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Rhabdoid Tumor Predisposition Syndrome : A Comprehensive Review of Genetics, Clinical Manifestations, and Management

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Rhabdoid tumor predisposition syndrome (RTPS) is a rare autosomal dominant disorder characterized by an increased risk of developing malignant rhabdoid tumors in early childhood. This syndrome is primarily caused by germline heterozygous loss-of-function pathogenic variants in the *SMARCB1* gene (RTPS1) and rarely in the *SMARCA4* gene (RTPS2). RTPS is characterized by the development of atypical teratoid rhabdoid tumors of the central nervous system, malignant rhabdoid tumors of the kidney, and/or extrarenal extracranial rhabdoid tumors. The syndrome demonstrates high penetrance, with most tumors developing before age 3 years, and carries a poor prognosis despite intensive multimodal therapy. Early diagnosis through genetic testing, implementation of surveillance protocols, and aggressive treatment approaches are crucial for improving outcomes. This review comprehensively examines the genetic basis, clinical manifestations, surveillance strategies, and current management approaches for RTPS, with particular emphasis on emerging therapeutic options and the importance of multidisciplinary care.

Key Words : Rhabdoid tumor predisposition syndrome · Epigenomics.

INTRODUCTION

Rhabdoid tumor predisposition syndrome (RTPS) was first proposed in 1999 as a rare hereditary cancer syndrome that dramatically increases susceptibility to the development of malignant rhabdoid tumors[15,49]. Initially recognized through observations of aggressive pediatric malignancies with characteristic rhabdoid histology, our understanding of this syndrome has evolved significantly with advances in molecular genetics and cancer biology.

The syndrome is primarily caused by germline mutations in *SMARCB1* located at chromosome 22q11.23 (RTPS1), or rarely in *SMARCA4* at chromosome 19p13.2 (RTPS2)[5,12,16,41,55]. Both genes are core components of the SWItch/sucrose non-fermentable (SWI/SNF) chromatin remodeling complex, which regulates gene expression and tumor suppression by altering chromatin structure[26,30,36,56]. Mutations in these genes disrupt this function, leading to uncontrolled cell proliferation and the development of aggressive malignancies.

The clinical spectrum of RTPS is characterized by the development of rhabdoid tumors at various anatomical sites. The central nervous system (CNS) is the most affected location,

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with atypical teratoid rhabdoid tumors (ATRT) accounting for approximately 65% of all cases. Renal involvement occurs in about 9% of cases as malignant rhabdoid tumors of the kidney (RTK), while the remaining 26% present as extrarenal extracranial rhabdoid tumors (EERT), often involving the liver, neck, thorax, or pelvis[12,16,39,41,43].

Patients with RTPS typically present at a younger age (median, 4–7 months) compared to those with sporadic rhabdoid tumors (median, 18 months), and they often demonstrate more extensive disease with poorer outcomes[17,18]. The presence of synchronous or metachronous tumors is particularly characteristic of RTPS, occurring in approximately one-third of affected patients[40,45]. Despite recent advances in molecular diagnostics, imaging techniques, and therapeutic approaches, the overall prognosis remains poor, with the 5-year survival rate below 30%, especially in patients with synchronous tumors or early-onset disease.

This review provides a comprehensive overview of RTPS, focusing on its genetic basis, clinical manifestations, surveillance, management strategies, and emerging therapeutic options. The importance of genetic counseling and coordinated multidisciplinary care is emphasized to improve outcomes for affected patients and their families.

MOLECULAR GENETICS AND PATHOGENESIS

RTPS results from germline alterations in key epigenetic regulator genes involved in the SWI/SNF chromatin remodeling complex. The presence of biallelic loss of *SMARC* (SWI/SNF-related, matrix-associated, actin-dependent regulator of chromatin) is the diagnostic hallmark of RTPS. RTPS exists in two forms : RTPS1, caused by mutations in *SMARCB1* (also known as *INI1/SNF5/BAF47*) located at chromosome 22q11.23, and more rarely RTPS2, caused by mutations in *SMARCA4* (also known as *BAF47/BRG1*) at chromosome 19p13[12,16,39].

The SWI/SNF complex is a critical molecular assembly of over 20 different genes that regulates chromatin remodeling and gene expression[31,44]. *SMARCB1* and *SMARCA4* encode core subunit proteins essential for the proper functioning of

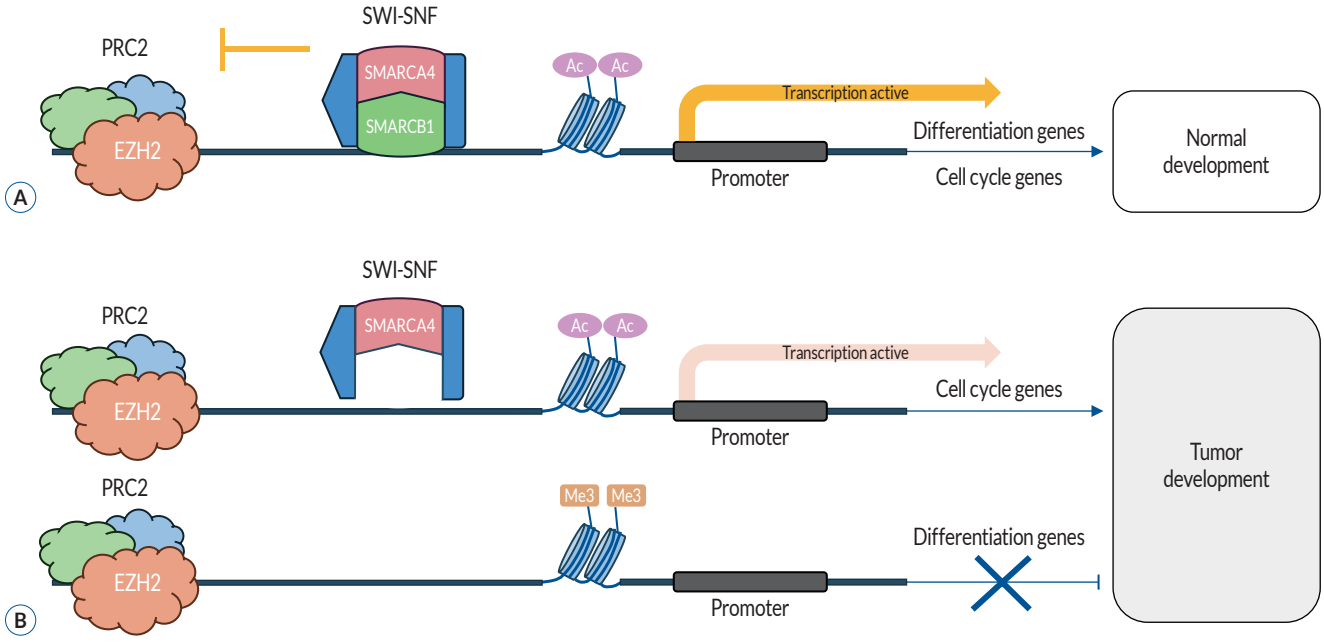

Fig. 1. Epigenetic regulation by SWI/SNF complex and polycomb repressor complex 2 (PRC2) in normal and tumor development. A : In normal cellular development, the SWI/SNF complex, including *SMARCB1* and *SMARCA4*, counteracts PRC2 activity. This balance allows transcription of pro-differentiation and cell cycle regulatory genes, supporting normal cell growth and differentiation. B : In rhabdoid tumors, the loss of *SMARCB1* leads to unopposed PRC2 activity, suppressing differentiation genes. At some promoters, residual SWI/SNF activity through *SMARCA4* enables transcription of cell cycle progression genes, contributing to tumor proliferation while differentiation pathways remain silenced. EZH2 : enhancer of zeste homolog 2, SWI/SNF : SWItch/sucrose non-fermentable, Ac : histone H3K27 acetylation (H3K26ac), Me3 : histone H3K27 methylation (H3K27me3).

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this complex. Mutations in *SMARCB1* or *SMARCA4* disrupt this balance, impairing nucleosome remodeling and promoting malignant transformation by deregulating cell cycle and differentiation pathways[30,31,44]. A key consequence of SWI/SNF loss is increased polycomb repressor complex 2 (PRC2) activity, mediated by the histone methyltransferase enhancer of zeste homolog 2 (EZH2). PRC2 promotes histone H3K27 methylation, silencing tumor suppressor and differentiation genes while enabling oncogenic pathways (Fig. 1)[20,33].

In rhabdoid tumors, residual SWI/SNF activity through *SMARCA4* enables selective transcription of cell cycle genes, contributing to aggressive proliferation while differentiation remains suppressed[20]. This selective transcriptional control explains why rhabdoid tumors typically demonstrate both aggressive proliferation and a block in cellular differentiation. The presence of residual SWI/SNF activity through *SMARCA4* also explains why targeting the PRC2-EZH2 axis has emerged as a promising therapeutic strategy, as it may help restore the balance between proliferation and differentiation signals.

The most frequent genetic event in rhabdoid tumors is biallelic inactivation of *SMARCB1*[55]. *SMARCB1* protein is normally expressed in the nuclei of all human cells, making its loss detectable through immunohistochemistry, which serves as a crucial diagnostic marker[35]. Approximately one-third of patients diagnosed with rhabdoid tumors harbor *de novo* germline *SMARCB1* mutations, following Knudson's two-hit hypothesis : an initial germline mutation is followed by somatic loss of the wild-type allele[2]. This mechanism often involves monosomy 22 or loss of heterozygosity, leading to complete protein loss and tumor formation.

RTPS1 demonstrates autosomal dominant inheritance with high penetrance, reported as greater than 90% for most truncating variants in *SMARCB1*, reaching this level by 5 years of age[18]. However, most cases (85–95%) are actually *de novo* due to the condition's early lethality. Gonadal mosaicism has been documented, where parents without detectable blood mutations can have multiple affected children[22,27]. By contrast, approximately 5% of cases result from truncating mutations at the *SMARCA4* locus. These mutations lead to near-complete gene inactivation and loss of the corresponding protein Brahma-related gene 1 (BRG1), which can be detected using immunohistochemistry[24,47,48]. RTPS2 demonstrate incomplete penetrance and are associated with a worse prognosis compared to *SMARB1*-mutated cases. Studies indicate that *SMARCA4* mutations often lead to earlier onset, aggressive tumor behavior, and poorer survival outcomes[17,26]. This finding highlights the clinical importance of distinguishing between *SMARCB1* and *SMARCA4* mutations for prognosis and management.

CLINICAL MANIFESTATIONS AND ASSOCIATED TUMORS

RTPS is characterized by the development of malignant rhabdoid tumors across multiple anatomical sites, often presenting at an unusually young age. Approximately one-third of newly diagnosed patients with rhabdoid tumors have an underlying genetic predisposition due to a germline SMARCB1 alteration[14]. Notably, studies have reported that germline mutations are more prevalent in patients diagnosed before six months of age, with an estimated frequency of approximately 55%, and this early onset is often associated with a poorer prognosis[40]. More than 70% of individuals with RTPS develop synchronous or metachronous tumors, often detected at advanced stages[37].

While the CNS is the most common site for primary rhabdoid tumors, the kidney is frequently involved in cases of synchronous tumors, often co-occurring with CNS rhabdoid tumors or other extracranial sites (Fig. 2)[2]. The presence of multiple tumors significantly impacts prognosis and therapeutic approach. Patients with RTPS typically demonstrate more aggressive disease characteristics compared to those with sporadic rhabdoid tumors, including earlier onset, more extensive disease, and lower survival rates[37].

Several factors are associated with poor prognosis in RTPS, including diagnosis before 12 months of age, presence of synchronous tumors, and metastatic disease. Data from the European Rhabdoid Registry (EU-RHAB) indicate that 84.5% of RTPS patients experience tumor progression during follow-up, with 48% progressing while on chemotherapy[37]. The prognosis is particularly challenging for patients with synchronous tumors, with one study reporting only 13% overall survival in patients with concurrent ATRT and EERT despite aggressive multimodal therapy[1].

This distinct clinical profile of RTPS necessitates early genetic testing and surveillance, particularly for young patients presenting with rhabdoid tumors and those with a concerning family history. The spectrum of manifestations has significant

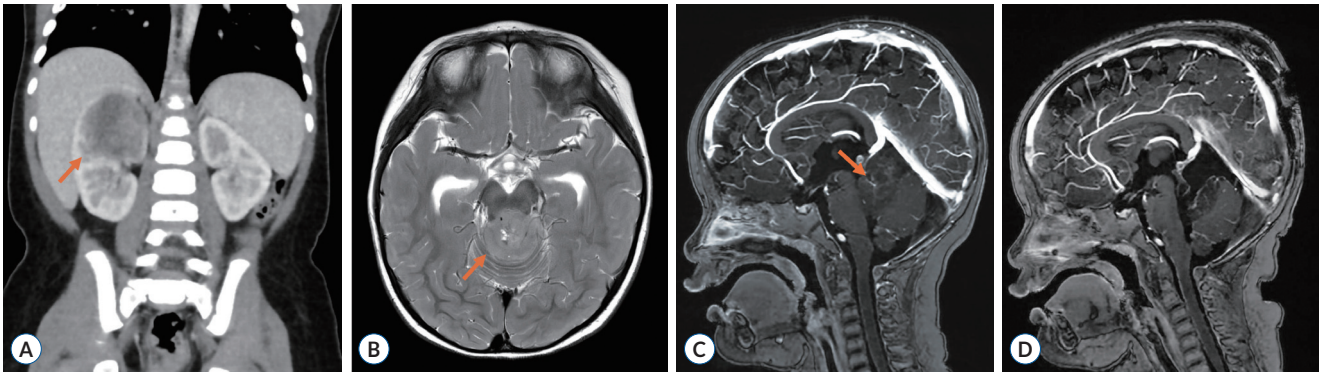

Fig. 2. Typical imaging findings in a patient with rhabdoid tumor predisposition syndrome (RTPS). A 15-month-old girl presented with hematuria. Kidney ultrasound revealed a renal mass, prompting further evaluation with computed tomography (CT). The patient underwent right nephrectomy, and pathology confirmed a rhabdoid tumor of the kidney. Subsequent brain magnetic resonance (MR) imaging screening detected a 3.1 cm mass in the midline posterior fossa. Surgical resection of this lesion demonstrated an atypical teratoid rhabdoid tumor on pathology. A : Coronal contrast-enhanced CT image of the abdomen shows a sharply circumscribed, predominantly hypoattenuating mass (thick arrow) located in the interpolar region of the right kidney. B : Axial T2-weighted MR image of the brain demonstrates a mixed cystic-solid mass lesion (arrow) in the midline posterior fossa. C : Mid-sagittal gadolinium-enhanced T1-weighted MR image shows heterogeneous enhancement of the posterior fossa mass (arrow). D : Postoperative mid-sagittal gadolinium-enhanced T1-weighted MR image demonstrates gross total resection of the lesion.

implications for clinical management and genetic counseling.

ATRT

First unequivocally described in 1987, ATRT is the primary CNS manifestation of RTPS and predominantly affects children under the age of 3[29]. The posterior fossa is the most common site (52% of cases), followed by the cerebral hemispheres or suprasellar region (39%), the pineal region (5%), and the spinal cord (2%)[8,35]. ATRTs tend to grow along the ventricles and into adjacent cisternal spaces, with direct ventricular system involvement. Imaging characteristics include peripheral cysts, variable enhancement, and restricted diffusivity (Fig. 2)[35,42,48]. Leptomeningeal dissemination is noted in approximately one-third of cases at diagnosis[8].

Molecular profiling has identified three subgroups of ATRT—ATRT-SHH, ATRT-TYR, and ATRT-MYC—based on DNA methylation and gene expression patterns. Each subgroup exhibits distinct characteristics in terms of tumor location, demographics, and clinical outcomes[25,29,52]. The ATRT-SHH subgroup, comprising approximately 30–35% of cases, is characterized by activation of the Sonic Hedgehog signaling pathway genes (*GLI2, BOC, PTCHD2*) and NOTCH signaling genes (*ASCL1, CBL, HES1*), along with MYCN upregulation[23,25]. This subgroup shows intermediate prognosis and can occur in both supratentorial and infratentorial regions, typically affecting older children (median age approximately 2 years)[11,34]. ATRT-TYR, accounting for about 35–40% of cases, predominantly occurs in the posterior fossa and affects very young infants[25,34]. This subgroup is characterized by overexpression of melanosomal genes (*TYR, TYRP, MITF*) and mesenchymal markers (*OTX2, PDGFRB, BMP4*), and shows relatively better prognosis, particularly when complete surgical resection is achieved[23,25,34]. The ATRT-MYC subgroup represents approximately 25–30% of cases and is mainly found in supratentorial regions[25]. These tumors are characterized by broad *SMARCB1* deletions and overexpression of *MYC*, *HOTAIR* and *HOX* cluster genes, and generally demonstrate the poorest prognosis among the three subgroups[11,23,25].

The rare ATRTs with underlying *SMARCA4* mutations demonstrate a higher frequency of germline mutations, manifest at younger ages, and show worse prognosis compared to *SMARCB1*-mutated cases[26]. These findings underscore the importance of molecular profiling in guiding prognosis and treatment strategies for ATRT.

RTK

RTK was first distinguished from Wilms tumor in 1978 as a distinctly aggressive entity with high mortality[21,50]. Comprising approximately 9% of RTPS-associated tumors, RTK typically presents before 12 months of age in syndromic cases. These tumors often demonstrate advanced disease at diagnosis, with pulmonary metastases being common.

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A characteristic imaging feature that may help differentiate RTK from Wilms tumor is the presence of a crescentic, nonenhancing hemorrhagic or necrotic subcapsular fluid collection, which may appear hyperintense on T1-weighted magnetic resonance imaging (MRI) due to blood products (Fig. 2)[35]. This differentiation is crucial for guiding treatment, as RTK requires aggressive multimodal therapy compared to Wilms tumor.

The prognosis for RTK remains poor, with a median survival of less than 1 year and a 5-year overall survival of approximately 20%[9,21]. Recent studies have identified several prognostic factors, including older age at diagnosis and extent of surgical resection as positive indicators, while presence of germline *SMARCB1* mutations and metastatic disease at presentation are associated with worse outcomes[53].

The EU-RHAB registry data suggests that gross total resection and radiotherapy are significantly associated with improved survival. However, high-dose chemotherapy (HDCT) with autologous stem cell rescue has shown no significant impact on outcomes[38]. This highlights the need for novel therapeutic strategies to combat the aggressive nature of RTK.

EERT

EERT can occur throughout the body, with common sites including the head and neck (14%), liver (13%), urinary bladder, and retroperitoneum[7]. On imaging, EERTs typically present as large heterogeneous masses, hypoattenuating at computed tomography, hypo- to isointense to muscle on T1-weighted images, and hyperintense to muscle on T2-weighted images, often containing regions of internal necrosis.

Some studies suggest that patients with EERTs may have better survival than those with RTK, which may be related to the fact that germline mutations in *SMARCB1*, an adverse prognostic marker, are found less frequently in EERT[38].

The clinical course of EERT is generally aggressive, with a reported 3-year overall survival of 27% and event-free survival of 21%[3]. Complete surgical resection has been identified as a significant prognostic factor, with a systematic review demonstrating improved survival in patients achieving complete resection[28]. Treatment outcomes appear to be influenced by several factors including age at diagnosis, tumor location, and extent of disease at presentation[54].

Regardless of anatomic location, these tumors share common molecular features through *SMARCB1* or *SMARCA4* mutations, though their clinical presentation, imaging characteristics, and treatment approaches may differ significantly. This molecular commonality underlies their aggressive behavior and poor prognosis, while their anatomic diversity necessitates site-specific management strategies. The presence of synchronous or metachronous tumors, particularly common in RTPS, requires thorough imaging surveillance and often impacts treatment planning and prognosis[12].

DIAGNOSIS AND SURVEILLANCE

The diagnosis of RTPS requires a comprehensive approach combining clinical features, imaging studies, and genetic testing. Early diagnosis is crucial given the aggressive nature and poor prognosis of associated tumors[16].

RTPS is diagnosed when a patient presents with either a rhabdoid tumor and/or a family history of rhabdoid tumors, along with identification of a pathogenic germline variant in *SMARCB1* (RTPS1) or *SMARCA4* (RTPS2) through molecular genetic testing[18]. Several clinical features should raise suspicion for RTPS, including congenital or early-onset rhabdoid tumors (age <12 months), advanced stage disease at diagnosis, and synchronous multiple primary rhabdoid tumors[6].

The diagnostic workup typically begins with imaging studies. Whole-body MRI is recommended at initial diagnosis for all individuals, regardless of age[18]. For brain imaging, standard protocols include T1-weighted, T2-weighted, fluid-attenuated inversion recovery sequences, diffusion-weighted imaging, and contrast-enhanced studies.

Molecular genetic testing approaches can involve either serial single-gene testing or multigene panels. If tumor immunohistochemistry shows a loss of *SMARCB1* protein expression, sequence analysis and gene-targeted deletion/duplication analysis of *SMARCB1* should be performed first. Similarly, if *SMARCA4* protein expression is absent, *SMARCA4* genetic testing should be prioritized[27]. Next-generation sequencing is especially useful in patients with a complex family history or ambiguous results from single-gene testing.

Given the high risk of tumor development in RTPS carriers, rigorous surveillance protocols have been established based on age groups (Table 1)[51]. For children from birth to 6 months, monthly (or at minimum every 2–3 months) thorough clinical examination including neurologic assessment, ultrasound of the abdomen and neck, and head ultrasound or brain and spine

Table 1. RTPS surveillance protocols by age group

Age group	Clinical & neurologic examination	Imaging studies	Frequency
Birth to 6 months	Thorough clinical and neurologic examination	Ultrasound of abdomen and soft tissues (neck) Head ultrasound or brain and spine MRI Whole-body MRI	Monthly (or at least every 2–3 months)
7 to 18 months	Thorough clinical and neurologic examination	Abdominal and neck ultrasound Brain and spine MRI*	Every 2–3 months
19 months to 5 years	Thorough clinical and neurologic examination	Abdominal and neck ultrasound Brain and spine MRI	Every 3 months
> 5 years	Thorough clinical and neurologic examination	Whole-body MRI Abdominal and pelvic ultrasound†	Clinical exam : every 6 months Whole-body MRI : annually Ultrasound : every 6 months (if applicable)

Initial whole-body MRI should be performed at diagnosis for all individuals regardless of age. *Whole-body MRI resolution may not be sufficient for brain structures. †For individuals with *SMARCA4*-related SCCOHT. RTPS : rhabdoid tumor predisposition syndrome, MRI : magnetic resonance imaging, SCCOHT : small cell carcinoma of the ovary, hypercalcemic type

MRI or whole-body MRI should be performed[18]. For ages 7–18 months, clinical and neurologic examination with abdominal and neck ultrasound should be performed every 2–3 months, and brain and spine MRI should be considered as whole-body MRI resolution may not be sufficient for brain structures[10]. For ages 19 months to 5 years, clinical and neurologic examination, abdominal and neck ultrasound, and brain and spine MRI should be performed every 3 months[46]. For patients older than 5 years, clinical examination including neurologic assessment should be performed every 6 months along with annual whole-body MRI, and for individuals with *SMARCA4*-related developing small cell carcinoma of the ovary, hypercalcemic type (SCCOHT), additional abdominal and pelvic ultrasound should be performed every 6 months[4].

Special consideration should be given to asymptomatic relatives at risk. Genetic counseling and testing should be offered to facilitate early detection and implementation of appropriate surveillance[13]. Identification of a pathogenic variant enables prenatal testing and preimplantation genetic testing for future pregnancies, offering options for early risk management[22].

Surveillance guidelines continue to evolve as our understanding of RTPS improves. Regular monitoring and adjustment of protocols may be necessary to account for individual patient factors and specific institutional protocols[18].

MANAGEMENT APPROACHES

The management of RTPS requires an intensive, multimodal approach, reflecting the aggressive nature of these tumors. Due to the rarity of RTPS, treatment protocols continue to evolve, with current strategies informed by clinical experience and ongoing research[17].

The cornerstone of RTPS treatment involves a combination of surgery, radiotherapy, and chemotherapy, with specific protocols developed by major research groups. The Children's Oncology Group has established a protocol that begins with surgery, followed by two cycles of induction chemotherapy utilizing cisplatin, cyclophosphamide, etoposide, vincristine, and methotrexate. This is followed by three cycles of HDCT with stem cell rescue using thiotepa and carboplatin as consolidation therapy, with radiotherapy administered according to age and disease stage[46]. In contrast, the Dana-Farber Consortium has developed an alternative combination therapy approach incorporating surgery, radiotherapy, and an intensive chemotherapy regimen including vincristine, dactinomycin, cyclophosphamide, cisplatin, doxorubicin, and temozolomide, along with intrathecal administration of methotrexate, cytarabine, and hydrocortisone[10]. For patients with extracranial rhabdoid tumors, the EU-RHAB registry recommends a combination therapy approach that emphasizes gross total resection when possible, followed by conventional chemotherapy including vincristine, dactinomycin, cyclophosphamide, doxorubicin, ifosfamide, carboplatin, and etoposide. This protocol also incorporates intrathecal methotrexate and allows for the use of HDCT with stem cell rescue using carboplatin and thiotepa, along with radiotherapy in patients older than 18 months[19].

Despite these intensive therapies, complications such as

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treatment toxicity are common, particularly in young children. To address this, strategies such as proton beam therapy, risk-adapted radiotherapy, and targeted therapies are being integrated into care[17]. For women with *SMARCA4*-related RTPS, prophylactic risk-reducing bilateral salpingo-oophorectomy may be considered after completion of family planning, given the high risk of developing SCCOHT[4].

Several targeted therapeutic approaches are currently under investigation to address the molecular pathogenesis of RTPS. EZH2 inhibitors, such as tazemetostat, target the epigenetic dysregulation characteristic of *SMARCB1*-deficient tumors. Additionally, immune checkpoint inhibitors including programmed cell death protein 1 (PD-1)/programmed death-ligand 1 (PD-L1) inhibitors are being evaluated for their potential to enhance anti-tumor immune responses. Novel approaches targeting cell cycle regulation through cyclin-dependent kinase 4 and 6 inhibitors and DNA damage repair through poly ADP-ribose polymerase (PARP) inhibitors are also being investigated. Ongoing clinical trials are exploring these targeted agents both as monotherapy and in combination with conventional treatment approaches[17].

Despite intensive multimodal therapy, prognosis remains poor, with fewer than half of children with RTPS becoming long-term survivors. Outcomes are particularly poor for patients with synchronous tumors and those diagnosed at very young ages. However, long-term survival has been achieved in some patients, particularly when complete surgical resection is possible and when intensive multimodal therapy can be administered successfully[32]. This comprehensive management approach requires careful coordination among multiple specialists, including oncologists, surgeons, radiation oncologists, and supportive care teams, all working together to optimize outcomes while minimizing treatment-related complications.

FUTURE DIRECTIONS

Research in the management of RTPS is advancing in several promising areas. A major focus is the development of more effective targeted therapies based on molecular profiling[29]. Agents such as EZH2 inhibitors aim to restore tumor suppressor activity, while PARP inhibitors target DNA repair deficiencies, potentially enhancing the efficacy of existing therapies. Ongoing investigations are also exploring novel combinations of these agents with conventional treatments to improve outcomes.

Immunotherapy is another area of active research. Checkpoint inhibitors, such as PD-1/PD-L1 inhibitors, aim to boost the immune system's ability to recognize and destroy cancer cells. CAR-T cell approaches, which engineer immune cells to specifically target tumor-associated antigens, hold promise for treating resistant or advanced cases[11].

Efforts are also underway to develop better predictive biomarkers for treatment response and to optimize risk stratification strategies[17]. Liquid biopsy techniques, such as circulating tumor DNA and tumor-derived exosome analysis, are being evaluated for their potential to monitor disease progression, detect recurrence, and assess treatment response in a minimally invasive manner[23]. Additionally, emerging technologies such as artificial intelligence and machine learning are being applied to refine risk assessment models and personalize treatment plans. These tools have the potential to analyze large datasets and identify patterns that can guide clinical decision-making.

International collaboration remains essential to advancing our understanding of this rare condition. Collaborative efforts enable the sharing of clinical data, standardization of treatment protocols, and the design of meaningful clinical trials that are otherwise challenging in rare diseases.

As these advancements continue to unfold, they hold the promise of improving outcomes for patients with RTPS.

CONCLUSION

RTPS remains a challenging condition requiring complex, multimodal management strategies. While advances in understanding the molecular basis of these tumors have led to the development of novel targeted therapies, outcomes remain suboptimal for many patients[25]. The success of treatment depends heavily on early diagnosis, appropriate risk stratification, and carefully coordinated multidisciplinary care. Continued research into targeted therapies, immunotherapy approaches, and biomarker development, combined with international collaborative efforts, holds promise for improving outcomes in this challenging patient population[11,29]. As our understanding of the molecular and genetic aspects of RTPS continues to evolve, the development of more personalized treatment approaches may ultimately lead to better outcomes for patients with this aggres-

sive disease. The future of RTPS management lies in combining scientific innovation with collaborative global efforts.

AUTHORS' DECLARATION

Conflicts of interest

Ji Hoon Phi has been editorial board of JKNS since October 2024. He was not involved in the review process of this original article. No potential conflict of interest relevant to this article was reported.

Informed consent

This type of study does not require informed consent.

Author contributions

Conceptualization : TK, JHP; Data curation : TK, JHP; Funding acquisition : JHP; Methodology : JHP; Project administration : JHP; Visualization : TK, JHP; Writing - original draft : TK; Writing - review & editing : JHP

Data sharing

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