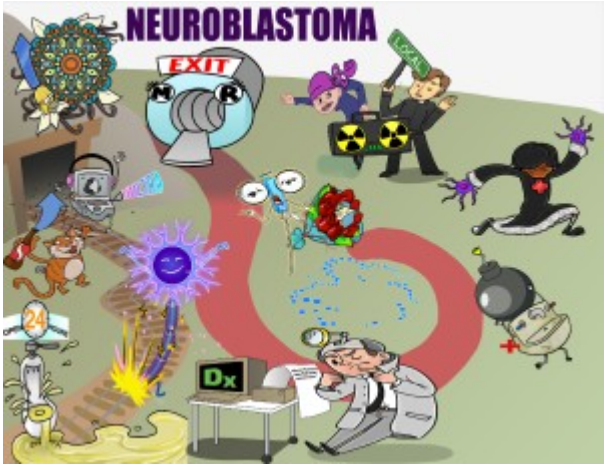
Neuroblastoma Diagnosis and Management

Neuroblastoma is the most common malignancy in infancy with a median age of presentation of 18 months. Diagnostic workup includes a 24-hour urine test for increased catecholamines, particularly homovanillic acid and vanillylmandelic acid. Since patients present with an abdominal mass, ultrasound and MRI are useful to assess tumor extent and imaging characteristics. The tumor may be located in the adrenal glands or anywhere along the sympathetic chain. Biopsy is necessary for genetic and histopathologic analysis. Findings include small, round blue cells, Homer-Wright rosettes, and positivity for bombesin and neuron-specific enolase. Treatment depends on the risk and tumoral characteristics. For low-risk neuroblastomas, observation or surgery can be curative. High-risk patients require multimodal therapy which includes radiotherapy, chemotherapy, and immunotherapy. Despite this multimodal therapy, cure rates for high-risk patients are only around 50%.



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Diagnosis

24-hour Urine Test

24-hour Urine Urinal

Neuroblastoma cells metabolize catecholamines, and therefore, over 90% of patients present with increased levels of homovanillic acid (HVA) and vanillylmandelic acid (VMA), which are catecholamine degradation products. Measuring HVA and VMA in a 24-hour urine test is usually performed initially. Urinary levels of HVA and VMA are also used for disease follow-up.

Increased Catecholamines

Up-arrow Cat-cola

Neuroblastoma cells express enzymes that metabolize catecholamines. The degradation of epinephrine, norepinephrine, and dopamine leads to the formation of homovanillic acid (HVA) and vanillylmandelic acid (VMA). Over 90% of patients with neuroblastoma present with increased levels of HVA and VMA in serum and urine.

Increased Homovanillic and Vanillylmandelic Acid

Up-arrow Homer-vanilla and Vanilla-Mandala

Homovanillic acid (HVA) and vanillylmandelic acid (VMA) are catecholamine metabolites. Elevated levels of HVA and VMA in a 24-hour urine study, in addition to positive imaging and clinical findings, should raise concern for neuroblastoma. Elevated HVA and VMA are present in over 90% of patients with neuroblastoma. 24-hour urine collection is no longer considered a required test since spot or random urinary catecholamine levels can be used instead in the diagnostic workup and are more practical.

Ultrasound

Ultrasound-machine

Ultrasound and plain radiographs are usually performed initially, depending on the presenting symptoms. When patients present with an abdominal mass, an ultrasound is usually performed first to exclude other causes such as Wilms tumor. Ultrasound findings include the presence of a heterogeneous mass arising from the adrenal gland or sympathetic chain ganglia, areas of calcification, and vascularity on Doppler.

Magnetic Resonance Imaging (MRI)

M-R-eyes Machine

Magnetic resonance imaging (MRI) is the preferred radiologic study for the evaluation of neuroblastoma. MRI should be conducted in the primary site and also in the chest, abdomen, and pelvis to evaluate for metastasis. Computerized tomography (CT scan) is also sometimes conducted to identify the primary site, but MRI is the imaging study of choice.

Biopsy

Biopsy-needle

Image-guided needle aspiration of the tumor is required for genetic and histological evaluation. The specimen must be evaluated for N-myc gene amplification and evaluation of DNA ploidy since these are markers of severity and help determine treatment. Bone marrow biopsy of iliac crests is also performed.

Pathology

Small Round Blue Cells

Small Blue-spots

One of the histological findings in neuroblastoma is the presence of small round blue cells with hyperchromatic nuclei. Other childhood tumors that present under light microscopy as small round blue cells include rhabdomyosarcoma, non-Hodgkin's lymphoma, and Ewing's sarcoma.

Homer-Wright Rosettes

Home Rose-bouquet

Homer-wright rosettes can be observed when analyzing aspirated bone marrow. They consist of round blue cells that are separated by a fibrillar matrix. Homer-Wright rosettes can also be found in medulloblastoma.

Bombesin Positive

Bomb-sink Positive

Bombesin is a neuropeptide released from neuroblastoma tumor cells and promotes cell growth. It serves as a tumor marker and is notable in small cell carcinoma of the lung and gastric cancer.

Neuron Specific Enolase Positive

Neuron Emo-lace Positive

Neuron specific enolase (NSE) is an important marker in neuroendocrine tumors. It is a clinical marker in neuroblastoma and has shown to be useful for prognostic evaluation.

Interventions

Local Excision

Local Exorcist

Surgery can be a definitive treatment for low-risk neuroblastoma. Low-risk neuroblastoma is characterized by features such as localized disease, favorable histological findings, no amplification of n-MYC, and age of presentation younger than 12 months. For high-risk neuroblastoma, surgery must be accompanied by multimodal treatment.

Chemotherapy

Chemo-head-wrap

Chemotherapy is part of the core management for patients with intermediate and high-risk neuroblastoma. Multiagent regimens are commonly used, which include drugs such as cyclophosphamide, cisplatin, vincristine, doxorubicin, etoposide, and topotecan.

Radiation

Radiation-radio

Due to the risks associated with radiation in children, radiotherapy is reserved for high-risk neuroblastoma.