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# Bilateral adrenal neuroblastoma and nephroblastoma occurring synchronously in a child with Fanconi's anemia and VACTERL syndrome

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**Abstract** Fanconi's anemia (FA) is an autosomal recessive inherited syndrome with a predisposition to malignancy. The association between FA and solid pediatric tumors is extremely rare. The authors report a rare case of VACTERL syndrome associated with FA and multiple solid pediatric tumors occurring in a very young girl. This child had numerous congenital anomalies (horseshoe kidney, cerebella hypoplasia, microcephaly, sacral agenesis) and esophageal atresia, which was repaired in neonatal period. Such association led quickly to the diagnosis of FA. At age of 11 months, she developed simultaneously a renal tumor in a horseshoe kidney and bilateral adrenal tumors. The left adrenal mass was removed, and partial nephrectomy was performed. Histological analysis concluded to adrenal neuroblastoma and nephroblastoma. We also evaluated the c-kit expression in these tumors to propose a therapeutic alternative to chemotherapy by oral agent STI-571 (Gleevec; Novartis, East Hanover, NJ). Strong cytoplasmic immunostaining of c-kit was found in both tumors. Unfortunately, she quickly developed a posterior cerebellar fossa tumor and died 1 month later. This clinical situation is very rare but suggests that young patients with FA and solid pediatric tumors may belong to a particular subgroup of FA. Further studies are necessary to test if STI-571 treatment could be efficient in such patients with pediatric tumors.


Fanconi's anemia (FA) is an autosomal recessive genomic instability syndrome characterized by developmental defects, short stature, renal and genital malformations, microcephaly, progressive bone marrow failure, and a predisposition to malignancy [1]. Solid tumors, which account for only 5% of total tumors, and pediatric blastemal tumors are exceptionally associated with FA [2].

We report clinical, histological, and genetic findings of bilateral neuroblastoma and nephroblastoma co-occurring in an very young girl with an FA and a VACTERL syndrome.

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## 1. Case report

Antenatal ultrasonography of a female fetus showed horseshoe kidney, cerebella hypoplasia, and microcephaly. Birth weight at 37 weeks' gestation was 2240 g (<10th percentile), and head circumference was 30.2 cm (<5th percentile) and length was 45 cm (<10th percentile). At day 1, surgery was performed for esophageal atresia. Chromosomal analysis showed increased spontaneous chromosomal and caryolysin-induced breakage in metaphase preparation of cultured peripheral blood lymphocytes, leading to the diagnosis of FA. Radiographic examination revealed sacral agenesis. Echocardiography showed a small ventricular septal defect. Renal ultrasonography and cystography revealed a horseshoe kidney with bilateral vesicoureteral reflux. Posterior cataract was also identified.

At 11 months, a 2-cm mass localized in the lower left part of the horseshoe kidney was detected by ultrasonography and tomodensitometry (Fig. 1A). The right and the left adrenal glands were noted to be enlarged. Urine vanillylmandelic acid level was 29.33 $\mu$mol/mmol of creatinine (normal value, <5.70 $\mu$mol/mmol) and the homovanillic acid level was 22.76 $\mu$mol/mmol of creatinine (normal value, <27 $\mu$mol/mmol).

After obtaining parental consent, explorative surgery with biopsy of the adrenal gland and partial nephrectomy was performed. During surgery, the left adrenal mass was removed and analyzed immediately, leading to the diagnosis of neuroblastoma. The other adrenal mass was not removed

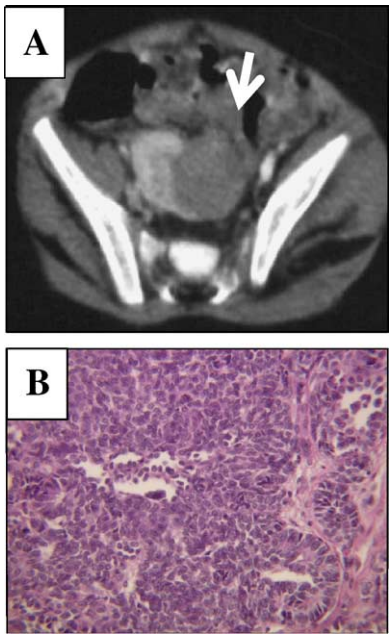


**Fig. 1** Nephroblastoma: abdominal computed tomographic scanner and histopathologic features. A, Abdominal computed tomographic scanner showing the nephroblastoma (arrow) in the horseshoe kidney. B, Histology reveals a predominantly epithelial nephroblastoma (hematoxylin-eosin staining, original magnification ×250).

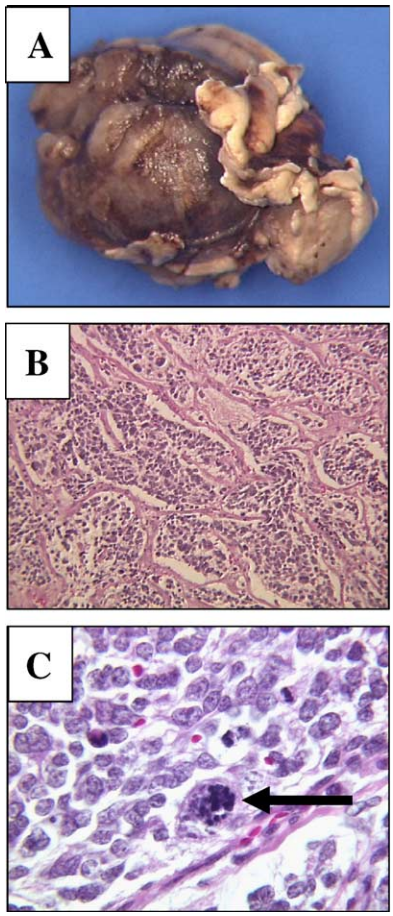


**Fig. 2** Left adrenal neuroblastoma: gross examination and histological features. The adrenal tumor measures 2.5 × 1.5 cm (A), and histology shows a stroma-poor, poorly differentiated neuroblastoma (B) with numerous atypical mitosis (C, arrow) (hematoxylin-eosin staining; B, original magnification ×160; C, ×400).

to preserve adrenal function. Partial nephrectomy with complete tumorectomy was also performed at the same time. Fresh samples of the neuroblastoma were immediately put in medium culture for cytogenetic studies and snap-frozen in liquid nitrogen. The nephroblastoma consisted mainly of epithelial elements forming tubules lined by basal crowded nuclei with marked mitotic activity or glomerular structures (Fig. 1B). The stromal element consisted of undifferentiated or fibroblastic cells. Scattered small foci of blastema were also present. No anaplasia was identified. The nephroblastoma was classified as an intermediate-risk tumor, nonaplastic nephroblastoma, and stage I.

Gross examination showed a 5.1-g adrenal tumor measuring 2.5 × 1.5 cm without calcifications (Fig. 2A). The peripheral neuroblastic tumor was classified according to International Neuroblastoma Pathology Committee recommendation as a neuroblastoma (Fig. 2B), stroma poor, poorly differentiated, mitosis-karyorrhexis index intermediate, high mitotic rate, no calcifications, younger than 18 months, and favorable [3]. It was remarkable by the high number of abnormal mitosis and numerous