ROLE OF MULTISLICE CT IN STAGING OF NEUROBLASTOMA.

Thesis
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In Radiodiagnosis

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دور الأشعة المقطعية المتعددة الشرائح في تحديد مرحلة ورم النيوروبلاستوما.

توطئه
للحصول على درجة الماجستير في الأشعة التشخيصية

مقدمة من
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List of Abbreviations

CCSG: Children's cancer Study Group.

COG: Children's Oncology Group.

CT: Computed Tomography.

GPOH: German Pediatric Oncology and Hematology group.

HVA: Homovanillic acid.

IDRFs: Image Defined Risk Factors.

IMA: Inferior Mesenteric Artery.

INRG: International Neuroblastoma Risk Group.

INRGSS: International Neuroblastoma Risk Group Staging System.

INSS: International Neuroblastoma Staging System.

JNBSG: Japanese Neuroblastoma Study Group.

LCA: Leucocyte Common Antigen.

LDH: Lactic Dehydrogenase.

LN: Lymph Node.

MIBG: Metaiodobenzylguanidine.

MRI: Magnetic Resonance Imaging.

NB: Neuroblastoma.

NCI: National Cancer Institute.

NSE: Neuron Specific Enolase.

PET/CT: positron emission tomography- computed tomography.

POG: Pediatric Oncology Group system.

SIOPEN: International Society of Pediatric Oncology Europe Neuroblastoma.

SMA: Superior Mesenteric Artery.

TNM: Tumor –Node-Metastasis staging system.

US: Ultra Sonography.

VMA: Vanillyl Mandelic Acid.

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الملخص العربى

يعتبر ورم النيوروبلاستوما أكثر أورام الأطفال الصلبة التى تحدث خارج الجمجمة شيوعا.هذا الورم له مسار متباين جدا، يمكن توقعه عادة من السمات الاكلينيكية و البيولوجية. يعتبر استخدام الأشعة المقطعية من التقنيات الهامة لتشخيص الورم و تحديد مرحلته وكذلك متابعة تطوره. كما تشمل أغلب أنظمة العلاج على استخدام الأشعة المقطعية بانتظام و ذلك لتقييم مدى فاعلية العلاج مما يؤدى الى توقع تطور المرض بشكل أفضل.

يتم تحديد مرحلة النيوروبلاستوما روتينيا و منذ فترة طويلة باستخدام نظام ال INSS العالمى. و لكن هذا النظام له بعض المعوقات، حيث أنه يطبق فقط بعد اجراء الجراحة. كما أنه يعتمد على مهارة الجراح و لا يصلح لمقارنة النتائج بين المراكز الطبية المختلفة بشكل موحد. و قد تم حديثا استخدام نظام ال INRGSS الذى يحدد مرحلة الورم قبل بداية العلاج حيث يعتمد على نتائج الأشعة المقطعية لتشخيص و تحديد مرحلة النيوروبلاستوما. يقسم هذا النظام الحالات الى موضعية و منتشرة بناء على وجود بعض العوامل (IDRFs) و كذلك الغدد الليمفاوية و انتشار الورم من عدمه.

اشتملت هذه الدراسة على ٢٠ حالة نيوروبلاستوما تمت دراستها بالأشعة المقطعية. نتائج هذا البحث مماثلة لمختلف الأبحاث السابقة حيث وجد الورم بنسبة عالية فى البطن (٨٥%) و كذلك كان الورم الأولى فى الغدة الأعلى كلوية بنسبة ٥٠%. كذلك كانت درجة الورم ضعيفة التمييزفى ٨٥ % وظهرت الغدد الليمفاوية فى ٧٠% من الحالات و كان الورم منتشرا فى ٣٥% من المرضى. أظهرت الدراسة وجود عوامل ال IDRFs بنسب أعلى من الأبحاث السابقة. باستخدام الأشعة المقطعية لتحديد المرحلة بنظام INRGSS تم تحديد أن نسبة حالات المرحلة L2 كانت الأكبر (٤٥%) ، تتلوها المرحلة M (٣٥%). أما المراحل L1 و MS فوجدت بنسب ١٥% و ٥% على التوالى. كما أمكن تحديد مرحلة الورم فى ٧ حالات بنظام INSS توفرت لهم أشعة مقطعية بعد اجراء الجراحة. اشتملت كل من المراحل IIB,III, IV على حالتين و المرحلة IIA على ٧/١ من الحالات.

خلصت هذه الدراسة الى أن نظام INRGSS لتحديد مرحلة ورم النيوروبلاستوما حديث و ذو قيمة، و يمكن استخدامه قبل الجراحة أو تلقى أى علاج. كما أنه يسهل مقارنة النتائج بطريقة موحدة بين المراكز الطبية. لايحل هذا النظام محل INSS ولكن يمكن استخدامهما بالتوازى. ثبت دورالأشعة المقطعية الهام لتشخيص و تحديد المرحلة و متابعة ورم النيوروبلاستوما.

على الرغم من ذلك، فاننا فى حاجة الى دراسات أخرى أكبر، لفهم دور نظام INRGSS بطريقة مفصلة و أكثر دقة مع تحليل علاقته بمستقبل المرض فى حالات ورم النيوروبلاستوما فى مصر.

Abstract

The International Neuroblastoma Risk Group Staging System (INRGSS) is a recent pretreatment staging system for neuroblastoma (NB), based on imaging by CT before surgery.

Purpose: This study aimed to stage NB cases using CT scan, in relation to available clinicopathologic data.

Patients and Methods: Twenty pathologically proven NB cases were included. All were reviewed for patients' characteristics, including age; sex, clinical picture, LN status and metastatic spread. All cases underwent CT scan for diagnosis. Staging was done using IDRFs, LN status and metastatic spread according to the INRGSS and INSS when available.

Results: An abdominal mass was found in 85% of cases and the suprarenal gland was the most common site of primary tumor (50% of cases). Concerning tumor grade, 85 % of cases were poorly differentiated. LNs were positive in 70%, and metastatic spread was found in 35% of patients respectively. Staging according to the INRGSS showed that L2 was the most common stage (45% of cases), followed by M stage (35%). L1 and MS stages were found in 15% and 5% of cases respectively. Only 7 cases had post surgical CT scans, and were staged according to the INSS.

Conclusion: It was concluded that the use of the INRGSS using CT scan, is a recent valuable pretreatment staging system, allowing accurate classification of neuroblastoma.

Key words: Neuroblastoma (NB), Computed tomography (CT) scan, Image Defined Risk Factors (IDRFs), International Neuroblastoma Risk Group Staging System (INRGSS), International Neuroblastoma Staging System (INSS).

Introduction

Neuroblastoma (NB) is the commonest extracranial pediatric solid tumor, and the most frequent solid neoplasm in the first year of life (El Bolkainy et al, 2013). It arises from the precursors of the sympathetic nervous system. The most common primary sites of neuroblastoma are the adrenal gland (40%), paraspinal ganglia in the retroperitoneum (25%), mediastinum (15%), neck (5%) and pelvis (3%) (Russel et al, 2008; Swift et al, 2018). The natural history of NB is extremely heterogeneous, but is usually predictable from clinical and biologic features (Kushner, 2004).Treatment and outcome of neuroblastoma depend on assessment of risk status and on stage of the disease.

Imaging by Computed Tomography (CT) plays an important role in the diagnosis, staging, response evaluation, and follow up of NB. Tumor size, location, calcification and spread can be well demonstrated. Most neuroblastoma protocols include regular CT assessment, to determine efficacy of therapy, thus helping to predict patient prognosis (Kembhavi et al, 2015).

There are two main staging systems for NB. For a long time; the International NB Staging System (INSS) was used for staging (Brodeur et al, 1993). However, this post surgical staging system depends on surgical skill; it can't be applied uniformly in different centers, or used for pretreatment risk classification(Swift et al, 2018).

Since 2004, the major cooperative Children Oncology Groups (COG) proposed the International Neuroblastoma Risk Group Staging System (INRGSS) as a recent pre treatment staging system for NB, based on the

imaging results taken before surgery. It was tested and finally published in 2009. In this system, imaging by CT or magnetic resonance imaging (MRI) plays a central role in the diagnosis, staging and follow up of neuroblastoma. It suggests that using a standardized nomenclature can facilitate international collaborative studies all over the world.

The INRGSS broadly classifies NB into localized and metastatic cases. The localized disease is further divided into L1 and L2 stages. The metastatic group is defined as stage M when the tumor has spread to other parts of the body, and stage MS where the tumor has spread only to skin, liver and/or bone marrow in patients younger than 18 months (Cohn et al, 2007; Monclair et al, 2009).

Aim of the work

This study aims to stage neuroblastoma cases using CT scan, in relation to available clinicopathologic data.

I- General Features of Neuroblastoma

Neuroblastoma is a tumor of adrenal medulla or sympathetic ganglia of neural crest cell origin (primitive cells of the neuroendocrine type). Embryogenesis of adrenal medulla continues during the first year of life. Persistence and transformation of these embryonal structures may give rise to neuroblastoma (El Bolkainy et al, 2013).Neuroblastoma was originally described by Virchow in 1863 (Lonergan et al, 2002).

Anatomy of adrenal gland:

The adrenal glands are small retroperitoneal paired endocrine organs, located on the upper pole of each kidney.Histologically, each gland is composed of cortex and medulla.

The adrenal cortex is divided into three zones with distinct endocrine function: zona glomerulosa, zona fasciculata, and zona reticularis that produce mineralocorticoids, glucocorticoids, and androgens, respectively. The normal adrenal cortex is 80–90 % of the volume of the normal gland. The adrenal medulla synthesizes and secretes catecholamines; it derives from neural crest and develops with sympathetic nervous system (Park et al, 2017).

Incidence of Neuroblastoma:

Neuroblastoma (NB) is the commonest solid extracranial tumor in childhood (Maris et al, 2007).It ranks as the third most common cancer of childhood, after leukemia and central nervous system tumors, accounting for 10% of all pediatric malignancies. It is also the second most common abdominal neoplasm, after Wilm's tumor, representing 90% of adrenal cancers (Pession et al, 2015). In Egypt, it constitutes 69.06% of primary malignant suprarenal

gland tumors presenting to the National Cancer Institute during the years 2000-2011(Salama and Abdel Azim, 2016).

Age at diagnosis:

About 90%of neuroblastoma cases are under 5 years of age, and 98% are under 10 years with peak incidence at the age of 2-3 years. The median age at diagnosis is 2years. It accounts for about 15% of childhood cancer deaths, a number which reflects its aggressive nature and frequency of metastatic disease at diagnosis. Most deaths occur within 2 years of diagnosis (Kushner, 2004).Neurobastoma is also the most frequent malignancy diagnosed in the first month of life (30-50%),and the most common cancer among infants less than 12 months of age (Lonergan et al, 2002). The tumor is slightly more common in boys than girls, with a male to female ratio of 1.1:1 in most large studies. Incidence of neuroblastoma is higher in white children than in black ones. However, race does not appear to have any effect on outcome (Brodeur and Maris, 2006).

Age of the patient and stage of the disease at diagnosis are the most important clinical variables predictive of disease outcome. It was reported that patients under 2 years of age have better prognosis than those older than 2 years at diagnosis (De Bernardi et al, 2003).

Aetiology and Risk Factors:

The cause of neuroblastoma is not well understood. It is not considered part of any developmental or congenital syndrome, and is not associated with any other malignancy. Exogenous causative factors have not been identified. The vast majority of cases are sporadic; approximately 1% only runs in families (Kushner, 2004).