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Bilateral Wilms' Tumor in Trisomy 18 Syndrome: Case Report and Critical Review of the Literature

Consolato Sergi^{1,2,3,4} and Marina Kos^{5,6}

¹Tianyou Hospital, Wuhan University of Science and Technology, Wuhan, Hubei, PR China

²Institute of Biomedical and Pharmaceutical Sciences, Hubei University of Technology, Wuhan, Hubei, PR China

³Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, Canada

⁴Stollery Children's Hospital

⁵Clinical Department of Pathology, Univ. Hospital Center "Sestre milosrdnice", Zagreb, Croatia

⁶Medical School University of Zagreb, Croatia

Address correspondence to Consolato Sergi, MSc, MD, PhD, FCPC, FCAP; Department of Laboratory Medicine and Pathology, University of Alberta, 8440 112 St, Edmonton, AB, Canada; e mail: sergi@ualberta.ca

Abstract

We present a patient with trisomy 18 syndrome and bilateral Wilms' tumor representing the second case of the literature. Physicians should remain alert to the possibility of WT in patients with trisomy 18 who may survive beyond infancy. In this event, it may be essential to consider periodic abdominal ultrasound for screening purposes. A critical review of the literature is presented.

Key words

trisomy 18 nephroblastoma karyotype

Introduction

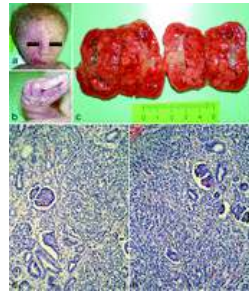
Wilms' tumor (WT) is the most common malignant renal tumor in children with triphasic component (blastemal, epithelial, and stromal components) and is bilateral in 4–13% of affected children. Nephroblastomatosis refers to the diffuse or multifocal involvement of the kidneys with nephrogenic rests (persistent metanephric blastema) and needs to be differentiated from WT as well as other renal tumors or dysplastic lesions [1–3]. Nephrogenic rests are found incidentally in 1% of infants and such foci of metanephric blastema able to persist beyond 36 weeks of gestation have the potential for malignant transformation into WT. Up to 40% of WTs may indeed originate directly from nephrogenic rests. Up to 5% of bilateral WT have a synchronous presentation and, in these cases, some predisposing syndromes should be considered. We present a case of WT found at autopsy in both kidneys of a newborn with trisomy 18 syndrome supporting the concept of a potential additional locus for WT.

Case Report

A 27-year-old woman (P2, G2) presented at 35 weeks gestation because of polyhydramnios. Her pregnancy was controlled outside the clinic until admission. The double test showed low risk, and previous routine ultrasound did not disclose further abnormalities. Following admission, an amniotic fluid drainage was performed. Two weeks after admission she complained of lower abdominal pain and an amniocentesis was performed during which the membranes ruptured. Caesarean section was completed, and a male infant (2350 g/47 cm, Apgar scores 6/10, 7/10) was delivered. The newborn died of respiratory failure a few hours later. The external examination showed a globular head with facial dysmorphism (slanted eyes, small and rounded mouth, micrognathia, low-set ears), clinodactyly and overlapping fingers on both hands (Figure 1a&b). The internal examination revealed enlarged kidneys for both kidneys, which were pale gray, slightly nodular with effacement of the corticomedullary junction (Figure 1c). No other abnormalities of the urinary system were found. Histopathological examination of both kidneys revealed the replacement of most kidney parenchyma by bilateral WT. The histology consisted of highly cellular blastematosus areas of small, round-to-oval, primitive cells and epithelial component characterized by the formation of tubular and glomerular structures (Figure 1d&e). Other organs were unremarkable, except for the lungs showing atelectasis. Postnatal cord blood karyotyping showed an extra chromosome 18.

Figure 1

(a) Globular head, slanted eyes, small rounded mouth, and micrognathia; (b) Clinodactyly and overlapping fingers on both hands; (c) The cut surface of both kidneys showed pale, nodular tissue effacing the corticomedullary junction; (d&e). Tumor areas showing cellular blastematosus areas of small



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blue cells and some primitive glomerular and tubular structures
(Hematoxylin-eosin staining x200).

Discussion

Wilms' tumor (WT) or nephroblastoma is one of the most common tumors in childhood and is apparently derived from renal blastemal cells, usually from several lines of differentiation, and the nephrogenic rest is the only precursor lesion of nephroblastomatosis [3]. WT is only exceptionally seen as a congenital neoplasm, and bilateral synchronous presentation in the newborn is extremely rare. Trisomy 18 is a condition that is associated with possible increased risk of WT [4]. Although it may develop in long-term survivors with trisomy 18, to our knowledge this is the second reported case of congenital, bilateral WT in a newborn with trisomy 18 syndrome. In the previous literature, we found 12 additional occurrences of WT presenting either mono- or bilaterally that are summarized in Table 1 [5]. The congenital anomalies most commonly associated with WT are aniridia, hemihypertrophy, Beckwith-Wiedemann syndrome, WAGR (Wilms tumor/Aniridia/Genitourinary anomalies/Retardation, mental) syndrome, and Denys-Drash syndrome. Other reported conditions associated with WT are Perlman syndrome, Turner syndrome, trisomy 8 syndrome, Sotos syndrome, 2q alterations, and several genitourinary anomalies.

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Table 1

MWT/BWT in Trisomy-18.

One of the abnormalities also due to failed meta-nephric differentiation is multicystic kidney dysplasia (MCKD). MCKD is characterized histologically by the presence in the kidney of abnormal lobar organization (primitive ducts and deficiency of vasa recta and loops of Henle) and dysplastic elements (metaplastic cartilage, undifferentiated mesenchyma, and immature collecting ductules) [3]. MCKD is almost always a unilateral lesion, but an associated abnormality of the contralateral kidney may be observed and we, previously, also found a renal cell carcinoma and a WT in an MCKD [3,6]. To date, MCKD is not an abnormal finding in trisomy 18 syndrome, being considered already in 1976 published Bolande's work. Dr. Bolande reviewed the types of congenital malformations associated with the development of neoplasms [7]. Substantially, these associations appear to be of central importance in developmental biology. In fact, there is the tendency for neoplasms to develop in anomalous or dysplastic tissues, including vestiges, undescended or dysgenic gonads, and some hamartomatous conditions. An increase of the incidence of tumors has been observed in: (I) specific disorders: aniridia, hemihypertrophy, Beckwith's syndrome, and basal cell nevus syndromes among others; (II) cytogenetic abnormalities (trisomy 21 syndrome, 13q- syndrome, and trisomy 18 syndrome); as well as (III) chromosomal instability syndromes, including Fanconi's anemia, ataxia-telangiectasia, and Bloom's syndrome. Some of the agents have been identified as both teratogenic and carcinogenic, although controversies among cancer agencies are, currently, not new [8–10]. Several compounds, known to be carcinogenic when administered postnatally to animals, are teratogenic in the fetus, while a few agents are both teratogenic and carcinogenic when applied to the fetus. As stated earlier, the timing of intrauterine insult is crucial in determining whether the effect on the offspring is teratogenic, oncogenic or may entangle both [7].

Trisomy or tetrasomy 7, trisomy 17, and loss of chromosome Y have been described in another tumor that can be seen in childhood, the papillary renal cell carcinoma (PRCC) of the kidney [11]. An interstitial 3p loss of heterozygosity has been observed in high-resolution studies in some PRCC, and trisomy 12, 16, and 20 have also been described and have been associated with tumor progression in specific cases. Investigations

involving the chromosome genomic hybridization showed gains of chromosome 7p and 17p in some subtypes of PRCC and allelic imbalances at 17q and 9p have also been noted, although their significance is probably still under inquiry [12].

It is unknown whether WT is related to trisomy 18 or to the presence of multiple renal anomalies (that were not present in our case). However, there is enough ground to justify an additional locus on chromosome 18. Moreover, the authors' clinical experience indicates that patients with trisomy 18 syndrome may survive for more extended periods. Thus, clinicians should remain alert to the possibility of WT in patients with trisomy 18 who may survive beyond infancy. In this event, it may be essential to consider periodic abdominal ultrasound for screening purposes.

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