



Fig. 3. Pulmonary metastasis, consisting of anaplastic cells, immunohistochemically strongly positive for glial acidic fibrillary protein (GFAP, $\times 600$).

differentiation and histologic type of the ependymoma, age at diagnosis, degree of surgical resection or prior treatment and subsequent development of extraneural metastases was found [4]. The exact route of extraneural metastases is not known, but

in the vast majority metastases occurred in the wake of craniotomy, suggesting iatrogenic vascular seeding [3]. Typically, extraneural metastases of ependymoma occur in the lungs, pleura, and lymph nodes while metastases to the mediastinum, liver, bone, and diaphragmatic muscle are even less common [4]. In most cases, the existence of pleuropulmonary metastases was disclosed only at autopsy usually coexisting with CNS recurrence and systemic metastases [5]. Extraneural metastases or relapses of ependymoma are extremely rare but physicians caring for ependymoma patients must remain aware of this possible complication.

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Thoracic Neural Crest Tumors in Beckwith–Wiedemann Syndrome

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Beckwith–Wiedemann syndrome (BWS) is an overgrowth syndrome associated with increased birth weight, macroglossia, omphalocele, neonatal hypoglycemia, craniofacial anomalies, and visceromegaly [1,2]. The syndrome is a complex genetic disorder caused by dysregulation of multiple growth regulatory genes within the 11p15 region. It is a cancer predisposition syndrome, and at least 7.5% of patients develop a malignant disease; most commonly Wilms tumor [3]. Other embryonal tumors have been reported including hepatoblastoma and rhabdomyosarcoma, but neural crest tumors are rare. We, therefore, add to the literature two children with BWS in whom thoracic ganglioneuroma and ganglioneuroblastoma were found.

The first child was diagnosed with BWS complicated by neonatal hypoglycemia, mild macroglossia, omphalocele and cleft palate. She did not have hemihypertrophy. At age 4 years, she underwent a cleft palate repair under general anesthesia when decreased air movement on the left side of her chest was noted. A chest radiograph revealed a large posterior mediastinal mass. Computed tomography (CT) of the chest, abdomen and pelvis showed a left-sided 5.3 cm \times 4.6 cm \times 7.4 cm posterior paraspinal mass with speckled calcification that proved to be ¹²³I-meta-iodobenzylguanidine (MIBG) avid. There was no evi-

dence of bone marrow involvement. A twenty-four hour urine collection showed an elevated vanillylmandelic acid (VMA) of 9.7 mg/total volume (tv) (normal 0–4) and an elevated homovanillic acid (HVA) of 23.5 mg/tv (normal 0–10). Ferritin was 22.5 ng/ml (normal 10–55). The mass was completely excised, and ganglioneuroma was confirmed on histologic examination of the surgical specimen. No adjunctive radio-

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TABLE I. Cases of Children With Beckwith–Wiedemann Syndrome (BWS) and Neural Crest Tumor

Case no.	Author/et al.	Location of tumor	Histology	Urine catecholamines	Symptoms	Hemihypertrophy
1	Wiedemann [10]	Paraspinal	Ganglioneuroma	ND	Asymptomatic	Yes
2	Sotelo-Avila [11]	Retroperitoneal	Ganglioneuroma	ND	ND	ND
3	Emery [1]	Thoracic	Neuroblastoma	Normal	Respiratory distress	No
4	Sirinelli [4]	Thoracic	Neuroblastoma	Elevated	Asymptomatic	Yes
5	Sirinelli [4]	Thoracic	Ganglioneuroma	Normal	Asymptomatic	No
6	Huber [8]	Thoracic	Neuroblastoma	Normal	Asymptomatic	No
7	Chitayat [7]	Adrenal	Ganglioneuroblastoma	ND	ND	No
8	DeBaun [9]	ND	Neuroblastoma	ND	ND	ND
9	DeBaun [9]	ND	Neuroblastoma	ND	ND	ND
10	Yoon [12]	Thoracic	Ganglioneuroblastoma	Elevated	Respiratory distress	No
11	Thornburg	Thoracic	Ganglioneuroma	Elevated	Respiratory distress	No
12	Thornburg	Thoracic and pararenal	Ganglioneuroblastoma	Elevated	Abdominal Mass	Yes

ND, not described.

therapy or chemotherapy was given, and the patient is now 5-year-old without recurrence or development of Wilms tumor.

A second child was diagnosed with BWS at birth. Her course was complicated by hypoglycemia, macroglossia, omphalocele, and right-sided hemihypertrophy. At eighteen months of age, she presented with an abdominal mass. On chest, abdomen, and pelvis CT, she was found to have a 5 cm × 5 cm × 7 cm abdominal mass anterior to the left kidney and also a 2 cm × 2 cm × 4 cm right thoracic paraspinal mass with speckled calcification. MIBG whole body scan showed uptake in the right paraspinal area and left pararenal area. A bone scan was negative as was the bone marrow evaluation. The urine VMA was 29 mg/tv (normal 0–1.5) and serum ferritin was 26 ng/ml (normal 10–55). The tumors were completely resected and assessed to be differentiating ganglioneuroblastomas. MYCN was non-amplified. The patient was diagnosed with two primary stage I ganglioneuroblastomas. She did not receive any chemotherapy or radiation therapy and has been in remission for 15 years.

DISCUSSION

Children with BWS are typically able to overcome hyperinsulinism, macroglossia, and omphalocele [2,4]. The long-term outcome is determined primarily by the development of a malignancy. Wilms tumor is the most frequently associated tumor. It has been recommended that children with BWS have abdominal ultrasonography every 3–4 months during childhood to screen for Wilms tumor [2,5,6].

Neural crest tumors are much less frequently associated with BWS than Wilms tumor. Table I summarizes all of the reported cases to date, including the two we describe. Among them, there was a fairly even distribution between neuroblastoma, ganglioneuroblastoma, and ganglioneuroma. Urine catecholamine levels were elevated in four of the seven patients for whom this information was available. Also, 30% of the children had hemihypertrophy.

Most important, many of the tumors were found during evaluation of non-specific respiratory symptoms. Of the twelve

reported cases of neural crest tumors in BWS, seven were thoracic in location. Therefore, abdominal ultrasound screening for detection of Wilms tumor would miss more than 50% of these neural crest tumors. Some clinicians have recommended periodic chest radiography with measurement of urinary HVA, VMA, and dopamine as a screening measure although the BWS Registry does not recommend specific screening measures for neural crest tumors [7–9]. Clinicians, thus, need to maintain a high index-of-suspicion for both thoracic and abdominal neural crest tumors in children with BWS.

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