Ain Shams University
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Role of Surgery in Advanced Stage Abdominal Neuroblastoma

ESSAY

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Abbreviations

- **13-cis-RA** 13-cis-RETINOIC ACID
- **4-HPR** The synthetic retinoid fenretinide
- **99mTc** Technetium-99m
- **ADCC** Antibody-Dependent Cellular Cytotoxicity
- **ATRA** All Trans Retinoid
- **BDNF** Brain-Derived Neurotrophic Factor
- **CCG** Child Cancer Group
- **ch14.18** human-murine chimeric antibody
- **COG** Children's Oncology Group
- **CT** Computed Tomography
- **DNA** DeoxyriboNucleic Acid.
- **EFS** Event- Free Survival
- **FISH** fluorescence in situ hybridization
- **GD2** Disialoganglioside
- **HVA** Homovanillic Acid
- **IDRFs** Image-Defined Risk Factors
- **IL-2** Interleukin-2
- **INRG** International Neuroblastoma Risk Group
- **INRGSS** INRG Staging System
- **INSS** International Neuroblastoma Staging System
- **LDH** Lactate Dehydrogenase
- **MDP** Methylene Diphosphonate

- **MIBG** Metaiodobenzylguanadine
- **MIS** Minimally Invasive Surgery
- **MRI** Magnetic Resonance Imaging
- **mRNA** Messenger-ribonucleic Acid
- **MSKCC** Memorial Sloan-Kettering Cancer Centre
- **NB** Neuroblastoma
- **NGF** Nerve Growth Factor
- **NSE** Neuron-specific enolase
- **OS** Overall Survival
- **POG** Pediatric Oncology Group
- **SFOP** French Society of Pediatric Oncology
- **SFOP** French Society of Pediatric Oncology
- **SIOPEN** International Society of Pediatric Oncology Europe Neuroblastoma Group
- **TBI** Total Body Irradiation
- **Tnm** Tumor Nodes Metastasis
- **TrkA** the primary receptor for NGF
- **TrkB** the primary receptor of brain-derived neurotrophic factor
- **TrkC** the receptor for neurotrophin-3
- **VMA** Vanilmandelic Acid

Introduction

Neuroblastoma is the most common extracranial solid tumor in infants and children, accounting for 6% to 10% of all childhood cancers and 15% of all pediatric cancer deaths. The overall incidence is estimated at about 1 case per 10,000 live births **(Gurney et al., 1995)**.

The incidence is highest in the first year of life during which approximately 30% of all cases occur, nearly half of newly diagnosed neuroblastomas are encountered between ages 1 and 4 years **(Brodeur et al., 1988)**.

Some neuroblastoma tumors undergo spontaneous regression or differentiate into benign ganglioneuromas **(Haas et al., 1988)**.

Most children with stages I and II disease can be cured with surgery alone **(Perez et al., 2000).**

Patients with stage III, IV neuroblastoma (metastatic neuroblastoma) refers to high-risk group of children with the primary tumor in the adrenal gland, mediastinum or pelvis associated with disease progression in other sites (bone marrow, cortical bone, liver, lymph node) **(Kaneko et al., 1997)**.

Role of surgery in advanced stage (III, IV) neuroblastoma is controversial. Cure will require control of the primary tumor and elimination of metastatic disease. There is still an ongoing discussion about the value of radical surgery for extended (stage III) and disseminated (stages III and IVs) neuroblastomas **(Schilling et el., 2003)**.


Definition

Neuroblastoma is the most common solid extra cranial malignancy of childhood and the most common malignant tumor in infants (patients younger than 1 year) **(Brodeur and Castleberry, 1993)**.

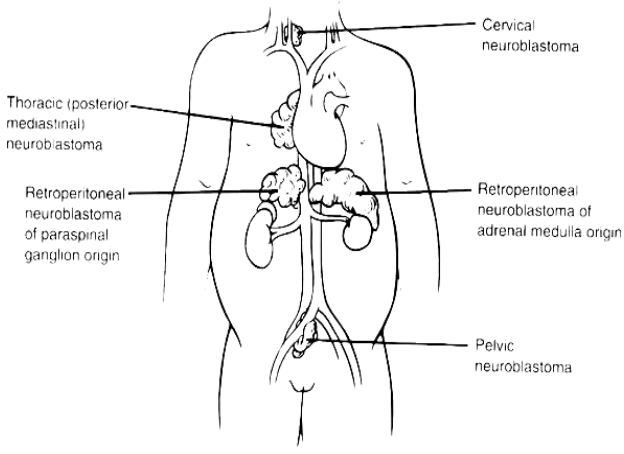

Figure 1: Primary sites of Neuroblastoma **(Young et al., 1986)**

Anatomically, neuroblastoma is an embryonic tumor of the sympathetic nervous system. These tumors arise during fetal or early postnatal life from sympathetic cells (sympathogonia) derived from the neural crest. Therefore, tumors can originate anywhere along the path that neural crest cells migrate, including the adrenal medulla, Para spinal sympathetic ganglia, and sympathetic paraganglia, such as the organ of Zuckerkandl **(Young et al., 1986).**

Grossly, neuroblastomas are purple, highly vascular, and friable mass. The tumor often becomes more nodular and frequently appears fleshy white with maturation or in response to therapy. Larger tumors frequently have calcifications resulting from necrosis or hemorrhage **(Brodeur and Nakagawara, 1992).**

Histologically, neuroblastomas are neuroblastic cells forming lobules separated by thin fibro vascular septa where Schwann cells (or their precursors) may be detected **(Shimada et al., 1984).**

The neuroblastoma is divided into early stage and advanced stage:

- **The early stage:** is localized resectable neuroblastoma which confined to the site of origin, with no evidence that it has spread to other tissues, and the cancer can be surgically removed.

-While **the advanced stage** is divided into:

1. Localized unresectable neuroblastoma which is confined to the site of origin, but the cancer cannot be completely removed surgically.
2. Regional neuroblastoma has extended beyond its original site, to regional lymph nodes, and/or surrounding organs or tissues, but has not spread to distant sites in the body.
3. Disseminated neuroblastoma which spread to distant lymph nodes, bone, liver, skin, bone marrow, and/or other organs. Stage 4S (or IVS, or "special")

neuroblastoma has spread only to liver, skin, and/or, to a very limited extent, bone marrow.

4. Recurrent neuroblastoma means that the cancer has come back, or continued to spread after it has been treated. It may come back in the original site or in another part of the body **(Brodeur and Castleberry, 1993)**.

Etiological Consideration, Diagnosis and Prognostic Factors

Risk Factors

1. Pregnancy and Childhood Factors

Several epidemiologic studies have investigated the role of reproductive history and birth characteristics in the etiology of neuroblastoma **(Olshan and Bunin 2000).**

Conflicting results have been found increase risk of neuroblastoma and maternal history of prior miscarriage, history of one or more induced abortions **(Buck et al., 2001).**

There is also link between incidence of neuroblastoma and repeated Cesarean birth, history of vaginal infection during pregnancy and sexually transmitted infection **(Hamrick et al., 2001).**

Breast feeding for more than 6 months was shown to decrease the risk of neuroblastoma by 40% in one study **(Daniels et al. 2002).**

2. Medication Use

Case series reports from Australia and Japan identified a possible relationship with maternal use of hormones for bleeding, history of miscarriage, and ovulation induction **(Olshan and Bunin 2000).**

Four case-control studies have examined hormone use before or during pregnancy. Positive associations have been reported with maternal use of sex hormones 3 months