

Case Study: Neuroblastoma of the Right Adrenal in a 17-year old Male

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Abstract:

Neuroblastoma is the most common solid extra-cranial tumor of infancy and also the most frequently diagnosed tumor of infancy.¹ The median age of diagnosis is 18 months with approximately 40% of cases being diagnosed in infancy. Because of this, it is considered one of the most important neoplasms that may arise from the sympathetic ganglia or in close proximity to the kidneys and adrenals. A right upper quadrant mass was incidentally noted on a 17-year old male while undergoing imaging for unrelated reasons. The mass was revealed to be a neuroblastoma, despite the patient having normal urine cortisol and metanephrine levels, and a right adrenalectomy was performed. However, bone marrow biopsy later showed metastasis and the patient was subsequently started on chemotherapy.

Case Report:

A 17-year old male was undergoing X-ray imaging for scoliosis when calcifications were noted in the Right Upper Quadrant. No previous patient history was noted. An abdomino-pelvic CT scan further revealed a 4.1 cm lobular right adrenal mass with coarse calcifications. Urine cortisol and metanephrine levels were normal. The patient subsequently underwent a right adrenalectomy. Gross examination of the specimen revealed a 4.2 cm encapsulated adrenal mass with red-brown to yellow cut surfaces and areas of calcifications. Gross photos of the specimen and cut surface are pictured in Figures 1-1, 1-2, and 1-4. Upon dissection of the surrounding soft tissue, multiple enlarged lymph nodes, grossly positive for metastatic disease, were identified. Microscopic examination demonstrated small, round, dark blue tumor cells in a background of fibrillary eosinophilic matrix. Immunohistochemical studies showed that the tumor was positive for CD56 and synaptophysin. Rare stromal cells were highlighted with S100. The final pathologic diagnosis was poorly differentiated neuroblastoma with a low Mitotic-Karyorrhectic Index (MKI). Based on this and the patient's age of 17.5 years at the time of diagnosis, the tumor was classified into the Unfavorable Histology Group according to the International Neuroblastoma Pathology Classification. Bone marrow biopsy later showed metastasis of the tumor and the patient was started on chemotherapy.

Prognostic Features in a Neuroblastoma:

Variable	Favorable	Unfavorable
Stage	Stage 1, 2A, 2B, 4S	Stage 3, 4
Age	< 18 months	> 18 months
Histology	Present	Absent
Evidence of schwannian stroma and gangliocytic differentiation	< 200/5000 cells	>200/5000 cells
Mitosis-karyorrhexis index		
DNA ploidy	Hyperdiploid or near-triploid	Near-diploid
N-MYC	Not amplified	Amplified
Chromosome 17q gain	Absent	Present
Chromosome 1p loss	Absent	Present
Chromosome 11q loss	Absent	Present
TRKA expression	Present	Absent
TRKB expression	Absent	Present
Telomerase expression	Low or absent	Highly expressed



Fig. 1-1: Intact specimen



Fig. 1-4: Specimen serial sectioned

Gross Description:

Received in formalin, labeled with the patient's name and medical record number and designated "Right adrenal mass, double stitch marks most inferior lymph node, shorter stitch superior, long lateral, proline marks anterior," is a 62.2 g adrenal gland and surrounding soft tissue (8.8 SI x 4.6 ML x 3.1 AP) with orienting sutures designated as follows: short suture superior, long suture lateral, proline suture anterior, and double stitch most inferior lymph node. The outer surface of the specimen is tan-pink to pink-red, smooth to shaggy and focally cauterized. The adrenal gland is inked as follows: anterior blue, posterior green. Abutting/arising from the adrenal gland is a grossly encapsulated, red-brown to yellow-tan, focally calcified mass (4.2 SI x 2.7 ML x 2.0 AP). The fibrous capsule of the mass grossly abuts the anterior, posterior, medial, lateral, and superior margins. The mass is 5.3 cm from the inferior margin. The uninvolved adrenal gland (4.4 SI x 3.9 ML x 1.3 AP) has a yellow-tan cortex measuring up to 0.2 cm surrounding a red-tan medulla measuring up to 0.2 cm.

The inferior half of the specimen is comprised of soft tissue (5.1 SI x 4.2 ML x 3.1 AP) within which are multiple distinct candidate lymph nodes. The most inferior candidate lymph node (designated by a suture) measures 2.3 x 1.4 x 1.0 cm and has white-pink to tan-white cut surfaces. The remaining lymph node candidates range in size from 0.5 to 3.6 cm in greatest dimension. The largest lymph node candidate measures 3.6 x 2.6 x 2.5 cm and has white-tan to pink-red, focally calcified cut surface.



Fig. 1-2: Cut surface of specimen. Green arrow is the encapsulated neuroblastoma. Orange arrow is the adrenal gland.

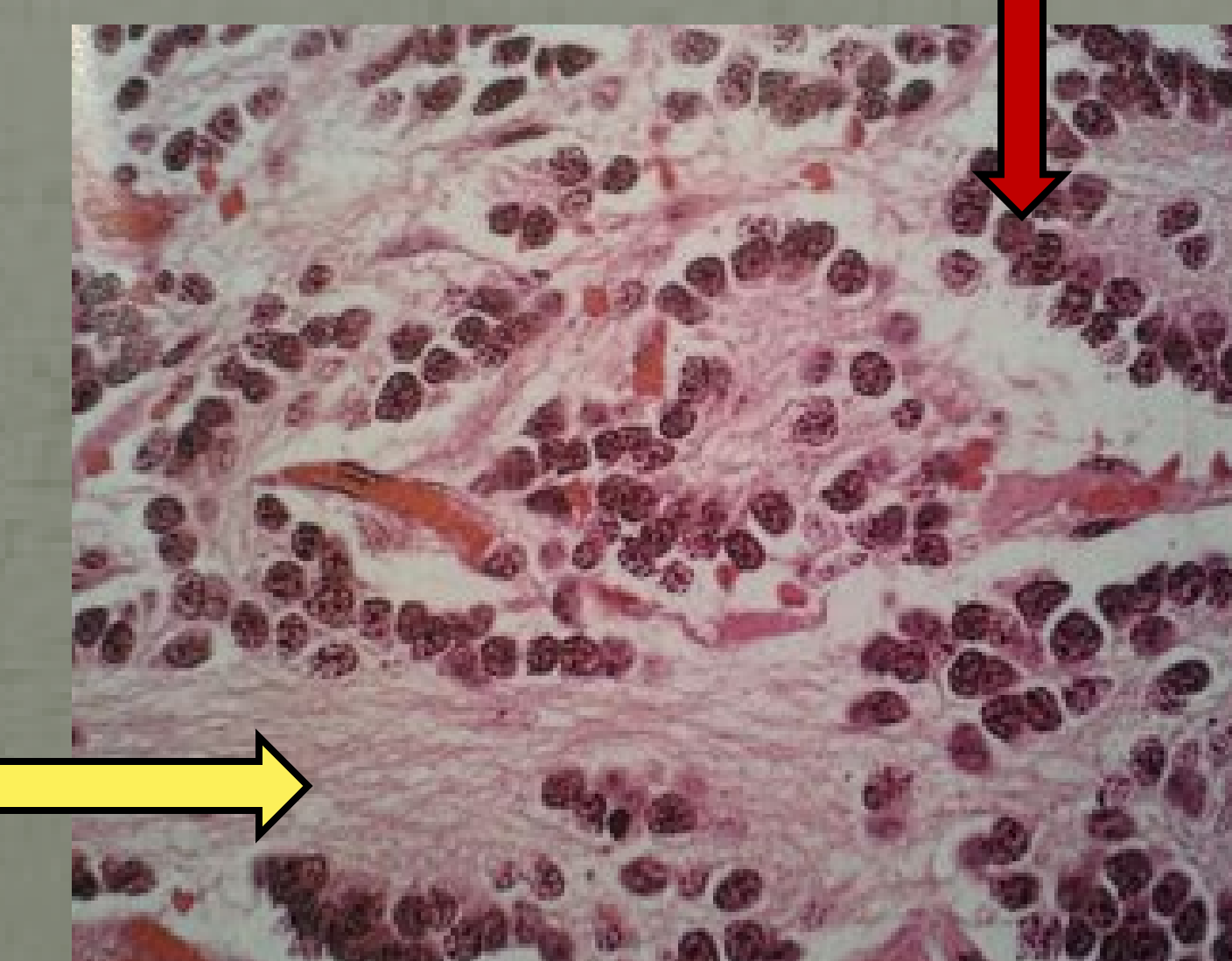


Fig. 1-3: Presentation of dark nuclei (red arrow) over a background of eosinophilic fibrillary material/ neuropil (yellow arrow). Image is stock from Robbins.⁵

Discussion:

The initial differential diagnosis for an adrenal mass in a 17 year-old male was adrenal adenoma or pheochromocytoma. Neuroblastoma was not suspected because the median age for occurrence is typically 18 months.² Microscopic review showed small round blue cell tumor and the differential diagnosis was adjusted to reflect the tumors commonly associated with this presentation. These include the following: neuroblastoma, Wilms tumor, desmoplastic small cell tumor, rhabdomyosarcoma, lymphoma, and Ewing sarcoma (PNET).

Neuroblastoma was confirmed as the diagnosis with the presentation of small cells with dark nuclei over a background of eosinophilic fibrillary material (neuropil). None of the other tumors in the small round blue cell tumor category will have a background containing neuropil. Additionally, neuroblastoma is typically the only one of the aforementioned tumors to stain positive for synaptophysin.³ Figure 1-3 demonstrates this classic presentation of a neuroblastoma on a H&E stain.

Conclusion:

This case was atypical in not only the relatively advanced age of the patient but also the lack of significant findings for urine cortisol and metanephrine levels. Approximately 90% of neuroblastomas will produce elevated blood levels of catecholamines.⁴ These are considered an important diagnostic feature. Neuroblastomas may also undergo spontaneous or therapy-induced differentiation. If cells representing ganglion cells in various stages of maturation combined with primitive neuroblasts are found, the tumor will be called a ganglioneuroblastoma. Further differentiation into more mature ganglion cells, fewer neuroblasts, and the appearance of Schwann cells, and the tumor will be called a ganglioneuroma. The appearance of schwannian stroma, highlighted by the S100 stain, is one of the prognostic factors in a neuroblastoma that is associated with a more favorable outcome. At least 50% of schwannian stroma is required in order for a neoplasm to be classified as either a ganglioneuroblastoma or a ganglioneuroma. The neuroblastoma of this case was noted to be poorly differentiated. This, as well as the >18 months age of the patient and advanced staging of the tumor led to the classification as unfavorable.

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5. Robbins. ⁵