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Neuroblastoma

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Introduction

Neuroblastoma is the most common, aggressive extracranial solid malignant type of cancer found in pediatric patients. "Neuro" refers to the nerves, "blastoma" indicates the type of cancer affecting immature cells during development, (American Cancer Society, 2018). Being a Pediatric RN at one of the top Childrens Hospitals, I often see many types of pediatric cancers in all stages. Neuroblastoma is one that I have found to be quite interesting due to the fact patients are often under the age of one year old, and each patient has experienced different effects from their tumor diagnosis. The exact pathophysiology of the disease is unknown., also making me curious to read the studies of all the different pathways potentially leading to Neuroblastoma.

Pathogenesis of Neuroblastoma

Origination begins during intrauterine life, when nerve cells are affected at their earliest form as a neuroblast, in the sympathetic nerve ganglia of the abdomen, adrenal glands or the venterolateral neural crest cells. Neuroblastoma develops when the neuroblasts don't mature correctly and can continue growing, creating a tumor. The deregulation of the neural crest tissue may contribute to the development of tumor cells. The cells that migrate away from the neural tube, or spine during embryogenesis have the ability to develop a new phenotype with other ligands throughout the body (Louis et. al., .2015). Metastasis sites include bone, bone marrow, liver, lungs, brain and areas of soft tissue. The symptoms the child is experiencing is dependent upon the location of the tumor and which organs are involved. Due to the migration of the neural crest cells, the maturation process of these cells can be studied as precursors to the transformation of malignant cells.

There are multiple different pathways in understanding the pathophysiology of Neuroblastoma and the specificities of its origin. Studies are being done on the neural crest tissue and inhibiting the maturation of malignant tumors and the effectiveness of interventions on a cellular level for early detection. Chromosomal studies are being performed to identify instability and the genomic rearrangements within the body. As explained in ***table 1,*** the presence of differentiation and the histology of the tumor and their specific stage and risk group. Studies are done not only to detect the disease early, but also determining the aggressiveness and progression of the disease on a genetic level once diagnosed (Neuroblastoma, 2020). There is no definitive answer biologically aside from the immaturity of neural crest cells forming clusters of neuroblasts as a solid malignant tumor.

Risk Groups

Neuroblastoma is classified into 4 different categories; very low risk, low risk, intermediate risk or high risk. With the use of The International Neuroblastoma Risk Group Staging System (INGRSS) and International Neuroblastoma Staging System (INSS) classification systems and imaging, risk groups can be predicted. Understanding the risks and behavior of the tumor, response to treatment can be predicted.
The following factors are used in order to determine the classification of the tumor:

- Stage of disease, with use of INRGSS/ INSS
- Age at time of diagnosis
- Histology
- Differentiation of tumor cells
- Presence of MYCN oncogene that provides instruction for making a protein that is important in tissue and organ formation during embryonic development. When mutated can cause normal cells to become cancerous.
- Chromosome 111q status
- DNA content of tumor cells

(Neuroblastoma, 2020)

Stages

There are two International Neuroblastoma staging systems used to determine the exact phase of the disease. The International Neuroblastoma Staging System was established in 1988, using a surgical, pathological staging system to classify the stages of Neuroblastoma. The International Neuroblastoma Risk Group Staging System was later developed in 2009, using imaging results taken before surgery to determine the stage of the disease, (American Cancer Society, 2018).

International Neuroblastoma Staging System (INSS)

- Stage 1: tumor is localized with complete gross resection, lymph node involvement near the tumor may occur
- Stage 2A: tumor is localized but unable to be resected in its entirety, no lymph node involvement
- Stage 2B: tumor is localized, complete resection may or may occur, ipsilateral lymph node involvement
- Stage 3: tumor is unable to be resected, metastasis to lymph nodes near tumor
- Stage 4: original tumor metastasized to distant lymph nodes in the bone, bone marrow, liver, skin and other organs
- Stage 4S: original tumor is located where it started and has only spread to the skin, liver and/or bone marrow – infants less than one year of age. Bone marrow involvement is minimal with less than 10% of cells testing positive

International Neuroblastoma Risk Group Staging System (INRGSS)

- Stage L1: tumor is located where it started, no image defined risk factors present in imaging scans
- Stage L2: tumor has not spread past nearby tissues from original location, imaging defined risk factors present on CT or MRI
- Stage M: tumor has spread to other parts of the body
- Stage MS: tumor has spread to only the skin, liver, and/or bone marrow in children under the age of 18 months

Clinical Presentation

- Abdominal pain
- Weight loss, anorexia
- Fatigue
- Bone pain, limping
- Numbness, tingling
- Unexplained fever
- Irritability
- Periorbital ecchymosis
- Tumors of the paraspinal sympathetic ganglia can cause: weakness, limping, paralysis, bladder/bowel dysfunction
- Thoracic tumors are often asymptomatic, but can cause mild airway obstruction and chronic cough
- Infants experience skin lesions similar to rubella
- Uncommon effects include diarrhea, hypertension, myoclonic jerking or rapid eye movements

Table 1: Risk Group and Stages of Neuroblastoma

Risk Group	Stage	Age	MYCN Amplification	Differentiation and Histology
Low	1	<18 months	Present	Favorable or Unfavorable
Low	2A/2B	< 18 months	Present or Absent	Favorable or Unfavorable
Low	4S	<12 months	none	Favorable
Low	L2	< 18 months	none	11q
Low	M	< 18 months	None	None
Intermediate	2A/2B	<12 months	Present	Favorable or Unfavorable
Intermediate	3	< 18 months >18 months	None None	None Favorable
Intermediate	4	<12 months 12-18 months	None None	None None
Intermediate	4S	<12 months	None	Unfavorable
Intermediate	M	<18 months >18 months	Present None	None None
Intermediate	MS	<18 months	Present or Absent	11q
High	2A/2B	<18 months	Present	Favorable or Unfavorable
High	L1/L2	<18 months	Present	Favorable or Unfavorable
High	4S	< 12 months	Present	Favorable or Unfavorable
High	M	<18 months >18 months	Present None	None None
High	MS	<18 months	Present	11q

Nursing Implications

Nurses are responsible for checking each patients chemotherapy road map with a second Chemo Certified Registered Nurse. The purpose of the road map is to verify that the medications being administered are appropriate during the specific week of chemotherapy they are in. Each patient has their own precise configuration of chemotherapy agents specific to their tumor growth, presence or absence of metastasis and the impending side effects. Infection, bleeding, and mucositis are three main symptoms to monitor closely during all stages of their treatment plan.

Continuous monitoring of each patients blood count, pain control, electrolyte and hydration status are key responsibilities of Nurses caring for children with Neuroblastoma due to all the side effects of their treatments and the aggressiveness of the tumor cells. Observing the patient after initiation of treatment for adverse effects and/or allergic reactions will allow their treatment to be adjusted to better treat their tumor with lesser adverse effects.

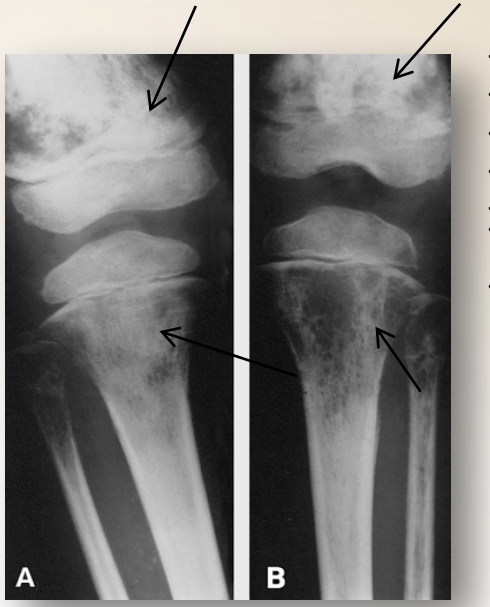

Image 1: Metastatic Neuroblastoma of the upper tibia and lower femur, (Adrenal Gland: Widely Metastatic Neuroblastoma in a 4 year old boy, (2008)[image])

Treatment

Imaging

- Chest/abdominal x ray
- CT of primary site and full body scan for metastasis
- MRI determines if the tumor is intraspinal or causing spinal cord compression
- MIBG scan identify primary and metastatic tumor
- Bone scans evaluate if tumor cells metastasized to the bone
- Skeletal survey will display metastatic lesions

Surgery

- Biopsies of the tumor site and surrounding tissue
- First line cure for localized tumors
- Metastasized tumors require biopsy for diagnosis and staging
- Resection following chemotherapy

Radiation

Chemotherapy is based on the stage of tumor cell growth and how the medication will affect tumor growth.

- Antineoplastics interfere with cell production
- Colony Stimulating factors are used in combination with other medications to prevent neutropenia
- Chemoprotective agents are included in the medication regimen to minimize side effects of the chemo

Statistics

- Most common cancer in children under the age of 1 year old
- 50-60% if children experience metastasis.
- Occurs more in White, Non-Hispanic boys
- Neuroblastoma is 6% of all childhood cancers
- 800 new cases per year
- 90% of children are diagnosed by age 5, rarely found in children over 10 years old
- 75% of children already have lymph node involvement when diagnosed

Conclusion

Neuroblastoma is an aggressive cancer affecting nearly 800 newly diagnosed children per year, (Key Statistics, 2020). The pathogenesis is studied at a cellular level in utero to the development of multiple different pathways, and the ability to metastasize to different areas of the body. In every 2 out of 3 cases, lymph node involvement was present at the time of diagnosis. From a genetic or chromosomal level, to the maturation of an immature cell forming a solid malignant mass, each Neuroblastoma case displays different side effects requiring different treatment combinations and interventions. By improving diagnosis and discovering a different, more effective pathway, early detection and interventions may decrease incidence rates of Neuroblastoma in children.

References

See attached Reference List

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