gy focal or cranial	OS and EFS 17 months
Van Gool et al., 2016[38]	Clinical trial	7	31.5	Multidrug chemotherapy, high-dose chemotherapy (intrathecal)	Irradiation 60 Gy	OS 56.04 months
Tekautz et al. (2005)[39]	Observational study		22 <3 years (12). 9 patients ≥3 years (3.9 years)	Multiple regimens	<3 years 2 local, 1 CSI + boost ≥3 years 7 patients CSI + boost	<3 years 2-year EFS 11% ± 6% 2-year OS 17 ± 8% ≥3 years 2-year EFS 78% ± 14% 2-year OS 89% ± 11%
Lafay-Cousin et al. (2012)[15]	Clinical trial —phase II	50	16.7	MTX, CDDP, CPM, VCR, VP, (CB, THIO) × 3 CDDP, CPM, VCR, VP16, (CB, THIO) × 3 CDDP, CPM, VCR, VP, (CB, THIO) × 3 Systemicor triple intrathecal: aracytine, hydrocortisone, MTX	45 Gy cranial/780 focal, or 36 Gy CSI/18 Gy focal boost, or 36 Gy CSI/18 Gy focal boost	2-year OS 36.4% ± 7.7%

ATRT, atypical teratoid/rhabdoid tumor; EU-RHAB, European Rhabdoid Registry; DFC, Docetaxel, Cisplatin and Fluorouracil; OS, overall survival; PFS, progression-free survival; POG, Pediatric Oncology Group; VCR, vincristine; CDDP, cisplatin; MTX, methotrexate; IRS-III, Third Intergroup Rhabdomyosarcoma Study; TMZ, temozolomide; VP, etoposide; CARBO, carboplatin; THIO, thiotepa; DOD, died of disease; IMRT, intensity-modulated radiation therapy; Fx, fractions; HDCT, high-dose chemotherapy; CSI, craniospinal radiation; IFOS, ifosfamide; AD, actinomycin; CR, complete response; CTX, cyclophosphamide; MELPH, melphalan; ICE, ifosfamide, carboplatin, etoposide; EFS, event-free survival; HSII, MTX methotrexate, CX cyclophosphamide, VP VP16, CPLT cisplatin, VCR vincristine; DFS, Disease-Free Survival.

making it challenging to identify which form of treatment had the most significant impact on survival.

Limitations

Our conclusions are limited because of the small number of included cases. Although there may be many ATRT cases in the literature, not all cases were confirmed neuropathologically. Thus, this new

Table 3. Multiple Regression Analysis for Survival

Survival	Unstandardized Regression Coefficient	95% Confidence Interval for Unstandardized Regression Coefficient		Standard Error of the Coefficient	β	R^2	Adjusted R^2
		Lower Limit	Upper Limit				
Model						0.328	0.235
Constant	65.526*	35.057	95.994	14.897			
Tumor location	−4.420	−19.083	10.242	7.169	−0.102		
Dissemination	−24.374†	−44.819	−3.929	9.996	−0.406†		
Resection	−5.512	−15.949	4.926	5.103	−0.172		
Adjuvant therapy	−4.424†	−8.747	−0.101	2.114	−0.359†		

Model = "Enter" method in SPSS; R^2, coefficient of determination.
*$P < 0.01$.
†$P < 0.05$.

definition of the tumor may impede our survival analysis, although it may be a cornerstone to a new and accurate understanding of pediatric ATRT. This phenomenon has also impeded our multiregression analysis, in which the differences in data completeness from one case to another prevented a more powered analysis. Another limitation was the heterogeneity of the chemotherapeutic, radiotherapeutic, and other adjuvant therapy protocols used in each study. This heterogeneity is primarily caused by the lack of a gold-standard protocol. This limitation has prevented a more powered analysis to investigate the impact of each protocol on survival.

CONCLUSIONS

ATRT is a rare malignant neoplasm of the CNS, with a poor prognosis. The average survival is <4 years. Although ATRT occurs most commonly in infratentorial or supratentorial regions, our systematic review shows that ATRT can also occur in the spine, significantly affecting survival, compared with intracranial ATRT. From our systematic review, the extent of resection was a statistically significant factor in prognosis, but adjuvant therapy may also significantly affect prognosis. However, conclusions are difficult to draw because of the small number of pediatric cases in the literature. Future trials are being conducted on chemotherapeutic regimens to elucidate an effective protocol to improve survival. Case reports and systematic reviews of rare malignant neoplasms remain an important component of the literature in neuro-oncology because they provide information that may show clinicopathologic patterns and factors that affect prognosis as well as direct future studies.

DATA AVAILABILITY STATEMENT

All datasets generated for this study are included in the text and the supplementary files.

REFERENCES

1. Horiguchi H, Nakata S, Nobusawa S, et al. Adult-onset atypical teratoid/rhabdoid tumor featuring long spindle cells with nuclear palisading and perivascular pseudorosettes. *Neuropathology*. 2017;37:52-57.
2. Samaras V, Stamatelli A, Samaras E, et al. Atypical teratoid/rhabdoid tumor of the central nervous system in an 18-year-old patient. *Clin Neuropathol*. 2009;28:1.
3. Dho YS, Kim SK, Cheon JE, et al. Investigation of the location of atypical teratoid/rhabdoid tumor. *Childs Nerv Syst*. 2015;31:1305-1311.
4. Hasselblatt M, Nagel I, Oyen F, et al. SMARCA4-mutated atypical teratoid/rhabdoid tumors are associated with inherited germline alterations and poor prognosis. *Acta Neuropathol*. 2014;128:453-456.
5. Hilden JM, Meerbaum S, Burger P, et al. Central nervous system atypical teratoid/rhabdoid tumor: results of therapy in children enrolled in a registry. *J Clin Oncol*. 2004;22:2877-2884.
6. Bartelheim K, Nemes K, Seeringer A, et al. Improved 6-year overall survival in AT/RT - results of the registry study Rhabdoid 2007. *Cancer Med*. 2016;5:1765-1775.
7. Frühwald MC, Hasselblatt M, Nemes K, et al. Age and DNA methylation subgroup as potential independent risk factors for treatment stratification in children with atypical teratoid/rhabdoid tumors. *Neuro Oncol*. 2020;22:1006-1017.
8. Biegel JA, Fogelgren B, Wainwright LM, et al. Germline INI1 mutation in a patient with a central nervous system atypical teratoid tumor and renal rhabdoid tumor. *Genes Chromosomes Cancer*. 2000;28:31-37.
9. Bourdeaut F, Lequin D, Brugières L, et al. Frequent hSNF5/INI1 germline mutations in patients with rhabdoid tumor. *Clin Cancer Res*. 2011;17:31-38.
10. Seeringer A, Reinhard H, Hasselblatt M, et al. Synchronous congenital malignant rhabdoid tumor of the orbit and atypical teratoid/rhabdoid tumor—feasibility and efficacy of multimodal therapy in a long-term survivor. *Cancer Genet*. 2014;207:429-433.
11. Nemes K, Clément N, Kachanov D, et al. The extraordinary challenge of treating patients with congenital rhabdoid tumors—a collaborative European effort. *Pediatr Blood Cancer*. 2018;65:e26999.
12. Rorke LB, Packer RJ, Biegel JA. Central nervous system atypical teratoid/rhabdoid tumors of infancy and childhood: definition of an entity. *J Neurosurg*. 1996;85:56-65.
13. Packer RJ, Biegel JA, Blaney S, et al. Atypical teratoid/rhabdoid tumor of the central nervous system: report on workshop. *J Pediatr Hematol Oncol*. 2002;24:337-342.
14. Burger PC, Yu IT, Tihan T, et al. Atypical teratoid/rhabdoid tumor of the central nervous system: a highly malignant tumor of infancy and childhood frequently mistaken for medulloblastoma: a Pediatric Oncology Group study. *Am J Surg Pathol*. 1998;22:1083-1092.
15. Lafay-Cousin L, Hawkins C, Carret AS, et al. Central nervous system atypical teratoid rhabdoid tumours: the Canadian Paediatric Brain Tumour Consortium experience. *Eur J Cancer*. 2012;48:353-359.
16. Athale UH, Duckworth J, Odame I, et al. Childhood atypical teratoid rhabdoid tumor of the central nervous system: a meta-analysis of

observational studies. *J Pediatr Hematol Oncol*. 2009; 31:651-663.

17. Olson TA, Bayar E, Kosnik E, et al. Successful treatment of disseminated central nervous system malignant rhabdoid tumor. *J Pediatr Hematol Oncol*. 1995;17:71-75.

18. Egiz A, Asl SF. The Impact of Extent of Surgical Resection and Adjuvant Therapy on Survival Outcomes in Paediatric Patients with Atypical Teratoid Rhabdoid Tumour: A Systematic Review and Meta-analysis. PROSPERO 2022 CRD 42022300996. Available at: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022300996. Accessed March 12, 2022.

19. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. *Syst Rev*. 2016;5:210.

20. Weber D, Ares C, Malyapa R, et al. Tumor control and QoL outcomes of very young children with atypical teratoid/rhabdoid Tumor treated with focal only chemo-radiation therapy using pencil beam scanning proton therapy. *J Neurooncol*. 2015; 121:389-397.

21. DiPatri AJ, Sredni ST, Grahovac G, Tomita T. Atypical teratoid rhabdoid tumors of the posterior fossa in children. *Childs Nerv Syst*. 2015;31: 1717-1728.

22. Inoue N, Watanabe H, Okamura K, et al. Atypical teratoid rhabdoid tumor in the cavernous sinus of a toddler presenting with oculomotor nerve palsy. *Childs Nerv Syst*. 2014;30:1463-1466.

23. Bush J, Hancock B, Israels S, Ellison D, Stefanovici C, Krawitz S. Intracranial Atypical Teratoid/Rhabdoid Tumor Presenting as an Axillary Mass: A Case Report and Review of Literature. *Pediatr Dev Pathol*. 2014;17:122-125.

24. Han Y, Zhao Y, He X, Ma J. Peritoneal metastasis of third ventricular atypical teratoid/rhabdoid tumor after VP shunt implantation for unexplained hydrocephalus. *World J Pediatr*. 2012;8:367-370.

25. Park E, Sung K, Baek H, et al. Tandem High-Dose Chemotherapy and Autologous Stem Cell Transplantation in Young Children with Atypical Teratoid/Rhabdoid Tumor of the Central Nervous System. *J Korean Med Sci*. 2012;27:135-140.

26. Bruggers C, Bleyl S, Pysher T, et al. Clinicopathologic comparison of familial versus sporadic atypical teratoid/rhabdoid tumors (AT/RT) of the central nervous system. *Pediatr Blood Cancer*. 2010; 56:1026-1031.

27. Heuer G, Kiefer H, Judkins A, et al. Surgical treatment of a clival-C2 atypical teratoid/rhabdoid tumor. *J Neurosurg Pediatr*. 2010;5:75-79.

28. Nicolaides T, Tihan T, Horn B, Biegel J, Prados M, Banerjee A. High-dose chemotherapy and autologous stem cell rescue for atypical teratoid/rhabdoid tumor of the central nervous system. *J Neurooncol*. 2010;98:117-123.

29. Chi S, Zimmerman M, Yao X, et al. Intensive multimodality treatment for children with newly diagnosed CNS atypical teratoid rhabdoid tumor. *J Clin Oncol*. 2009;27:385-389.

30. Fidani P, De Ioris M, Serra A, et al. A multimodal strategy based on surgery, radiotherapy, ICE regimen and high dose chemotherapy in atypical teratoid/rhabdoid tumours: a single institution experience. *J Neurooncol*. 2009;92:177-183.

31. Gidwani P, Levy A, Goodrich J, Weidenheim K, Kolb E. Successful outcome with tandem myeloablative chemotherapy and autologous peripheral blood stem cell transplants in a patient with atypical teratoid/rhabdoid tumor of the central nervous system. *J Neurooncol*. 2008;88:211-215.

32. Janson K, Nedzi L, David O, et al. Predisposition to atypical teratoid/rhabdoid tumor due to an inheritedINI1 mutation. *Pediatr Blood Cancer*. 2006; 47:279-284.

33. Abu Arja M, Patel P, Shah S, et al. Synchronous central nervous system atypical teratoid/rhabdoid tumor and malignant rhabdoid tumor of the kidney: case report of a long-term survivor and review of the literature. *World Neurosurg*. 2018;111:6-15.

34. Johann P, Hovestadt V, Thomas C, et al. Cribriform neuroepithelial tumor: molecular characterization of a SMARCB1-deficient non-rhabdoid tumor with favorable long-term outcome. *Brain Pathol*. 2016;27:411-418.

35. Lee J, Kim D-S, Han JW, Suh C-O. Atypical teratoid/rhabdoid tumors in children treated with multimodal therapies: the necessity of upfront radiotherapy after surgery. *Pediatr Blood Cancer*. 2017;64:e26663.

36. Byers H, Adam M, LaCroix A, et al. Description of a new oncogenic mechanism for atypical teratoid rhabdoid tumors in patients with ring chromosome 22. *Am J Med Genet A*. 2016;173:245-249.

37. Wang R, Guan W, Yan Y, et al. Atypical teratoid/rhabdoid tumours: clinicopathological characteristics, prognostic factors and outcomes of 22 children from 2010 to 2015 in China. *Pathology*. 2016;48:555-563.

38. van Gool SW, Holm S, Rachor J, et al. Immunotherapy in atypical teratoid-rhabdoid tumors: Data from a survey of the HGG-Immuno Group. *Cytotherapy*. 2016;18:1178-1186.

39. Tekautz TM, Fuller CE, Blaney S, et al. Atypical teratoid/rhabdoid tumors (ATRT): improved survival in children 3 years of age and older with radiation therapy and high-dose alkylator-based chemotherapy. *J Clin Oncol*. 2005;23:1491-1499.

40. Rao SJB, Konar SK, Shukla D, et al. Factors influencing survival of children with atypical teratoid/rhabdoid tumors: a single-institute experience in a developing country. *World Neurosurg*. 2019;129:e264-e272.

41. Mousa A, Al-Kofide A, Siddiqui K, Alhindi H, Alshaikh N, Alshail E. Atypical teratoid rhabdoid tumors (ATRT): King Faisal Specialist Hospital and Research Centre experience. *Int J Pediatr Adolesc Med*. 2021;8:154-159.

42. Appaji L, Aruna Kumari BS, Babu KG, et al. Atypical teratoid rhabdoid tumor of the central nervous system: case series from a regional tertiary care cancer centre in South India. *J Cancer Res Ther*. 2017;13:1015-1022.

43. Chan V, Marro A, Findlay JM, Schmitt LM, Das S. A systematic review of atypical teratoid rhabdoid tumor in adults. *Front Oncol*. 2018;28:567.

44. Benesch M, Nemes K, Neumayer P, et al. Spinal cord atypical teratoid/rhabdoid tumors in children: clinical, genetic, and outcome characteristics in a representative European cohort. *Pediatr Blood Cancer*. 2020;67:e28022.

45. Johann PD, Erkek S, Zapatka M, et al. Atypical teratoid/rhabdoid tumors are comprised of three epigenetic subgroups with distinct enhancer landscapes. *Cancer Cell*. 2016;29:379-393.

46. Makuria AT, Rushing EJ, McGrail KM, Hartmann D-P, Azumi N, Ozdemirli M. Atypical teratoid rhabdoid tumor (AT/RT) in adults: review of four cases. *J Neurooncol*. 2008;88:321-330.

47. Moretti C, Lupoi D, Spasaro F, et al. Sella turcica atypical teratoid/rhabdoid tumor complicated with lung metastasis in an adult female. *Clin Med Insights Case Rep*. 2013;6:177-182.

48. Yang M, Chen X, Wang N, et al. Primary atypical teratoid/rhabdoid tumor of central nervous system in children: a clinicopathological analysis and review of literature in China. *Int J Clin Exper Pathol*. 2014;7:2411-2420.

49. Fleming AJ, Hukin J, Rassek R, et al. Atypical teratoid rhabdoid tumors (ATRTs): the British Columbia's Children's Hospital's experience, 1986—2006. *Brain Pathol*. 2012;22:625-635.

50. Fischer-Valuck BW, Chen I, Srivastava AJ, et al. Assessment of the treatment approach and survival outcomes in a modern cohort of patients with atypical teratoid rhabdoid tumors using the National Cancer Database. *Cancer*. 2017;123: 682-687.

51. Schrey D, Carceller Lechón F, Malietzis G, et al. Multimodal therapy in children and adolescents with newly diagnosed atypical teratoid rhabdoid tumor: individual pooled data analysis and review of the literature. *J Neurooncol*. 2016;126: 81-90.

52. Warmuth-Metz M, Bison B, Dannemann-Stern E, Kortmann R, Rutkowski S, Pietsch T. CT and MR imaging in atypical teratoid/rhabdoid tumors of the central nervous system. *Neuroradiology*. 2008; 50:447-452.

53. Meyers SP, Khademian ZP, Biegel JA, Chuang SH, Korones DN, Zimmerman RA. Primary intracranial atypical teratoid/rhabdoid tumors of infancy and childhood: MRI features and patient outcomes. *AJNR Am J Neuroradiol*. 2006;27: 962-971.

54. Nowak J, Nemes K, Hohm A, et al. Magnetic resonance imaging surrogates of molecular subgroups in atypical teratoid/rhabdoid tumor. *Neuro Oncol*. 2018;20:1672-1679.

55. Arrazola J, Pedrosa I, Méndez R, Saldaña C, Scheithauer BW, Martínez A. Primary malignant rhabdoid tumour of the brain in an adult. *Neuroradiology*. 2000;42:363-367.

56. Sugita Y, Takahashi Y, Hayashi I, Morimatsu M, Okamoto K, Shigemori M. Pineal malignant

rhabdoid tumor with chondroid formation in an adult. *Pathol Int*. 1999;49:1114-1118.

57. Kanoto M, Toyoguchi Y, Hosoya T, Kuchiki M, Sugai Y. Radiological image features of the atypical teratoid/rhabdoid tumor in adults: a systematic review. *Clin Neuroradiol*. 2014;25:55-60.

58. Han L, Qiu Y, Xie C, et al. Atypical teratoid/rhabdoid tumors in adult patients: CT and MR imaging features. *AJNR Am J Neuroradiol*. 2011;32:103-108.

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