

INTRODUCTION

Lymphomas account for approximately 8% of all known malignancies; they are generally subdivided into two groups: Hodgkin's disease (HD) and non-Hodgkin lymphoma (NHL). Hodgkin's disease accounts for about 10% of all lymphomas and non-Hodgkin lymphoma accounts for the remaining 90% of all lymphomas. Non-Hodgkin lymphoma is the fifth most common cancer in Egypt, in both males and females, the exact causes for this increase are not clear but could be related to HCV infection which is prevalent among Egyptians. Hodgkin lymphoma is the seventh most common cancer in the United States. Each year, about 70, 000 Americans are diagnosed with non-Hodgkin lymphomas, and about 20, 000 people die because of that disease. Since the 1970s, non-Hodgkin lymphoma incidence rates have doubled. Part of the reasons for this dramatic rise may be due to AIDS, which increases the risk for high – grade (aggressive) lymphomas (*Lenz and Staudt, 2010*).

The risk of non-Hodgkin lymphomas (NHL) increase with age. Most patients are diagnosed when they are in their 60s and 70s. However, non-Hodgkin lymphomas can develop in people of any age, including children. Also, people who have immune system impairment which leads to develop infectious diseases or people who exposed to certain types of chemicals

appear to have increased risk to develop the disease. Still, people without any known risk factors can develop non-Hodgkin's lymphomas (NHL) (*Shankland et al., 2012*).

Survival rates for non-Hodgkin lymphomas vary widely, depending on many factors e.g. the type of lymphoma, age of the patient and staging of the cancer. After the diagnosis and before the treatment, lymphomas are staged; this refers to deduce how far the cancer has spread in local tissue or to other sites. Staging is reported as a grade between I (confined) and IV (spread). Staging is carried out because it impacts lymphomas prognosis and treatment (*Flowers et al., 2010*).

There have been many significant advances in the staging of lymphomas. FDG positron emission tomography (PET) scanning is more sensitive and specific than contrast materials enhanced computed tomography (CT) in staging of lymphomas. The accuracy can be improved by combining FDG-PET and CT scanning as (PET/CT). The FDG-PET component provides information about metabolic activity. Whereas, CT component helps in localizing the sites of activity accurately (*Riad et al., 2010*).

Newer PET/MRI has already preceded promising results in staging of lymphomas, as a new powerful imaging tool because of advantages that MRI offers over CT, like improved

soft tissues contrast e.g. bone marrow lesions and soft tissue tumors. The explicit role of newer PET/MRI in staging of lymphomas still needs further researches and awaits to be thoroughly evaluated (*Philipp et al., 2013*).

AIM OF THE WORK

The aim of this work is to highlight the differences between role of PET/MRI and PET/CT in staging of lymphomas.

ANATOMICAL CONSIDERATIONS OF LYMPHOMAS

LYMPHOMAS

Lymphomas are malignant neoplasms of lymphoid lineage. Broadly classified as either Hodgkin lymphoma (Hodgkin's disease) or as non-Hodgkin lymphoma (NHL), lymphomas are clinically, pathologically, and biologically distinct (*Jaffe, 2009*).

I-Non-Hodgkin lymphoma (NHL)

Non- Hodgkin lymphoma (NHL) is a heterogeneous group of lymph proliferative malignancies with differing patterns of behavior and responses to treatment. NHL usually originates in the lymphoid tissues and can spread to other organs. However, unlike Hodgkin's disease, NHL is much less predictable and has a far greater predilection to disseminate to extra nodal sites (*Toma et al., 2007*).

- **Incidence**

The incidence of NHL is 20 per 10, 000. The prevalence of NHLs differs greatly from country to country, being much higher in developing countries. Unlike in HD, the prevalence of

NHLs increases steadily with age throughout life. NHLs are twice as frequent in males as in females (*Toma et al., 2007*).

The age-specific incidence of non-Hodgkin lymphoma only slightly increases over the first 2 decades of life. By comparison, the incidence of Hodgkin's disease increases more dramatically than this as children age (see image below). In adulthood, the risk of non-Hodgkin lymphoma steadily climbs, whereas the age-specific incidence of Hodgkin's disease is biphasic (Fig.1) (*Horner et al., 2008*).

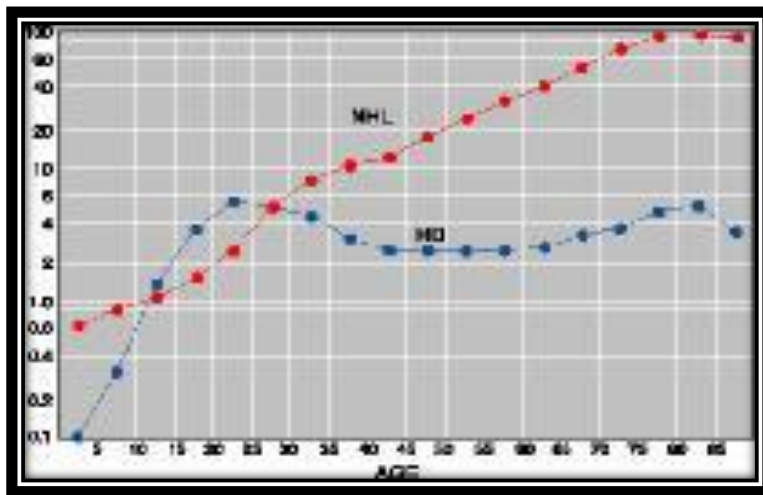


Figure (1): Incidence of lymphoma as a function of age per 100, 000 population. Data are from the Surveillance, Epidemiology, and End Results (SEER) (*Horner et al., 2008*).

- **Mortality/Morbidity**

Its 5 year survival ranges from 40 to 70 % (*Poeppel et al., 2009*).

II-Hodgkin lymphoma

Hodgkin lymphoma (Hodgkin's disease) is a highly curable malignant disease. The recent understanding and insight into the biology of Hodgkin-Reed-Sternberg (HRS) cells as B-cell derived have lead to the classification of Hodgkin's disease as a lymphoma or Hodgkin lymphoma (HL) (*Alarcon et al., 2008*).

Hodgkin lymphoma was the first cancer to be cured with radiation therapy alone or with a combination of several chemotherapeutic agents. The cure rate for children and adolescents with Hodgkin lymphoma has steadily improved, particularly with the introduction of combined radiation and multiagent chemotherapy (*Ayra et al., 2005*).

- **Incidence**

The incidence of HD is 3 per 10, 000. HD has a bimodal age distribution: In developed countries the first peak occurs in the middle to late 20s and the second peak after the age of 50 years, whereas in developing countries the early peak occurs before adolescence. HD is very rare in children younger than 5 years. The prevalence in males and females is roughly the same (*Toma et al., 2007*).

- **Mortality/Morbidity**

The 5-year disease-specific survival for patients with stages I and II Hodgkin's disease (Hodgkin lymphoma) is 90%; III, 84%; and IV, 65% (*Toma et al., 2007*).

Organs involvement in Lymphomas

Table (1). Relative Prevalence of Lymphomatous Involvement of Organs (*Toma et al., 2007*).

Anatomic Sites	HD	NHLs
CNS	Absent or very rare	Rare
Head and neck		
Jaw	Absent or very rare	Frequent
Paranasal sinuses	Absent or very rare	Rare
Waldeyer ring	Rare	Somewhat frequent
Cervical lymph nodes	Very frequent	Somewhat frequent or frequent
Salivary glands	Absent or very rare	Rare
Chest		
Mediastinum	Very frequent	Frequent
Lungs	Somewhat frequent	Rare
Abdomen		
Bowel	Somewhat frequent	Very frequent
Mesenteric and retroperitoneal lymph nodes	Frequent	Frequent
Spleen	Frequent	Somewhat frequent
Liver	Somewhat frequent	Somewhat frequent
Pancreas	Rare	Rare
Peritoneum and omentum	Somewhat frequent	Somewhat frequent or frequent
Kidneys	Rare	Somewhat frequent
Gonads	Absent or very rare	Somewhat frequent
Bone		
Bone marrow	Rare	Frequent
Cortical bone	Rare	Somewhat frequent

Central Nervous System

Primary involvement of the CNS by lymphoma occurs almost exclusively with NHLs and is uncommon in children. It may manifest as cranial nerve palsy or spinal cord compression. Unlike in adults, primary cerebral lymphomas manifesting as discrete masses or infiltrations involving the corpus callosum are very rare in the pediatric age group. Uncommon intracranial locations include the pituitary stalk, in which case affected children present with central diabetes insipidus and growth hormone deficit. At MR imaging, a relative decrease in signal intensity on both T1-weighted and T2-weighted images probably reflects hypercellularity, meningeal infiltration can also be seen (Fig 2). Subarachnoid nodules, diffuse leptomeningeal carcinomatosis, or both can be seen on post contrast MR images (*Tortori-Danti et al., 2005*).

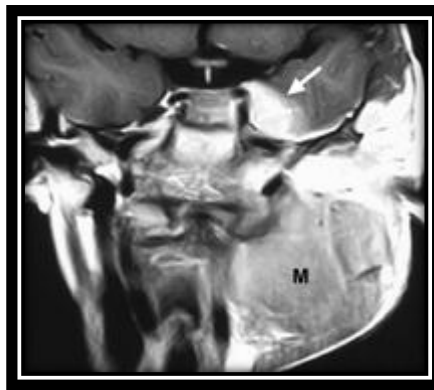


Figure (2): NHL of the neck in a 4-year-old boy. Coronal contrast-enhanced T1-weighted MR image shows a large laterocervical mass (*M*) involving the parapharyngeal space. Infiltration of the left cavernous sinus (arrow) and dural involvement with intracranial extension are evident (*Toma et al., 2007*).

Intramedullary spinal cord involvement by either HD or NHL is rare and is usually a manifestation of widespread disease (Fig 3).

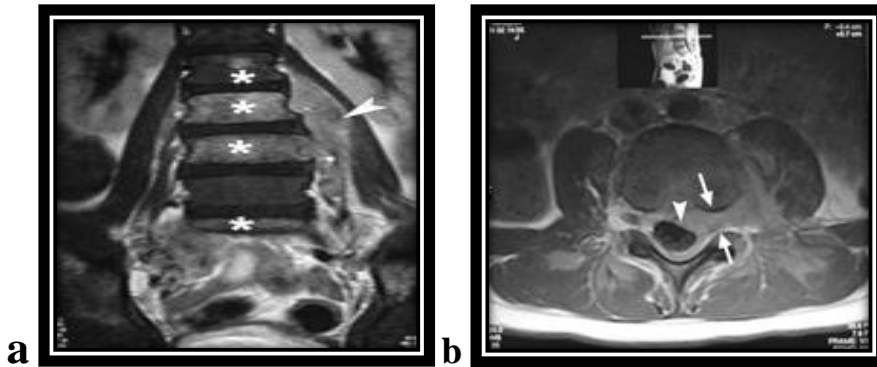


Figure (3): HD in a 6-year-old girl. **(a)** Coronal T2-weighted MR image shows a left-sided paraspinal mass (arrowhead). The second, third, and fourth lumbar vertebrae and first sacral vertebra show infiltration (*). **(b)** Axial contrast-enhanced T1-weighted MR image shows extension into the spinal canal (arrows) and compression of the dural sac (arrowhead) (*Toma et al., 2007*).

Head and Neck

• Jaw

The jaw is a frequent site of disease in African patients with Burkitt lymphoma, whereas disease in this location is very uncommon in white patients. In African patients, the jaw is the initial site of disease in 50% of cases, and involvement often begins at the angle of the mandible. Radiography shows loss of the lamina dura and osteolysis of medullary and cortical bone, with a concomitant periosteal reaction producing lamellar and perpendicular spicules of new bone in the mandible or maxilla.

An extra osseous soft-tissue mass usually develops in parallel with bone destruction (*Toma et al., 2007*).

- **Para nasal Sinuses**

The paranasal sinuses are very rarely involved. At CT or MR imaging, lymphomatous infiltration appears as a nonspecific soft-tissue mass partially or completely obscuring the involved lumen. Destruction of the surrounding bone may be associated (*Toma et al., 2007*).

- **Waldeyer Ring**

The Waldeyer ring comprises a network of lymphoid tissue in the nasopharynx, base of the tongue, and tonsils including the soft palate. Involvement of the Waldeyer ring is rather rare in children and is more frequently observed in large B-cell NHL, whereas HD very rarely involves the Waldeyer ring. The lymphomatous mass may involve all sites of the Waldeyer ring or may be localized in one site, most commonly the faucial tonsils, followed by the nasopharynx and the base of the tongue (Fig 4). At CT, it appears as an isoattenuating to muscle, homogeneous, submucosal mass most often associated with enlarged lymph nodes in the neck. At MR imaging, the lymphomatous mass usually has low signal intensity on T1-weighted images and intermediate signal intensity on T2-weighted images (*Weber et al., 2005*).



Figure (4): Burkitt lymphoma of the palatine tonsils in a 3-year-old boy. Sagittal contrast-enhanced T1-weighted MR image shows a huge, well-defined mass (M) of the soft tissues of the rhino pharynx that penetrates into the nasal choanae (*Toma et al., 2007*).

- **Cervical Lymph Nodes**

The cervical nodes are the most common sites of HD manifestation. HD is typically confined to this area in up to 80% of cases. In contrast, NHL manifesting as cervical adenopathy is frequently more widespread. In lymphomas, involved lymph nodes are enlarged and painless. The nodal groups in the upper neck, especially the internal jugular and spinal accessory nodes, are more commonly enlarged than those in the lower neck (*Toma et al., 2007*).

However, enlargement of the cervical lymph nodes is a very common finding in children and, in most cases, is a benign, reactive condition secondary to inflammatory processes in the lymphoid tissue of the nasopharynx and tonsils. US is probably

the imaging technique best suited to studying enlarged superficial lymph nodes. Several US features have been described for differentiating reactive lymphadenopathy from lymphomatous involvement. Enlargement, round shape, absent or eccentric hilum, hypoechoic parenchyma, absence of calcifications, tendency to aggregate into a mass, and distorted branching and amputation of nodal vascularization are US characteristics that can often be observed in lymphomatous nodes (Figs 5, 6). However, not rarely and especially in children, similar findings may also be observed in reactive, benign lymph nodes, thus making differential diagnosis very difficult. Therefore, in the presence of dubious findings, only biopsy makes diagnosis possible (*Toma et al., 2007*).

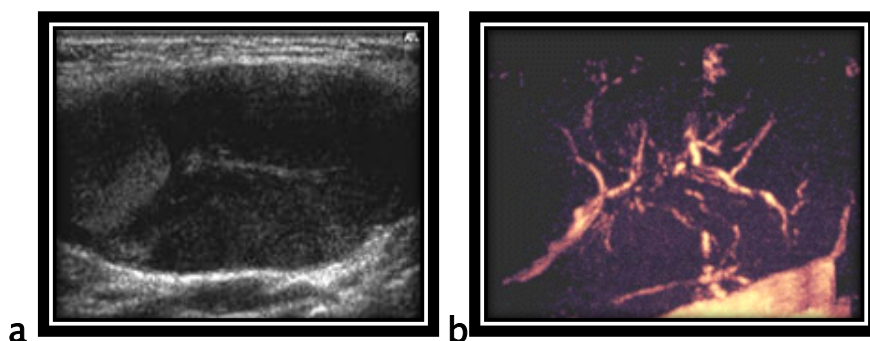


Figure (5): HD of the cervical lymph nodes in a 21-year-old girl. (a) US scan shows lymphomatous infiltration of a cervical lymph node, which appears enlarged, non homogeneous, and partially hyperechoic. (b) Three-dimensional power Doppler US scan of the same lymph node shows distorted vascular branching and vessel amputation (*Toma et al., 2007*).



Figure (6): HD of the cervical lymph nodes in a 10-year-old girl with a right lateral cervical mass. US scan shows multiple roundish, hypoechoic lymph nodes with a tendency to aggregate. The nodal hila are not visualized or appear eccentric (arrowheads) (*Toma et al., 2007*).

At CT, the involved lymph nodes may be discretely enlarged or appear as a soft-tissue mass. Necrosis in lymphomatous nodes is very rare both before and after treatment and appears as central areas of lower attenuation. Intravenous contrast enhancement greatly facilitates distinction of vessels from the adjacent lymph nodes and detection of solid organ involvement. Similarly to US, CT may show findings similar to those of inflammatory adenopathy, and tissue sampling is often required for diagnosis (*Bragg et al., 2005*).

At MR imaging, lymph nodes show low to intermediate signal intensity on T1-weighted images and intermediate to high signal intensity on T2-weighted images. The multiplanar capability and superb soft-tissue contrast resolution of MR

imaging make it an excellent modality for assessing both nodal and extra nodal disease in the neck region. MR imaging is also valuable for assessing lower cervical nodes near the clavicles, where beam-hardening artifacts at CT often obscure the complex anatomy (*Bragg et al., 2005*).

- **Salivary Glands**

All salivary glands can be affected by lymphoma in adults, although in children this is a very rare event. The most frequently involved gland is the parotid (Fig 7). Salivary gland lymphoma is almost invariably secondary to diffuse disease. Lymphoma of the parotid gland lymph nodes has the non specific appearance of a single mass or multiple masses, and the gland may be displaced(*Toma et al., 2007*).

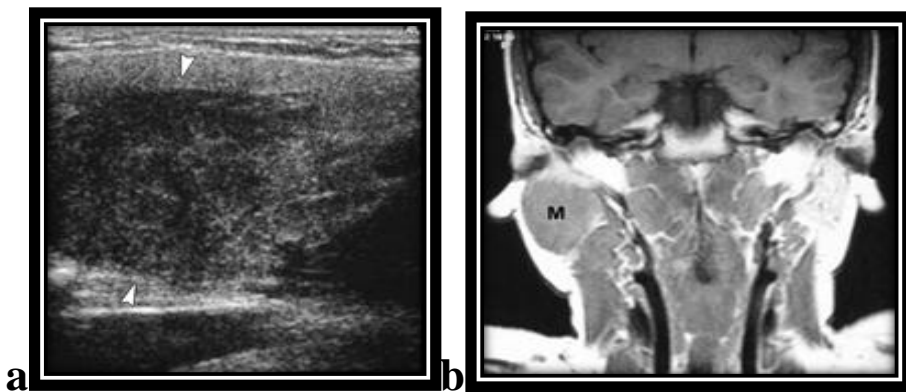


Figure (7): NHL in a 10-year-old girl. (a) US scan of the right parotid gland shows infiltration, which appears as an ill-defined, non homogeneous hypoechoic area (arrowheads). (b) Coronal T1-weighted MR image shows that the infiltrated gland (M) is isointense relative to the neck muscles (*Toma et al., 2007*).