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Utility of vascular flow pattern in diagnosis of cervical lymphadenopathy- Literature review

Suwarna Dangore-Khasbage[1], Monika Khubchandani[2], Khushboo Durge[3]

[1] Professor, Oral Medicine and Radiology, Sharad Pawar Dental College, Datta Meghe Institute of Medical Sciences, (Deemed to be University) Sawangi (M), Wardha, India

[2] Reader, Pedodontia, Sharad Pawar Dental College, Datta Meghe Institute of Medical Sciences, (Deemed to be University) Sawangi (M), Wardha, India

[3] Senior Lecturer, Periodontia, Sharad Pawar Dental College, Datta Meghe Institute of Medical Sciences, (Deemed to be University) Sawangi (M), Wardha, India

SUMMARY

Abstract: Cervical lymphadenopathy is a quite common condition with variable etiologies. Appropriate investigations to detect the correct cause of lymphadenopathy is vital for perfect management and a good prognosis. Though several imaging modalities are proved to be helpful in the diagnosis of the condition, one of the advancements in radio diagnosis, that is, colour doppler ultrasound plays a key role in evaluating the status of cervical lymphadenopathy. Colour Doppler ultrasound is less time-consuming, non-invasive, reliable, and reproducible.

Key words: Cervical, Lymphadenopathy, Ultrasonography, Lymph nodes, Lymphadenitis

Address for correspondence:

Dr. Suwarna Dangore -Khasbage, Professor, Oral Medicine and Radiology, Sharad Pawar Dental College, Datta Meghe Institute of Medical Sciences, (Deemed to be University) Sawangi (M), Wardha, India, Email: dangore_suwarna@rediffmail.com

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INTRODUCTION

The neck swelling due to enlarged cervical lymph nodes is one of the common findings observed in clinical practice. The common cause for which is benign such as lymphoid hyperplasia or reactive lymphadenitis and is easy to treat. Nevertheless, rarely the reason for cervical lymphadenopathy can be a major disease like primary malignancy of lymph nodes, metastatic lymphadenopathy, or acquired immunodeficiency syndrome. It became imperative for the clinician to evaluate the correct reason for cervical lymphadenopathy which is very much required for an appropriate management as well as a good prognosis of the condition.

Although the clinical examination is the first step, assessment of cervical lymphadenopathy by using imaging techniques provides additional information regarding its cause. Several advanced imaging techniques such as Computed Tomography, Magnetic Resonance Imaging (MRI), Ultra-Sonography (US), and Colour Doppler Ultra Sonography (CDUS) are the modalities sensitive in the detection of lymph nodes.

The US is one of the well-known popularly used modalities for the detection of lymph node status as it can demarcate alterations in the internal architecture of the node. The US has been reported to be a highly sensitive technique than clinical examination for the diagnosis of cervical lymphadenopathy. The US can also detect or discover the nodes which are missed on clinical examination [1-3]. However, CDUS which is an advancement in the US detects actual pathology present within the lymph node based on the presence of vascularity of the lymph node [3].

The angioarchitecture and the hemodynamics within a lymph node vary from disease to disease. For example, in inflammatory or reactive nodes, there is dilatation of intranodal vessels while in metastatic nodes internal nodal vasculature is destroyed due to neoplastic infiltration. These vascular alterations in a diseased lymph node are diagnostic of pathology and thus aid in the differentiation of benign from malignant lymph nodes [4].

CDUS provides additional information than grey scales in the US about the presence of vascularity within the node, vessel location or flow pattern, intravascular resistance estimation, and

spectral Doppler analysis. The type of vascular flow pattern and increased vascular resistance are the significant features used to differentiate between benign and malignant nodes [5]. Even one can assess treatment response by periodic monitoring of nodal size as well as vascularity [6].

Considering all these factors, one is determined to accept the fact that, CDUS is not only a valuable diagnostic tool but also it is a vital, safe (as no ionizing radiations are used), non-invasive and painless investigation in the evaluation of cervical lymphadenopathy.

LITERATURE REVIEW

Colour Doppler Ultrasound (CDUS)

An Austrian Physicist, Johann Christian Doppler 1842 first described the colour Doppler effect. He postulated that certain properties of light emitted from stars depend upon the relative motion of the observer and the wave source. He suggested that the coloured appearance of certain stars was caused by their motion relative to the earth. He has explained the "Doppler effect". Doppler effect is used to detect the details regarding the vascularity within a US image such as the presence or absence of vascularity, its direction, and velocity. The velocities are distinguished by different colours [7,8]. Usually two Colours –Red denotes the flow /reflector is coming towards Blue denotes the flow is moving away the Doppler shift frequency can also be recorded in frequency spectrum analyzers. The waveform seen on the screen is called a flow velocity waveform or a spectral waveform. Using this, one can detect blood flow in its direction as well as the velocity of blood flow.

One of the vital factors is new blood vessel formation is required for the growth of tumour cells. For this, a hormonal substance known as the tumour angiogenesis factor plays a role. This new vessel formation mainly takes place along the periphery of the lymph node while the central part remains devoid of vascularity and often undergoes necrosis. These vascular events are responsible for the characteristic appearance of CDUS and are helpful to identify the basic pathology of lymphadenopathy in a particular case [9]. Based on the presence of vascular changes in a lymph node, the detection of even small, round inflammatory, or benign lymph nodes is also possible [10]. Thus, CDUS is a widely used investigation in Oral and Maxillofacial disorders.

CDUS is a non-invasive technique, safe technique and can be performed in a short time. Vascular flow pattern and vascular resistance are the two main parameters studied on CDUS that assist in the diagnosis of the cause of cervical lymphadenopathy.

Vascular flow pattern

The anatomy of the lymph node shows that the lymphatic artery enters through the hilus, and the lymphatic vein exits through the hilus. Thus, the hilar area or central area of a normal node appears vascular on CDUS. Rarely a normal cervical lymph node may appear avascular but the vascularity is never at the periphery in a reactive lymph node. The reason for avascularity in benign or reactive nodes on CDUS is difficulty in the detection of intranodal vasculature in small-sized nodes. This happens usually in parotid nodes or the nodes of the posterior triangle of the neck. Nonetheless, the submental and submandibular nodes which are comparatively bigger show significantly high vascularity [10, 11]. All the vascularity-related parameters which include blood flow and velocity (peak systolic velocity and end diastolic velocity) are related to the size of the nodes. These features are more prominent in bigger nodes as compared to small nodes as the bigger nodes allow faster and more flow of blood in the node which is easily detectable on CDUS [3, 4, 11, 12]. Vascular flow pattern on CDUS is classified into 4 groups and their pathologic co-relation is as under:

No colour flow:

The lymph node is replaced by highly keratinized tissues and necrotic debris suggestive of the metastatic or malignant node.

Central flow:

Suggestive of the benign or inflammatory node with the presence of adequate vasculature and normal sinuses in the hilar region.

Displaced flow**:**

The remaining vessels are displaced as the maximum lymph node is replaced by metastatic tissue and vessels are destroyed.

Peripheral flow:

This correlates with the feature of neo angiogenesis at the periphery while destruction of hilar vessels.

Francesco Giovagnorio et al. classified CDUS vascular flow patterns into three types. Type I- hilar normal (frequently associated with inflammation), type II- hilar activated (frequently associated with lymphoma), and type III- peripheral (metastatic) [13].

All these classifications of vascular flow patterns describe the difference between benign and malignant lymph nodes. But then again, the additional feature is vascular flow pattern can differentiate between primary and secondary malignancy also as the spread of neoplastic cells within lymph node vary between metastasis node and lymphomatous node. In metastasis, the tumour cells travel through the afferent lymphatic vessels and thus invade the node from outside. Then the neoplasia advances in a centripetal fashion, that is from periphery to centre while in lymphoma, the disease originates within the lymph node, and progresses to involve the lymph node completely in a centrifugal fashion. However, the exception to this can be observed in high-grade aggressive lymphomas in which there is the involvement of multiple nodes. In this case, the involvement of the lymph node may be from outside when the adjacent lymph node infiltrates the remaining nodes [13].

In this regard, Takako Shirakawa, et al. mentioned the importance of extra hilar vessels as a key feature of malignancy [14]. An extra hilar vessel enters the lymph node not from the hilus but from the surface of the node that is from outside. Tuberculous nodes also show similar features as the destruction of the nodal architecture takes place the same as that of the metastatic node. But, in a study by Rohan K et al., tuberculous nodes depicted variable vascular flow patterns, with both benign patterns as well as malignant patterns [15].

Ahuja AT et al. stated that some factors are responsible for variation in the flow pattern and vascular resistance amongst various diseased lymph nodes [16]. These include the histopathological features of tumour cells, the severity of nodal infiltration, and arteriovenous shunting. Does this explain the fact why metastatic nodes of different malignancies behave differently? Nonetheless, different parts of the same node that is metastasized from the same malignancy may also depict variable features [11].

Ozerk Omur Okten, et al. explained the concept of the number of vascular poles to identify the type of cervical lymphadenopathy [17]. According to them, a single vascular pole with linear and even branches suggests a benign lymph node while multiple peripheral poles with alteration and shift of the internal vessels is a sign of a malignant node. The authors stated that based on this concept, it is probable to distinguish between benign and malignant nodes. However, the differentiation between lymphomatous cervical lymphadenopathy and metastatic cervical lymphadenopathy is not possible based on this concept.

Vascular resistance -Resistivity Index (RI) and Pulsatility Index (PI)

In an advanced stage of the disease, the maximum portion of the lymph node is replaced by tumour cells. This causes compression of blood vessels by tumour cells within the node due to limited space therein. This further leads to an increase in vascular resistance and thus an increase in RI [13,18]. Although this is the explanation for increased RI in malignant nodes controversial results and contradictory explanations are also reported in the literature. The studies reporting lower RI and PI in malignant nodes explained that the absence of a muscle layer in tumour vessels and the presence of arteriovenous shunting as the reasons for low RI and PI [18].

In regards to age-wise alterations in blood flow and vascular resistance of lymph nodes, the vascular flow is reported to be quite higher in the elderly. The reason for this is the reduced compressibility of the small vessels with ageing thus blood flow is easily detected. However, there is no variation in vascular resistance in regards to the size of lymph nodes. There is no variation between men and women for both parameters [11].

Zeran Brnic and Andrija Hebrang have reported differences in RI and PI between all types of lymphadenopathy [18]. Resistance is greater in metastatic nodes. But, no difference in RI and PI is observed between lymph nodes with primary malignancy and benign nodes. In lymphomatous nodes, CDUS is useful for monitoring the response to the treatment. A rapid decrease in blood flow is suggestive of a positive response to the treatment and prediction of a good prognosis but the persistence of high vascularity following the treatment indicates subsequent relapse after chemotherapy [19]. Although, assessment of RI and PI in post-chemotherapy lymphoma patients gives no noteworthy results [19].

CONCLUSION

CDUS is one of the popular and routinely used valuable investigations in the field of Medical Radio-diagnosis. It assesses intranodal architecture based on vascular flow patterns or Doppler spectrum analysis of nodal blood vessels. The modality is less time-consuming, non-invasive, reliable, and reproducible. Thus, the vascular flow pattern in CDUS can be trusted as a reliable marker for the diagnosis of cervical lymphadenopathy.

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