Extranodal lymphomas: a pictorial review for CT and MRI classification

Alfonso Reginelli¹, Fabrizio Urraro¹, Angelo Sangiovanni¹, Gaetano Maria Russo¹, Carolina Russo¹, Roberta Grassi¹, Andrea Agostini¹, Maria Paola Belfiore¹, Michaela Cellina¹, Chiara Floridi², Andrea Giovagnoni², Antonello Sica³, Salvatore Cappabianca¹

¹ Department of Precision Medicine, University of Campania Luigi Vanvitelli, Naples, Italy; ² Department of Clinical, Special and Dental Sciences, University Politecnica delle Marche, Ancona, AN, Italy; ³ Department of Radiology, Ospedale Fatebenefratelli, ASST Fatebenefratelli Sacco, Milan, Italy; ⁴ Oncology and Hematology Unit, Department of Precision Medicine, University of Campania; "Luigi Vanvitelli", Naples, Italy

Summary. Extranodal lymphomas represent an extranodal location of both non-Hodgkin and Hodgkin lymphomas. This study aims to evaluate the role of CT and MRI in the assessment of relationships of extranodal lymphomas with surrounding tissues and in the characterization of the lesion. We selected and reviewed ten recent studies among the most recent ones present in literature exclusively about CT and MRI imaging of extranodal lymphomas. Contrast-enhanced computed tomography (CT) is usually the first-line imaging modality in the evaluation of extranodal lymphomas, according to Lugano classification. However, MRI has a crucial role thanks to the superior soft-tissue contrast resolution, particularly in the anatomical region as head and neck. (www.actabiomedica.it)

Keywords: Extranodal lymphomas, Computed Tomography, Magnetic Resonance Imaging.

Introduction

Lymphoma is a neoplastic proliferation of lymphoid cells in lymph nodes and lymphatic tissues primarily, with bone marrow, spleen, and thymus involvement in many cases (1). In addition to lymphoid organs and tissues, lymphomas can have an extranodal location, with or without contextual nodal involvement (2). This presentation can be primitive or secondary to hematogenous spread from nodal site to extranodal site (3). The extranodal engagement occurred more frequently for non-Hodgkin lymphomas (NHL, 25-40%) than for Hodgkin lymphomas (HL, 1%). Approximately one-third of non-Hodgkin lymphomas (NHL) arise from sites other than lymph nodes, spleen, or the bone marrow (4). The median age at diagnosis for patients with NHL is 67.2 years; however, because of AIDS and organ transplantation increase, lymphoma may become more prevalent in middle-aged patients (5). The most common types of extranodal lymphomas (ENL) are diffuse large B-cell lymphoma (DLBCL) and Malt lymphoma (6).

In 43% of cases, extranodal involvement is localized in the gastrointestinal tract, followed by head and neck with 14% of cases, lung (2%), skin (7%), bone (5%), and brain (6-7%) (7). The head and neck localization represent the second most common malignant neoplasm of these anatomical regions, involving nodal and extranodal sites or both (8, 9), and Waldayer’s ring is most frequently involved (10).

Diagnosis and accurate localization and staging are fundamental to choosing the best treatment strategy (11); to this end, PET/CT role has become increasingly important in recent years (12, 13) thanks to the ability to identify metabolically active tumors. At the same time, as regards ENLs and the relationships that lesions contract with surrounding tissues and organs, an accurate morphological characterization is essential, therefore the use of methods such as CT and MRI for the study of these pathologies and many
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...others remains fundamental. Cross-sectional imaging (MRI, CT and US) techniques gained large application in radiology; in the setting of inflammatory and oncological diseases, they are advised as techniques in the diagnosis, staging and follow-up (14-20).

The purpose of our study was to illustrate, with a pictorial review based on our case studies, typical characteristics of extranodal lymphomas found with CT and MRI, site by site.

**Role of Imaging**

Contrast-enhanced computed tomography (CT) is usually the first-line imaging modality for newly diagnosed neck masses to determine lesion extent and bony involvement, according to Lugano classification (21). CT diagnostic criteria for characterizing ENL include two diameters measurement (longest and shortest diameter) (22), although an interobserver variation up to 15% was observed, caused by lesions irregularity or an inferior lesion to background contrast (23). Intravenous contrast medium is fundamental, and an optimal bowel opacification is necessary for abdomen evaluation (22). ENL in CT images is reported in **Figures 1 and 2**.

Magnetic resonance imaging (MRI) provides more excellent soft-tissue contrast. It is crucial in accurately determining invasion of sophisticated anatomical planes and skull base, besides evaluating spinal or intracranial extension (**Figures 3 and 4**). Generally, the soft-tissue contrast resolution of MRI is superior to that of CT; however, ENLs MRI in the detailed region as head and neck, have been reported to show variable homogeneity and signal intensity of tumor on both T1WIs and T2WIs (24). After intravenous contrast medium administration, ENL lesions have homogeneous diffuse enhancement, predominantly peripheral thick band-like enhancement and marginal septal enhancement in 68%, 21%, and 11%, respectively, as shown by Chun et al. (25). CT and MRI play a crucial role in clinical staging, assessment of prognosis, and treatment planning for ENLs and other various pathologies (26-33).

ENLs should be in the imaging differential of any soft tissue mass showing (10): imaging homoge-
nous attenuation or signal; absence of calcification; hemorrhage or significant necrosis or cystic changes; the intermediate-to-low signal on fluid-sensitive MRI sequences, and marked diffusion restriction (hypercellular nature of the mass); encasement of vessels without luminal compression and moderate to intense homogenous enhancement. Whatever organs are involved by ENL, these lesions show standard features that suggest diagnosis and indicated that biopsy samples should be taken, avoiding unnecessary surgery, as in many others tumors (34). For this reason, imaging has a vital role in direct diagnosis through imaging-guided biopsy, with accuracy at around 90% (35).

**Head and neck**

Lymphomas arising in the head and neck area constitute the second most frequent extranodal site after the gastrointestinal tract (36). Hereafter we will analyze ENLs characteristics in the individual subsites.

**Waldeyer’s ring**

Waldeyer’s ring is the most common site where the extranodal disease occurs in head and neck lymphomas. Together with the paranasal sinuses and the nasal cavity, Waldeyer’s ring is the most frequently extranodal sites involved. More often, there are more sections of involvement within the ring, and their appearance can identify the extranodal lesions; in fact, Waldeyer’s ring looks like squamous carcinoma (37). In MRI, the classical imaging appearance of the EHNLI in the Waldeyer’s ring is a well-demarcated mass that shows the T2w intermediate signal conformed to space/surrounding structures with a smooth interface in contrast to epithelial malignancies. T1w shows an isointense signal, and the enhancement is homogenous (10, 38, 39). The margins are sharply demarcated also in the invasion of the adjacent spaces. Multiple subsite involvement is frequently, such as the lack of skull base destruction and unilateral or bilateral non-necrotic lymphadenopathy (40). In order of frequency, the common subsites of Waldayer’s ring are (38): palatine tonsils, nasopharyngeal tonsil (or adenoids), lingual tonsils; most Waldayer’s ring lymphomas are of B-Cell

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**Figure 3.** MRI with contrast enhancement show rounded nodular lesion in the context of the left parotid gland with shaded margins and peripheral enhancement.

**Figure 4.** MRI T2w with nodular solid lesion right mandible inhomogeneously hypointense with lobulated margins.
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Origin, and more than half occur in the palatine tonsil (41, 42). Symptoms are similar to squamous cell carcinoma in these locations. Still, on clinical inspection, the EHNLS is not ulcerated mucosal masses like in the squamous cell carcinoma, and they appear mostly submucosal (43). Clinical symptoms depending on the area involved: e.g., sore throat or tonsillar swelling are present in tonsils involving; nasal obstruction, cervical mass, obstruction of Eustachian tube with decreased hearing in nasopharyngeal tonsil (40); foreign body sensation in lingual tonsils. EHNLS of Waldeyer’s ring is associated with gastric disease in 10 percent of patients (43). The appearance of Waldeyer’s ring ENLs is shown in Figure 5.

**Sinonasal region**

Sinonasal lymphomas are very rare; they affect less than 1 percent of all malignant tumors of the head and neck and are mainly non-Hodgkin lymphomas (44).

They are divided into two groups that have different symptoms, prognosis, and treatment: B-cell lymphomas, more frequent, less aggressive but with better prognosis; T/NK cell lymphomas: rarer but most found in the nasal cavity (45).

Regarding symptoms, high-grade lymphomas are aggressive with a non-healing ulcer, pain, cranial nerve manifestations, facial swelling, and epistaxis. Lower-grade lymphomas present with a sinonasal mass associated with obstructive symptoms, meanwhile high-grade diffuse large B-cell tumors are used to present with bone or soft tissue destruction; T-cell lymphomas are associated with perforation or damage of the nasal septum (44, 46).

In imaging, they are bulky masses with intermediate signal intensity on MRI with moderate contrast improvement. ENL is presented as a destructive soft tissue mass that can mimic squamous cell carcinoma but tends to be more homogeneous in T2 imaging with less intense carcinoma enhancement. Although the areas of development are different, lymphomas are more frequent in the nasal cavity or the maxillary sinus, and the lesions can reshape or erode adjacent bones. Sites like frontal or sphenoid sinuses or the ethmoid are infrequent (47) (Figure 6).

![Figure 5. (a-b) Waldeyer’s ring lesion. MRI T2w. Nodular capsulated solid lesion in the left parapharyngeal space with reduction of the pharyngeal airspace. (c) After i.v administration the lesion show midly inhomogeneous enhancement.](image1)

![Figure 6. CT of a bulky masses inhomogeneous hypodensity. The CT show a destructive soft tissue mass can mimic squamous cell carcinoma.](image2)
**Thyroid**

Primary thyroid lymphoma is a rare tumor accounting for 1 to 5% of all thyroid malignancies and approximately 2% of all malignant extranodal lymphomas (48). Pure thyroid MALT lymphomas comprise about 6 to 28% of primary thyroid lymphomas and are recognized as extranodal marginal zone B-cell lymphomas (49, 50). Thyroid lymphoma is a rare pathology associated with about 80% by cases with Hashimoto thyroiditis and more frequent in women, especially between 70 and 80 years (51, 52). The most frequent sign is a palpable mass with neck enlargement, but patients may also present a cold thyroid nodule or symptoms as dysphagia, hoarseness, and suffocation. Primary thyroid lymphoma can be confused radiologically with anaplastic thyroid carcinoma; however, these lesions are characterized by typical features, classified into three types detectable in CT and MRI exams (53):

- type 1 is a solitary nodule surrounded by healthy thyroid tissue, which rapidly enlarges the mass by imitating anaplastic thyroid carcinoma or other aggressive carcinomas;
- type 2 consists of several thyroid nodules that mimic the goiter;
- type 3 shows a homogeneous enlargement of both thyroid lobes with reduced attenuation, with or without peripheral hyper-attenuating thyroid tissue.

A difference between thyroid lymphoma and carcinoma is the presence on transverse imaging of a more homogeneous signal, whereas the lack of calcification, cystic degeneration, or necrosis distinguishes it from goiter (52).

**Tongue**

Extranodal lymphomas of the tongue are a very rare disease. The alterations are identifiable with the physical examination, while MRI is useful for defining exact disease extension.

**Salivary gland**

Primary salivary gland lymphoma represents 2-5% of all salivary gland neoplasms, involving parotid gland (70%) and submandibular gland more frequently (54). The diagnosis of primary lymphomatous involvement of the parotid gland requires that three criteria must be fulfilled: involvement of organ is the first disease manifestation; disease must involve gland parenchyma and not adjacent nodes; lymphoid infiltrate is malignant (55). For instrumental diagnosis, CECT should be performed from skull base to clavicles for intraparotid lesions to evaluate the extent of cervical disease fully. In the case of NHL clinical suspicion, special attention must be paid as they may be isodense and, therefore, invisible in CECT. If MRI performed, T2 MR, FS, or STIR make intraparotid lesions more conspicuous; a single unilateral mass of relative soft-tissue homogeneity with a poorly defined margin was thought to be the most common sign of a parotid lymphoma (56). Diffusion-weighted imaging is beneficial in unusual cases with shallow apparent diffusion coefficient values.

**Cranial vault and skull base**

The primary NHL of calvarial bones is extremely rare. If present, initial symptoms, and signs usually include painless scalp nodules, headaches, convulsions, or focal neurological deficits, also not to be forgotten as a complication is cerebrospinal fluid diffusion. In the imaging findings of the cranial vault, lymphoma may be present cerebral infiltration and orbital involvement (57, 58). Even though CT is superior to assess cortical bony destruction, MRI allows for better soft tissue characterization, the extent of involvement, and marrow infiltration. Although MRI cannot diagnose lymphoma with certainty, its inclusion in the differential can be critical, since the surgical approach can be very different.

In the skull base, ENLs mainly involve clivus, and principal CT is permeative bony destruction. Other less common imaging features include destructive lytic pattern, sclerosis, or bone expansion beyond cortex, or “traversing” bone lesion with preserved cancellous bone and minimal attenuation of the cortex. Typically, the injury is often isointense to the gray matter on T1WI and intermediate signal on T2WI.

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