Concurrent Development of Hepatoblastoma and Wilms Tumor in a Child with Trisomy 18

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Children with trisomy 18 are predisposed to developing hepatoblastoma and Wilms tumor (WT) ; however, the simultaneous occurrence of these two malignancies in the same patient has not been previously documented. We report a rare case of synchronous hepatoblastoma and renal tumor in a child with trisomy 18. The hepatoblastoma was treated with surgical resection followed by chemotherapy. The renal lesion, initially suspected to represent intralobular nephrogenic rests, showed rapid progression and was clinically diagnosed as WT. This case underscores the increased susceptibility of patients with trisomy 18 to multiple malignancies and emphasizes the need for careful oncologic surveillance in this population. *Shinshu Med J 74 : 111—116, 2026*

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Ⅰ Introduction

The occurrence of multiple primary malignancies in children is uncommon and typically associated with underlying genetic predispositions[1)]. Trisomy 18 has been linked to an increased risk of certain tumors, particularly hepatoblastoma and WT[2)3)]. To date, no cases of concurrent hepatoblastoma and WT in a child with trisomy 18 have been reported. We describe the clinical course and management of a child with trisomy 18 who developed both hepatoblastoma and a renal tumor later diagnosed as WT.

Ⅱ Case report

A 6-month-old female with trisomy 18 was referred for evaluation of an abdominal mass. Prenatal trisomy 18 was confirmed by amniocentesis at 27 weeks of gestation. Following genetic counseling, the parents opted for standard neonatal care. The patient was delivered at 40 weeks by emergency cesarean section due to fetal distress and admitted to the neonatal intensive care unit for respiratory distress, requiring intubation and mechanical ventilation for 1 day. Her respiratory function stabilized without further support.

Echocardiography revealed a small ventricular septal defect with preserved cardiac function. Type 4 radial longitudinal deficiency was identified by X-ray photographs of the arm, while a horseshoe kidney with grade Ⅰ hydronephrosis was identified by abdominal ultrasound. No other structural anomalies were detected.

At 6 months of age, a well-defined 5×5-cm mass in the left upper abdomen was incidentally detected on routine abdominal ultrasound. Magnetic resonance imaging (MRI) showed a hepatic mass in the left lateral segment with heterogeneous T2-weighted signal intensity, consisting of interspersed high- and low-intensity areas **(Fig. 1A)**. On diffusion-weighted

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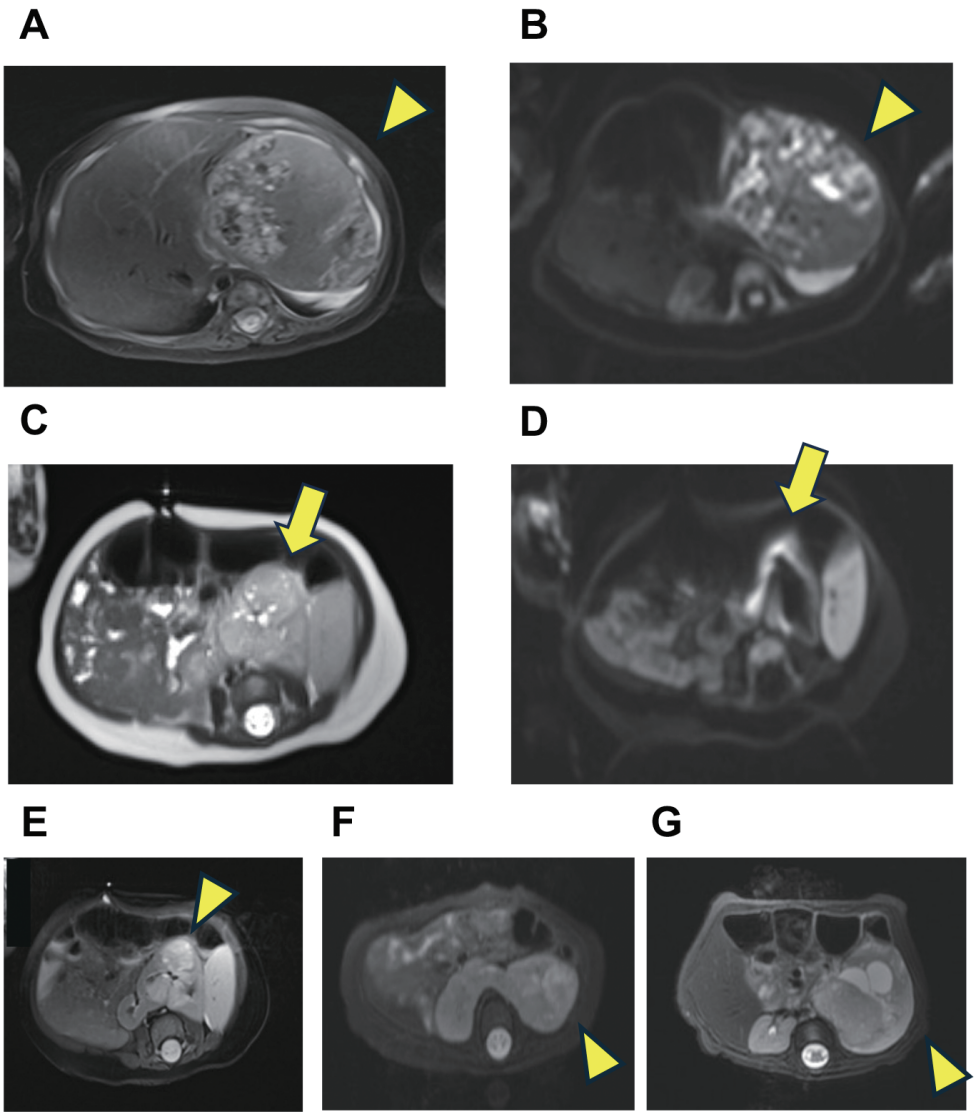

Fig. 1 Magnetic resonance imaging findings of liver and kidney tumors
(A) Axial T2-weighted image (T2WI) showing hepatoblastoma at initial diagnosis (yellow arrowhead). (B) Diffusion-weighted image (DWI) showing hepatoblastoma at initial diagnosis (yellow arrowhead). (C) Axial T2WI showing the kidney tumor at initial diagnosis (yellow arrow). (D) DWI showing the kidney tumor at initial diagnosis (yellow arrow). (E) Fat-suppressed T2WI of the kidney tumor in a horseshoe kidney at 6 months (time of biopsy). (F) Fat-suppressed T2WI of the kidney tumor in a horseshoe kidney at 11 months, after completion of chemotherapy for hepatoblastoma. (G) Fat-suppressed T2WI image of the kidney tumor in a horseshoe kidney at 14 months, demonstrating tumor enlargement with associated hydronephrosis.

imaging (DWI), the mass exhibited focal hyperintensity **(Fig. 1B)** and poor enhancement on dynamic contrast-enhanced MRI-findings consistent with hepatoblastoma[4]. The markedly elevated serum alpha-fetoprotein (AFP) level (244,470 ng/mL) supported this presumptive diagnosis.

In the same MRI, a 4-cm lesion was detected in the left kidney, demonstrating high signal on both T2WI and DWI **(Fig. 1C, D)**. Although the imaging characteristics suggested malignancy, the relatively homogeneous appearance and minimal necrotic change were compatible with an intralobar nephrogenic rest[5]. Metastatic hepatoblastoma could not be ruled out.

Due to gastrointestinal obstruction and rapid hepatic tumor growth, a left lateral segmentectomy was performed. Resection of the renal mass was deferred because of the risk of postoperative renal failure associated with the patient's horseshoe kidney and con-

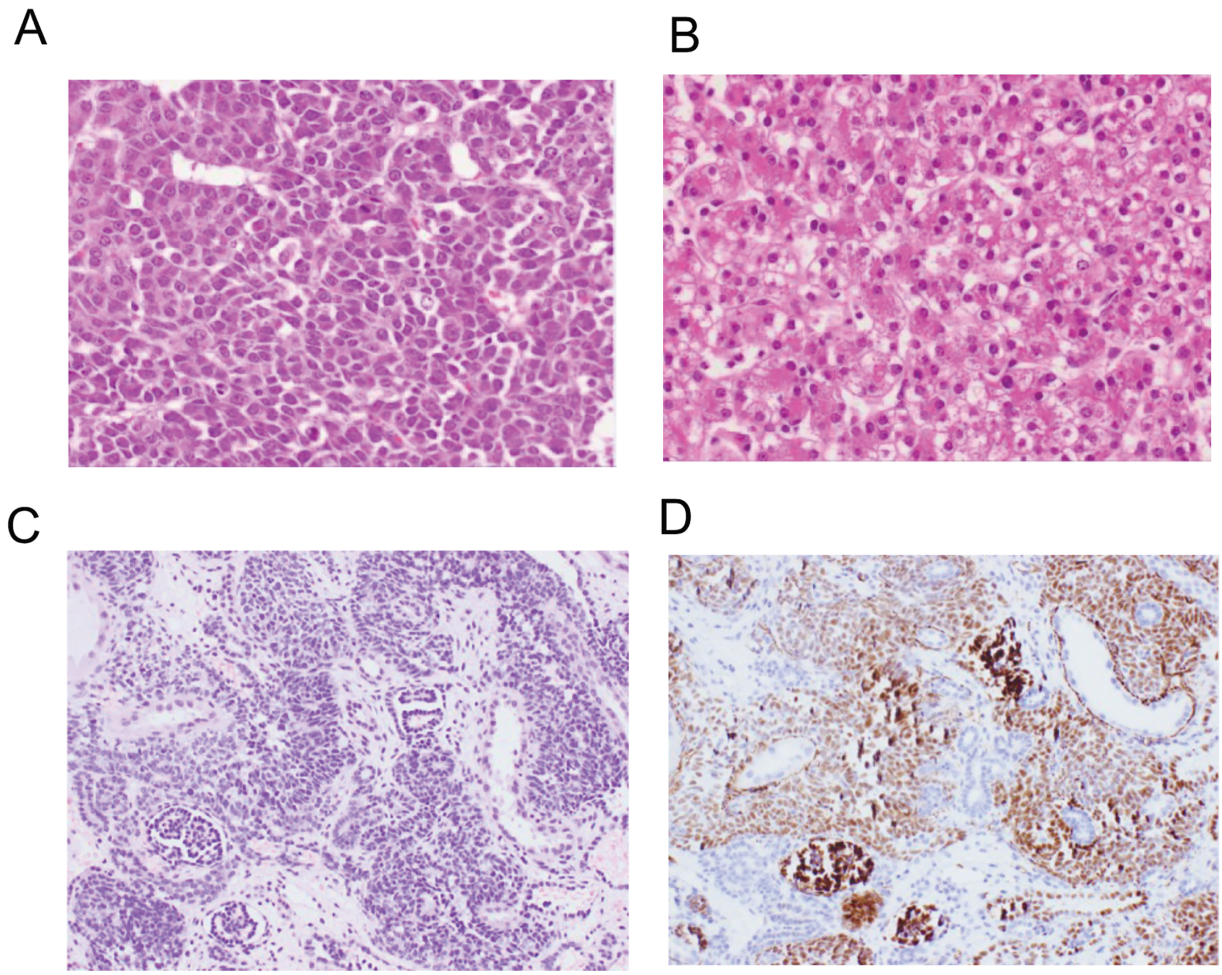

Fig. 2 Histological findings of liver and kidney tumors
(A, B) Hematoxylin–eosin (H & E) staining of the liver tumor showing both embryonal (A) and fetal components (B), consistent with mixed-type hepatoblastoma. (C) H & E staining of the kidney tumor reveals atypical immature round-cell proliferation forming nests and partial immature glomerular differentiation. (D) Immunohistochemical analysis demonstrating diffuse WT-1 positivity in tumor cells.

tralateral renal involvement. A needle biopsy was therefore performed for histopathological evaluation of the renal lesion.

Histology confirmed complete (R0) resection of a hepatoblastoma of the mixed fetal and embryonal subtype **(Fig. 2A, B)**. The renal biopsy showed atypical immature round-cell proliferation forming nests, with partial glomeruloid differentiation **(Fig. 2C)**. Immunohistochemical staining revealed diffuse positivity for WT-1 **(Fig. 2D)**. No capsule was identified between the lesion and the surrounding renal parenchyma. Although the findings were suggestive of intralobar nephrogenic rest, nephroblastoma could not be excluded due to limited tissue sampling.

If WT had been definitively diagnosed, neoadjuvant therapy with vincristine and actinomycin D would have been initiated to reduce tumor size before considering nephron-sparing surgery. However, given that the postoperative regimen for hepatoblastoma involved cisplatin monotherapy–and platinum agents have demonstrated limited activity against recurrent WT[6]–cisplatin was prioritized, with close monitoring of the renal lesion.

The patient received six cycles of cisplatin monotherapy, which were well-tolerated without severe adverse effects. Serum AFP levels decreased markedly to 6.1 ng/mL. Serial imaging during treatment demonstrated no interval growth of the renal mass

(Fig. 1E, F, 6 and 11 months**)**.

Three months after completing chemotherapy, follow-up MRI showed significant enlargement of the renal lesion **(Fig. 1G**, 14 months**)**, consistent with clinical progression to WT. A mild elevation of serum AFP (130 ng/mL) was also observed, likely reflecting WT progression rather than hepatic recurrence. After detailed discussions regarding further management, the parents declined intensive treatment for WT. The patient succumbed to tumor progression at 17 months of age.

Ⅲ Discussion

This report describes a child with trisomy 18 who simultaneously developed hepatoblastoma and Wilms tumor (WT). Although trisomy 18 is known to confer an elevated risk for these malignancies, this is, to our knowledge, the first documented case of their concurrent occurrence.

Histological examination of the renal lesion suggested an intralobular nephrogenic rest ; however, a definitive distinction from WT was not possible owing to limited tissue sampling. Nephrogenic rests represent residual embryonic metanephric cells that persist beyond 36 weeks of gestation in normal kidneys[7]. Both clinical[8] and molecular[7] studies indicate that nephrogenic rests may serve as precursors of WT and are associated with an increased risk of malignant transformation. For instance, Brown et al.[8] reported that 33 % of patients monitored for nephrogenic rests developed WT during follow-up. In this case, the limited biopsy sample may have failed to capture overt WT regions. Furthermore, the rapid tumor progression and the clinicopathological features observed were consistent with WT behavior, supporting a clinical diagnosis of WT during disease evolution.

During postoperative cisplatin monotherapy for hepatoblastoma, the renal mass showed no interval growth, suggesting that cisplatin may have exerted a transient suppressive effect. In retrospect, given the later rapid progression, earlier consideration of WT-directed neoadjuvant therapy when tumor stability was first noted might have enabled more timely surgical intervention.

Multiple primary cancers are uncommon in children because most pediatric tumors arise from disruptions in developmental pathways (e.g., transcriptional or chromatin dysregulation) rather than the progressive accumulation of somatic mutations[9]. When dual primaries occur, they are usually linked to an inherited cancer predisposition syndrome, such as Li-Fraumeni syndrome[1]. Whole-exome sequencing has identified genetic predispositions in 33.3 % (42 of 126) of WT cases, underscoring the strong association between WT and germline abnormalities[10]. Chromosomal aberrations, including those observed in Beckwith-Wiedemann syndrome and trisomy 18, have also been associated with an increased risk of hepatoblastom[11].

Collectively, our findings, together with previous reports, indicate that children with trisomy 18 have a particularly high predisposition to both hepatoblastoma and WT. This underscores the need for vigilant tumor surveillance and multidisciplinary coordination in managing malignancies in this population. Current recommendations for trisomy 18[3)12)] include a comprehensive abdominal ultrasound with serum alpha-fetoprotein (AFP) measurement every three months from birth to four years of age, followed by renal ultrasound every three months from 4 to 7 yr, and semiannual abdominal ultrasound thereafter[3)12)]. Our patient's development of a renal tumor in infancy, in the presence of a horseshoe kidney, highlights the importance of early and comprehensive abdominal screening. Once a malignancy is diagnosed, continued three-monthly imaging is appropriate, with intervals adjusted through shared decision-making to balance early detection with minimization of radiation exposure and sedation risks.

Although palliative management has historically been the mainstay of care for children with trisomy 18, recent evidence indicates that standard intensive neonatal and pediatric treatments can significantly improve survival outcomes[13]. Moreover, standard therapeutic approaches-including surgery and chemotherapy-have been associated with favorable outcomes for hepatoblastoma in children with trisomy 18 who do not have severe cardiac dysfunction[14]. In

our case, standard postoperative chemotherapy for hepatoblastoma was administered. However, following progression of the renal tumor, the family chose to decline further aggressive treatment due to concerns regarding quality of life, the risk of renal failure, and the potential need for long-term dialysis.

Had definitive therapy been pursued, we planned to initiate neoadjuvant vincristine and actinomycin D, reassess vascular anatomy and split renal function, and consider nephron-sparing resection if feasible. Contingency measures, including peritoneal dialysis in the event of postoperative renal failure, were also discussed. This case highlights the importance of individualized, family-centered decision-making when determining the optimal therapeutic strategy for children with trisomy 18[15].

In conclusion, we present a rare case of a child with trisomy 18 who developed both hepatoblastoma and WT. Together with existing literature, this report reinforces the concept of a strong tumor predisposition in trisomy 18 and emphasizes the critical role of early surveillance, multidisciplinary management, and shared decision-making in improving clinical outcomes.

Author Contributions

Y.F. and S.S. contributed to the conception and design of this study. H.M., Y.F., Y.M., M.K., K.Y., E.O., K.H., and S.S. were involved in patient care. M.K. provided genetic counseling. Y.N. and S.S. supervised the study. H.M., Y.F., and S.S. drafted the manuscript. All authors critically revised the manuscript, approved the final version, and agreed to be accountable for all aspects of the work to ensure its integrity and accuracy.

Conflicts of interest

Authors have no conflicts of interest to declare.

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