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CONGENITAL MESOBLASTIC NEPHROMA: COMPARATIVE HISTOLOGICAL STUDY OF THREE CASES AT DIFFERENT AGES

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In 1967 Bolande et al described a series of benign kidney tumors discovered at birth or during the neonatal period under the name "congenital mesoblastic nephroma" [1]. Subsequently, in 1973, Bolande identified in the literature approximately 48 examples of the same tumor, which prior to 1966 had been diagnosed under various names such as spindle cell sarcoma, fibrosarcoma, leiomyosarcoma, fibroma, leiomyoma and most frequently as Wilms' tumor or hamartoma[2]. The benignity of this tumor was first recognized by Kay et al, who suggested nephrectomy without chemotherapy or irradiation as the treatment of choice[3]. Because it was Bolande's studies which identified the tumor as a distinct benign entity, it is also known as Bolande's tumor.

The purpose of the present study is two-fold: to present three cases of mesoblastic nephroma, one of which was associated with neurofibromatosis, and to discuss whether it is in fact a benign tumor or a hamartoma.

Case Reports

Case 1. A 4-day-old male infant was brought to the Hacettepe Children's Hospital because of an enlarged abdomen. A firm, mobile abdominal mass, five cm in size, was palpated. Intravenous pyelography (IVP) disclosed a right kidney mass with minimal distortion of the renal pelvis. At the age of 10 days, a right nephrectomy was performed. Both the clinical and operative diagnoses were Wilms' tumor. The kidney with tumor weighed 100 gm (normal 12-20 gm) and measured 7 × 6 × 3.5

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cm. On sectioning, an intrarenal tumor 5 cm in diameter without a capsule was seen located in the lower pole. The cut surface was firm, grayish white and had a trabeculate appearance. No softening, cysts, hemorrhage or necroses were seen (Figure 1). The postoperative course was uneventful, and no additional therapy of any form was given. Follow-up studies of the patient a year later were normal.

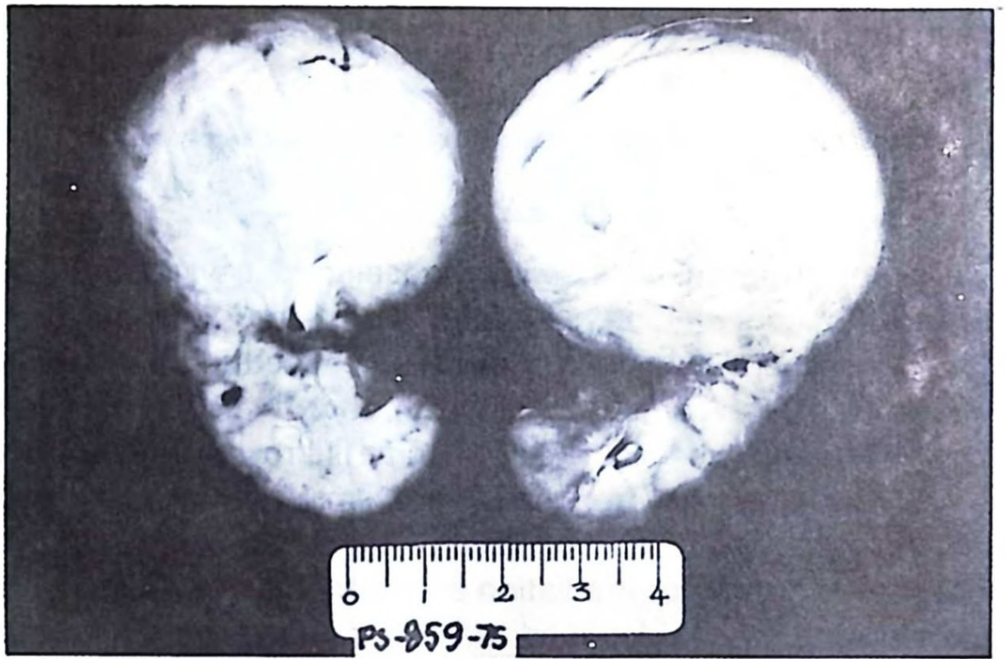

Figure 1

Cut surface of mesoblastic nephroma showing characteristic solid and trabeculate appearance resembling a uterine leiomyoma.

Case 2. A 14-month-old female was referred to the hospital because of a slowly growing mass in the abdomen which had been the size of a walnut when first noted five months prior to admission. A firm, fixed 20 cm mass in the abdomen was palpated. The IVP revealed a large mass almost filling the abdominal cavity and marked compression of the right ureter. The x-ray surveys for metastasis were negative. A right nephrectomy and para-aortic lymph node biopsy were performed. The clinical and operative diagnoses were Wilms' tumor. The kidney with tumor weighed 1670 gm (normal 40 gm) and measured 19 × 16 × 10 cm. The tumor, without a capsule, replaced much of the renal parenchyma and was globoid, grayish white in color and firm in consistency with areas of softening. No extension of the tumor beyond the renal parenchyma was seen. There was no invasion of the renal pelvis or the ureter. Histological examination of the lymph node showed no metastasis. The patient received no chemotherapy or irradiation before or after surgery. She was followed for three years and found to be normal.

Case 3: A 5-year-old male child admitted to a local hospital is the third case reported were. Case material (a slice of kidney tumor and biopsy of skin nodule) and the following case history were referred to the Hacettepe Children's Hospital for consultation.

The patient complained of abdominal enlargement for the preceding year and blood in his feces for the preceding three months. Physical examination showed abducens nerve paralysis, exophthalmos, optic nerve atrophy, several cafe-au-lait spots and a large firm fixed mass palpable in the abdomen. The IVP showed a large left kidney tumor and distortion of the renal pelvis. Chest x-rays and bone survey revealed no metastasis. Clinical diagnosis of Wilms' tumor was made and 1800r irradiation and one dose of actynomycin-D were administered preoperatively. On operation, a large kidney with a lobular mass adherent to the peripheral tissue was removed. No rupture or neoplastic invasion of the capsule was present. During the postoperative period a wound infection developed. Chemotherapy was continued, but no radiation therapy was given. Three small subcutaneous nodules clinically thought to be metastases were noted in the left scapular, clavicular and suboccipital areas. Microscopic examination of these nodules revealed neurofibromatosis. The patient died three weeks after the operation and the death was attributed to therapeutic complications.

Clinical and pathological features of the cases are summarized in Tables I and II.

Comparative microscopic study: In all three cases, the tumors showed no capsule and consisted mainly of interlacing bundles of cells forming collagen with no neoplastic nephronic elements (Figure 2). Decreasing numbers and increasing maturity of the tubules were noted as the patients' ages increased (Figures 3-5). Similarly cystic dilatation of tubuli, degeneration and intravascular thrombosis were noted in the cytological details. In Case 1, the tumor cells were more tightly packed, their nuclei often spindle-shaped with elongated cytoplasm. The nuclei showed stipling, with lighter staining of nuclear material. Mitotic figures were very rare. In Case 2, some focal areas showed variation of the nuclear size and slight hyperchromatism, and two or three mitotic figures were noted in one high-power field. In Case 3 the nuclei were less crowded and more rounded and vesicular than in Cases 1 and 2. No mitoses were seen. In all three cases the tumor had infiltrated the adjacent renal parenchyma but did not extend beyond it. Fetal glomeruli within the tumor were seen in Case 1 and within the outer normal cortex in Case 2 but none in Case 3.

Discussion

Bolande's studies of mesoblastic nephroma in neonates demonstrated that in the past they have sometimes been erroneously diagnosed as Wilms' tumor or various

TABLE I

CLINICAL SUMMARIES OF THREE CASES OF MESOBLASTIC NEPHROMA

	Case 1	Case 2	Case 3
Age of presentation	4 days	9 months	4 years
Age of operation	10 days	14 months	5 years
Sex	Male	Female	Male
Clinical findings	Palpable mass. IVP: Right renal mass and distorted pelvis	Palpable mass. IVP: Right renal mass with uretral compression	Abdominal mass and pain. IVP: Left renal mass. Exophthalmos, nerve paralysis, cafe-au-lait spots
Clinical diagnosis	Wilms' tumor	Wilms' tumor	Wilms' tumor with metastasis
Therapy given	Nephrectomy only	Nephrectomy only	Nephrectomy and chemotherapy, preoperative radiotherapy
Follow up	One year and well	Three years and well	Died 3 weeks after surgery from complications of therapy

TABLE II

PATHOLOGICAL FINDINGS OF THREE CASES OF MESOBLASTIC NEPHROMA

	Case 1	Case 2	Case 3
Tumor and kidney weight	100 grams	1670 grams	Unavailable
Approximate diameter of tumor	5 cm	14 cm	10 cm
Tumor capsule	None	None	None
Tumor consistency	Solid, firm	Solid, firm	Solid, firm
Tumor color	Grayish white	Grayish white	Grayish white
Extension of tumor	Extended into but not outside of renal parenchyma	Extented into but not outside of renal parenchyma	Extended into but not outside of renal parenchyma
Cystic changes and necrosis of tumor	None	3 small cystic changes but no necrosis	Larger cystic changes and necrosis
Microscopic findings	Monotonous, mature interlaced spindle cells, dysplastic nephronic elements, rare mitotic figures.	Similar to Case No. 1 (see "comparative microscopic study" section in text).	See "comparative microscopic study" section in text.

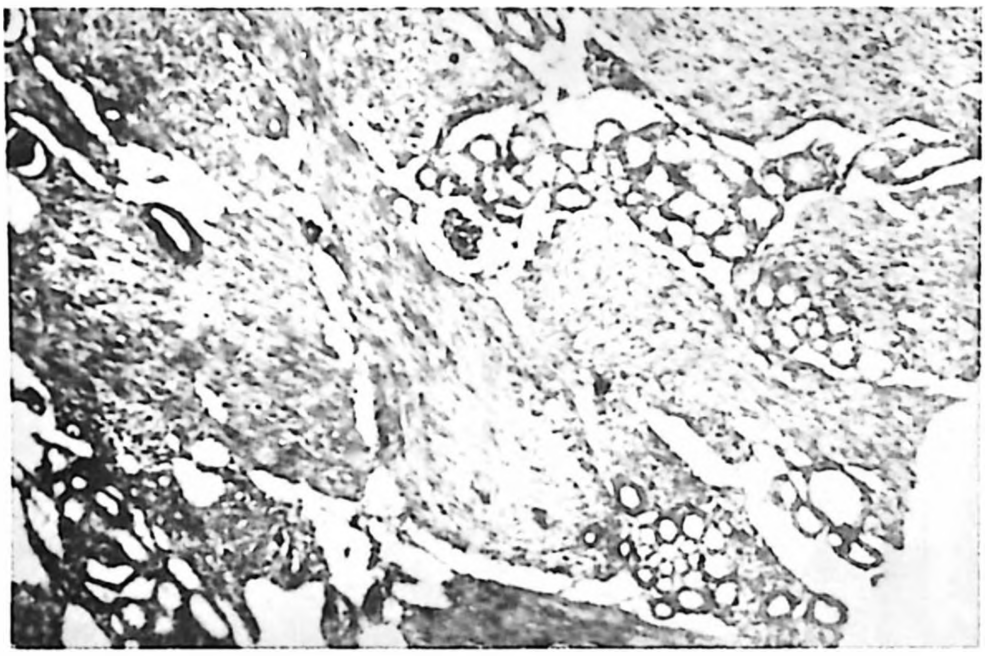

Figure 2

The tumor is composed of interlaced bundles of spindle cells and differentiated glomerular and tubular elements.

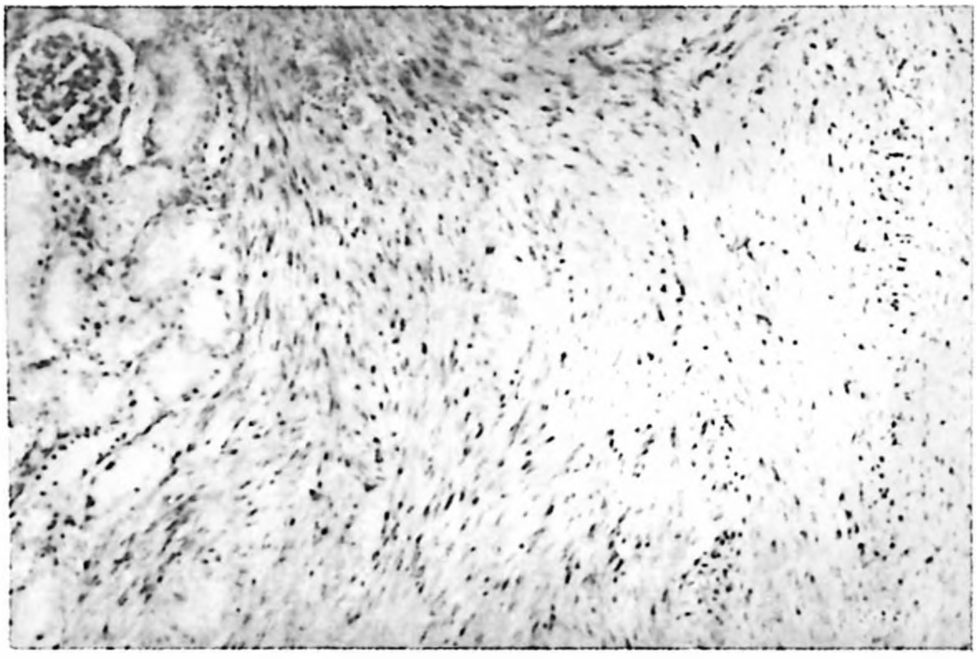

Figure 3

Junction of the tumor and renal parenchyma. Note the absence of a capsule and entrapped tubuli.

types of benign or malignant mesenchymal neoplasma[1,2]. Until 1973, no recurrences had been reported and they were generally accepted to be benign tumors, but some authors considered them to be hamartomas[3-5]. This stimulated interest in this type of tumor. Since 1973 cases with recurrences, metastasis and death unrelated to the form of therapy[5-8] and more recently renin-secreting mesoblastic nephroma have been reported[9]. This recent evidence of recurrences, metastasis and functional features, although rare, argues against the idea that these tumors are hamartomas. We have therefore concluded that they are real tumors, and opted to classify our three cases as mesoblastic nephroma.

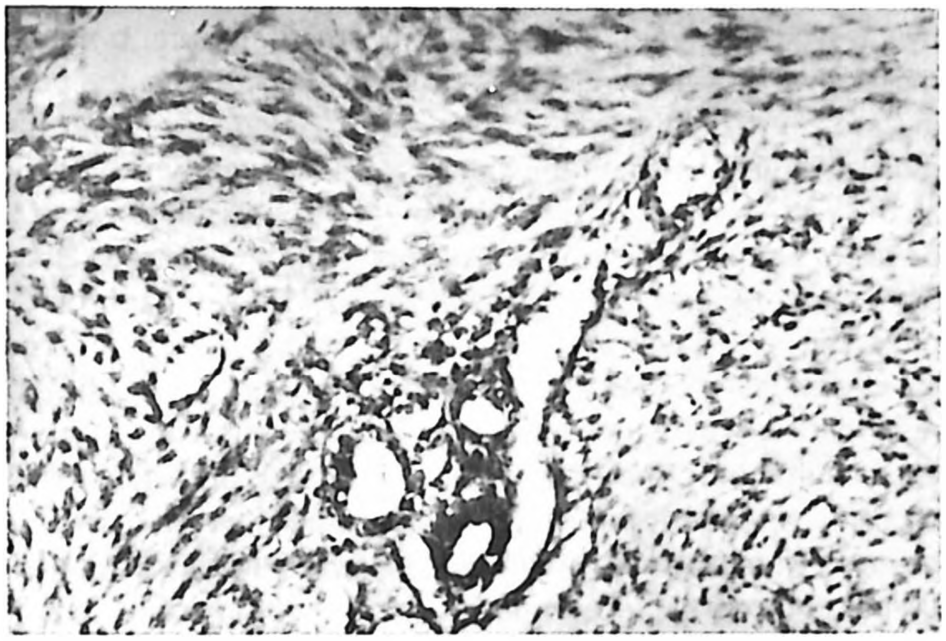

Figure 4

Differentiated tubuli within the tumor and rich vascularity of the tumor.

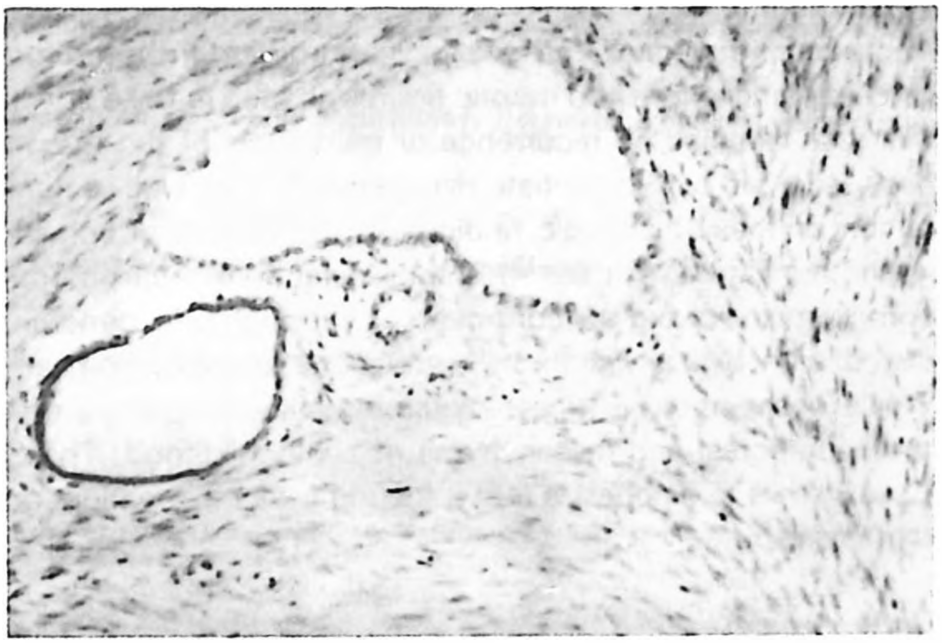

Figure 5

Cystic dilatations of the differentiated tubuli within the tumor.

Another question which needs clarification is the relation of this tumor seen in the neonatal period to the similar tumor noted in older age groups. Mesoblastic nephroma has been reported in children as old as three, eight, eleven and fifteen years[2]. Our comparative histological findings in different age groups gave some clues to this relation. Our random review of the Wilms' tumor series of 150 cases revealed that only the three cases reported in the present study showed similar and distinct morphologic features consisting of spindle cells in fibromyxoid stroma and some non-neoplastic nephronic elements. Nephronic elements in Case 1 were

dysplastic (fetal type), in Cases 2 and 3 more mature, but compressed by the tumor mesenchyma. Fetal type glomeruli were also noted in the outer cortex of the kidney in Case 2. We postulate that the nephronic elements may reflect retained differential multipotentiality of the fetal kidney mesenchyma which may decrease or disappear as the age advances, after which a tumor consisting only of spindle-type cells may be seen. Normal development of metanephric blastema is completed in about the 34th week of gestation[10]; nevertheless, similar nephronic elements have been produced experimentally and are reported to occur in secondary renal diseases of newborns[11]. These observations support the hypothesis that mesoblastic nephroma in younger children and mesenchymal tumors may be the same. The latter, in contrast to the mesoblastic nephroma, are usually small, present no clinical problems and tend to occur in adults rather than children. Similarly, the biological behavior of mesoblastic nephroma and congenital mesenchymal tumors of the soft tissues is interesting. Kauffman and Stout's study of the latter emphasized that they do become malignant, albeit rarely, and suggested that while resembling histologically those appearing in older age groups, they differ biologically[12].

Another controversy in mesoblastic nephroma is the interpretation of areas of cellularity, pleomorphism and mitotic figures as seen in Case 2. A three-year follow-up of this case revealed no recurrence or metastasis of the tumor. These findings have been recorded to substantiate malignancy[5,6,8] as well as benignity[1,2,4]. The contribution of these histologic findings to the biological behavior of the mesoblastic nephroma is not yet clear[13]. The association of neurofibromatosis in Case 3 may contribute to solving the controversy. Although rare, generalized fibromatosis associated with Wilms' tumor[14,15] and ectomesenchymomas[16] has been reported. These observations suggest pluripotentiality as well as an interrelation between the neural crest and mesenchyma of early childhood. The clinical observations in Case 3 serve to emphasize that a second tumor in a patient does not always mean a metastasis.

Summary

Three benign mesoblastic nephroma cases aged 10 days, 14 months and five years are presented. A comparative histological study of the tumors with a review of the literature suggested that they are essentially benign and may be considered mesenchymal tumors, similar to those seen in older age groups and probably differing only in size and in the age-dependent retained differential potentiality of the metanephric blastema of very young children. The unique association of neurofibromatosis in one of these cases suggested some relationship between the neural crest and mesenchyma in very young children. Although biologically different, mesoblastic nephroma may be one of the congeners of Wilms' tumor, not a hamartoma.

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