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Research Article

ROLE OF HIGH RESOLUTION ULTRASOUND AND COLOR DOPPLER IN EVALUATION OF CERVICAL LYMPH NODES AND CORRELATION WITH HISTOPATHOLOGY

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ABSTRACT

Introduction and objective: Cervical lymphadenopathy is one of the most common causes of neck masses and to find out the cause is often a diagnostic challenge for proper treatment and follow up. The main objective of our study is to study the gray scale and Doppler characteristic of different causes of cervical lymphadenopathy and compare with the histopathology

Methods: Gray scale Ultrasound and Doppler study was done on 100 patients with cervical lymph nodes enlargement, Gray scale ultrasound and Doppler features were compared with histopathology

Results: Normal and reactive nodes were oval in shape with central echogenic hilum on gray scale ultrasound and showed hilar vascularity, low RI and PI values on color Doppler. Abnormal lymph nodes showed more round in shape (loss of normal oval shape), loss echogenic hilum and necrosis on gray scale ultrasound and peripheral and chaotic vascularity and sometime absent vascularity due to extensive necrosis on color Doppler. Infective nodes showed indeterminate doppler features. RI and PI of malignant nodes were significantly higher than benign nodes.

Conclusion: High resolution Ultrasonography together with Color Doppler features are the primary modality of investigation in head and neck lymphadenopathy. Using clinical examination, ultrasonography and color Doppler criteria (S/L ratio, border sharpness, hilum, echogenicity, necrosis, matting and vascular pattern) it is possible to differentiate malignant and non malignant head and neck lymphadenopathy.

Keywords: Lymph nodes, Gray scale ultrasound, Doppler, Resistive Index (RI), Pulsatility Index (PI).

INTRODUCTION

Cervical lymph nodes enlargement is common in various diseases of head and neck and non–head and neck. Evaluation of cervical nodes is an important because it assesses the prognosis of the patients and helps to select appropriate treatment. Noninvasive imaging techniques such as CT and US be used for improved detection of metastasis in lymph nodes. Regardless of the primary tumor, the presence of a metastatic node reduces the 5-year survival rate by 50%, and the presence of another metastatic node on the contra lateral side further reduces the survival rate to 25%[1]. Metastatic nodes are site-specific[2], and nodal metastasis of a particular head and neck cancer in an unexpected level indicates that the neoplasm is more aggressive[3]. Sonography has proved highly effective for detection, localization and delineation of enlarged lymph nodes of the neck. Infiltration of adjacent structures, specifically the common, internal and external carotid arteries and the neck muscles are reliably demonstrated.

Cervical lymph nodes are also common sites of involvement of lymphoma in the head and neck[4-6].

Tuberculous lymphadenitis remains a diagnostic dilemma and lymph nodes in the head and neck regions are common sites of this infection[7,8]. Tuberculous lymphadenitis is common in underdeveloped countries, and with the spread of acquired immune deficiency syndrome (AIDS), tuberculous lymphadenitis is now frequently encountered in developed countries[9,10]. Although the incidence of AIDS-related tuberculous lymphadenitis is increasing, it may also be found in patients without AIDS.

The role of high-resolution ultrasound in assessment of cervical lymph nodes is well established, and grey-scale ultrasound is widely used to assess cervical nodes for their number, site, size, nodal boundary, hilum, matting, adjacent soft tissue oedema and other internal nodal echo patterns[2,11-16]. With the use of colour Doppler sonography (CDS), the amount of information that can be obtained during an ultrasound examination of cervical lymph nodes has increased. However, when CDS was initially applied in the assessment of cervical lymphadenopathy, its value in daily practice was often doubted because of inconsistent results and disagreement on methodology[17,18]. With the development of technology assessment of the vascularity of lymph nodes by ultrasound has become more accurate[19-23]. Doppler sonography is more accurate in the assessment of small vessels, such as those found in lymph nodes

The main objective of our study is to study the gray scale and Doppler characteristic of different causes of cervical lymphadenopathy and compare with the histopathology. The results obtained were correlated with histopathological findings and specificity and sensitivity of color Doppler parameters in differentiation of benign and malignant lymphadenopathy was determined.

MATERIALS AND METHODS

Prospective study of 100 with cervical lymph node enlargement referred from other department and high resolution ultrasonography and color Doppler study was performed in the Department of Radiodiognosis

All studies were subjected for High resolution Ultrasonography and Color Doppler of cervical lymph nodes with SIEMENS ACUSON 300 PE Ultrasound Scanner with a linear probe with 7.5 MHz frequency with patient in supine position with neck extended. Doppler examination was preceded by grey scale sonography and we looked for size (L/S ratio), shape, echogenicity, nodal border and echogenicity of hilum. Calcification, intra nodal necrosis, matting and adjacent soft tissue edema if present were also noted.

Colour Doppler parameters were adjusted for detection of low-velocity or low- volume flow and included:

- The color gain was first increased to a level which shows color noise, and then decreased to the level where the noise just disappeared.
- For measuring Doppler indices (RI and PI), the more prominent vessels were selected.
- For measuring Peak systolic velocity, (PSV) and end diastolic velocity (EDV), angle correction was made to an angle of 60 degree or less.

Fine Needle Aspiration was done in all the cases and smears were sent for cytology and the results were compared with High resolution Ultrasound and Doppler findings.

Chi- square test was used for overall efficacy of Doppler and spectral parameters in accurate differentiation of benign and malignant lymphadenopathy and student's t-test was used for determining significance of difference of means of roundness index, RI /PI in benign and malignant nodes.

RESULTS

The present study was undertaken in the department of Radiodiagnosis Al-Ameen medical college Bijapur-Karnataka state on 100 patients with lymph node masses in neck that were referred to our department for Doppler Ultrasonography.

Malignant nodes outnumbered benign cases in our study as patients who were very sick and admitted on inpatient basis were usually referred to us. 58 of 100 cases in our study were malignant with metastatic nodes accounting for 38 cases.

Grey scale features (Table 1)

Solbiati Index (SI) or roundness index of lymph nodes is most important grey scale feature in differentiating benign from malignant nodes

Mean Roundness index in benign nodes was 2 and in malignant nodes was 1.48. Highest mean rounded index in benign node was 2.94 and lowest was 1.70. Highest mean rounded index in malignant node was 1.75 and lowest was 1.09. The difference was statistically significant with p value < 0.05

However, 7 out of 21 reactive nodes i.e 33% and 13 out of 26 tubercular nodes i.e 50% had SI < 2, whereas none of malignant nodes had SI > 2 in our study.

So 19 of 27 nodes (70%) having SI < 2 were malignant. So there will be high false positive rate for predicting malignant nodes if roundness index is used as the only criteria.

Necrosis and displaced hilum as a feature was seen more frequently in tubercular nodes and necrosis was not seen in any of the reactive lymph nodes.

Vascular Distribution in Nodes (Table 2)

Vascular distribution has been classified differently by different researchers. In our study, we have taken classification of **Wu et al[23] who** in addition to Avascular group classified vascularity into four types as

Hilar type:a simple short feeding vessel, or a central longitudinal vessel, or a hilar vessel with regular and symmetric centrifugal branching;

Spotted or multifocal type: scattered specks or segments of vessel signals distributed chaotically within the node;

Peripheral type: vascular signals distributed only around the node or in a basket pattern with centripetal branching;

Mixed type: a mixture of more than one of the foregoing types

Hilar vascularity was common in reactive and Lymphomatous nodes and mixed pattern was frequently seen in metastatic nodes. **(Figure 1, 2, 3)**

SPECTRAL INDICES OF NODAL VESSELS (Table 3 & Table 4)

Resistive index of benign nodes was low with minimum value of 0.33 and maximum value of 0.7 while as Resistive index of malignant nodes was high with minimum value of 0.65 and maximum value of 1.15 Most of malignant nodes have RI value more than 0.7 and most of the benign nodes have RI value less than 0.7. Pulsatility index of benign nodes was low with minimum value of 0.42 and maximum value of 1.3 while as Pulsatility index of malignant nodes was high with minimum value of 1.1 and maximum value of 4.5 Most of malignant nodes have RI value more than 1.3 and most of the benign nodes have RI value less than 1.3.

There was a significant difference in the mean RI and PI values of benign and malignant values with mean RI and PI of malignant nodes as 0.86(SD=0.11) and 1.76 (SD=0.72) respectively and mean RI and PI of benign nodes as 0.58(SD=0.1) and 0.85(SD=0.23) respectively . Difference of means were found statistically significant using student's t-test with a p-value < 0.0001

Mean RI and PI of lymphoma and metastatic nodes was almost similar with no significant difference. Mean RI and PI of tubercular nodes is more than reactive nodes but less than malignant nodes.

EDV of lymph nodes (Table 5)

EDV of malignant nodes varied from -4.6 to 11.1 cm/s with mean of 2.8cm/s and EDV of benign nodes varied from 3.4 to 19.4 cm/s with mean value of 7.5cm/s. 23 of 28 vascular malignant nodes showed EDV < 5cm/s and vascular benign nodes showed EDV >/= 5cm/s. None of the benign node had EDV < 3.4 and none of the malignant node had EDV > 11.1cm/s. **(figure 4, 5, 6, 7).**

PSV of lymph nodes

PSV of malignant nodes varied from 7.79 to 43 cm/s with mean of 19.84cm/s and PSV of benign nodes varied from 8.4 to 29.4 cm/s with mean value of 17.37cm/s

DISCUSSION

Grey scale features most important in differentiation of benign and malignant lymphadenopathy were roundness index and hilum changes. Grey scale features had acceptable sensitivity for detecting a malignant node but had low specificity as half of tubercular nodes and 18% of reactive nodes had SI< 2.

Hilar vascularity is commonly seen in reactive lymphadenopathy. 82% of cases in our study showed hilar vascularity. **Ayata et al**[24] noticed hilar vascularity in 88% of reactive lymph nodes. **Ahuja et al**[25] noticed hilar vascularity in 96% of reactive nodes

Tubercular nodes usually have variable vascularity. In the present study, hilar (40%) and avascular (30%) forms were most common together accounting for 70% of cases. Multifocal and mixed vascularity was seen in 20% and 10% of cases respectively. In a study conducted by **Wu et al**[23] they found 72% of tuberculous lymphadenopathy lesions revealed either an avascular pattern or a hilar vascular pattern. Malignant nodes are characterized by extrahilar vessels which are induced by neovascularisation however incidence of extrahilar vessels in lymphoma is lower than metastatic nodes [26].

In the present study, vascular distribution was variable with mixed vascularity being the most common form of vascularity in metastatic nodes and was found in 79% of cases. **Wu et al**[23] also found mixed vascularity the most common form and was seen in 53% of cases**. Na et al**[27] also noticed mixed vascularity in 82% of malignant nodes

Spotted / Multifocal and Peripheral vascularity were the main vascular components present in the metastatic nodes with 15 of 19 nodes (79%) showing multifocal and 14 of 19 (74%) showing peripheral with both being together in mixed form usually. Only peripheral vascularity was only seen in 5.3% of cases. **Na et al**[27] also noticed similar findings with 47 of 52 nodes (90%) showing peripheral and 42 of 52(81%) showing multifocal with both forms being together usually in mixed form, they noticed pure peripheral vascularity in 6% of cases.

Lymphomatous nodes usually showed hilar preponderance. In our study, 40% of nodes showed only hilar vascularity and 60% showed mixed vascularity with hilar component seen in all the cases showing mixed vascularity. Hilar vascularity in lymphoma was different from benign nodes in being more profuse and showing few large branches and it was also noticed by **Giovagnorioet al**[28] and they called it hilar activated or type 2 hilar vascularity. They also concluded that lymphoma and metastatic node can be differentiated by vascular pattern as hilar vascularity is more common in lymphoma and peripheral subcapsular vascularity is more a feature of metastasis. **Wu**[23] **et al 1998** also found that hilar vascularity is the most common vascularity seen in lymphoma and is different from benign hilar vascularity as high vascular density is seen in lymphoma cases.

Lymphadenopathy due to benign and malignant diseases can be distinguished with a high degree of accuracy by means of spectral waveform analysis. RI and PI of malignant nodes is significantly higher than benign nodes. In the present study, RI values ranged from 0.33 to 0.7 in benign nodes and 0.65 to 1.15 in malignant nodes and Mean RI of benign and malignant nodes in our study was 0.58 and 0.86 respectively. **Choi et al**[29] in their study noticed that RI ranged from 0.38 to 0.82 in benign nodes and 0.44 to 1.24 in malignant nodes with a mean RI of 0.59 in benign nodes and 0.92 in malignant nodes.. **Ferrari et al**[30] found mean RI of 0.58 and 0.84 in benign and malignant lymph nodes respectively almost in close agreement with the present study.

PI values ranged from 0.42 to 1.3 in benign nodes and 1.1 to 4.5 in malignant nodes and mean PI of benign and malignant nodes in our study was 0.85 and 1.76 respectively. . **Choi et al**[29] in their study noticed that PI ranged from 0.46 to 1.43 in benign nodes and 0.59 to 6.16 in malignant nodes with a mean PI of 0.90 in benign nodes and 2.66 in malignant nodes. **Ahuja et al**[25] found a mean PI of 1.89 for malignant nodes and 1.07 for reactive nodes almost close to the values obtained in the present study.

In the present study, mean RI and PI in reactive nodes was 0.54 and 0.77, in tubercular nodes was 0.65 and 1.03, in Lymphomatous nodes was 0.86 and 1.83 and in metastatic nodes was 0.86 and 1.72 respectively. **Na et al**[27] found mean RI and PI of 0.57 and 0.85 in reactive nodes, 0.64 and 1.03 in tubercular nodes, 0.7 and 1.2 in lymphoma and 0.83 and 1.62 in metastatic nodes which.. In our study mean RI and PI of lymphoma cases was not much different from metastasis because most of our lymphoma cases were aggressive Non Hodgkin lymphoma as has been noticed by **Picardi et al**[31], that mean RI value of aggressive NHL was 0.85 and was significantly higher than the mean values of 0.74 in Hodgkin lymphoma.

Different researchers have suggested different cut off for RI and PI for differentiating benign and malignant lymphadenopathy. **Wu et al**[23] suggested cut off of 0.7 for RI and 1.1 for PI and found that accuracy was 73% and 76%, respectively. **Chang et al**[32] suggested a cut off of 0.6 for RI and 1.2 for PI and found sensitivity and specificity of 81% each. However, they had selected the lowest indices from each node. **Shirakawa et al**[26] suggested cut off of 0.72 for RI and 1.3 for PI and found it appropriate for acceptable sensitivity, specificity and **Ahuja et al**[33] suggested the cut off of 0.7 for RI and 1.4 for PI.

In the present study sensitivity and specificity was seen at three different values of RI and PI and it was noticed that at RI of 0.7 and PI of 1.3 high sensitivity (93%,89%) and specificity (94%,94%) was obtained with a p-value <0.0001 (using Chi Square test) while increasing the cut off to 0.8 for RI increased the specificity to 100% but reduced sensitivity to 68% and by decreasing cut off to 0.6 sensitivity increased to 100% but specificity was reduced to 45. **Na et al**[27] also looked for sensitivity and specificity at different cut off values and found sensitivity for labeling a node malignant at RI of 0.6 was >90% but specificity was 50%, at RI of 0.8 sensitivity reduced to around 50% but specificity was 100%. Likewise, for a cut off PI value of 1.1, sensitivity was > 80% but specificity was around 70% but at a cut off value of 1.5 sensitivity reduced to 55% but specificity reached 100%

Mean Peak systolic velocity in the present study was similar in benign and malignant lymph nodes with malignant nodes showing mean PSV of 19.84cm/s and benign nodes showing mean PSV of 17.37cm/s and mean End diastolic velocity in malignant nodes was 2.8cm/s which was significantly lower than mean EDV of benign nodes which was 7.5 cm/s. EDV in malignant nodes varied from -4.6 to 11.1cm/s and EDV in benign nodes ranged from 3.4 to 19.4 cm/s. So in our study EDV> 11.1 cm/s has 100% negative predictive value for nodal metastasis, and EDV<3.4 cm/s has 100% specificity and PPV for metastasis.

Choi et al[29] also found mean PSV similar in two groups with mean PSV of 25cm/s in malignant and 24cm/s in benign nodes. Mean EDV of malignant and benign nodes was 2cm/s and 10cm/s respectively. EDV in benign nodes varied from -10cm/s to 14cm/s and EDV in benign nodes ranged from 3cm/s to 51 cm/s

Brnic and Hebrang[34] **also** noticed that EDV>9 cm/s has 100% negative predictive value for nodal metastasis, and EDV<1 cm/s has 100% specificity and PPV for metastasis.

Most important marker for differentiation of benign and malignant node in our study was RI with a sensitivity of 93%, specificity of 94% and accuracy of 93.5% at a cut off value of 0.7 with a p-value of < 0.0001.

Issing et al[35] also concluded that most valuable parameter was Pourcelot index (RI) with a specificity of 92% for detecting malignant node. **Ayata et al**[24] also suggested RI as the most important marker with a sensitivity of 84.6, specificity of 100% and accuracy of 95.7% at a cut off value of 0.7 for differentiating benign from neoplastic lymphadenopathy.

CONCLUSION

1. Ultrasound with Color Doppler is the primary modality of investigation in head and neck lymphadenopathy
2. Using clinical examination, ultrasonography and color Doppler criteria (S/L ratio, border sharpness, hilum, echogenicity, necrosis, matting and vascular pattern) it is possible to differentiate malignant and non malignant head and neck lymphadenopathy
3. Ultrasonography being a bedside and outpatient procedure can be used by radiologists as well as surgeons and physicians for the evaluation of cervical lymphadenopathy.
4. Though histopathological examination is the gold standard for detection of lymphnode metastasis, ultrasonography with color doppler can be used alternatively.

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Table 1: Grey scale feature

Diagnosis	mean Roundness index (L/S)	Hilar features			Necrosis
		Normal	Absent	Displaced	
Reactive	**2.10**	**20**	**0**	**1**	**0**
Tuberculosis	**1.83**	**7**	**5**	**9**	**5**
Lymphoma	**1.60**	**10**	**7**	**0**	**1**
Metastatic	**1.35**	**5**	**22**	**6**	**3**

Table 2: Vascular Distribution in Nodes

TYPE OF VASCULARITY	Patients with reactive (n =22)	Patients with tuberculosis (n =20)	Patients with metastasis (n =38)	Patients with lymphoma (n =20)
Hilar	**18**	**8**	**2**(5.26%)	**8**
Multifocal	**2**	**4**	**2**(5.26%)	**0**

Peripheral	**0**	**0**	**2**(5.26%)	**0**
Avascular	**0**	**6**	**2**(5.26%)	**0**
Hilar, peripheral and multifocal	**0**	**0**	**4**(10.52%)	**0**
Peripheral and multifocal	**0**	**0**	**20**(52.6%)	**0**
Hilar and peripheral	**2**	**2**	**2**(5.26%)	**10**
Hilar and multifocal	**0**	**0**	**4**(10.52%)	**2**

SPECTRAL INDICES OF NODAL VESSELS (Table 3 & Table 4)

Table 3

DIAGNOSIS	MEAN RI	MEAN PI
BENIGN	0.58	0.85
MALIGNANT	0.86	1.76

Table 4

DIAGNOSIS	MEAN RI	MEAN PI
METASTASIS	0.86	1.72
LYMPHOMA	0.86	1.83
REACTIVE	0.54	0.77
TUBERCULOSIS	0.65	1.03

Table 5: EDV of lymph nodes

EDV(cm/s)	BENIGN	MALIGNANT
< 0	0	2
0-4.9	3	21
5-9.9	12	4
>=10	3	1

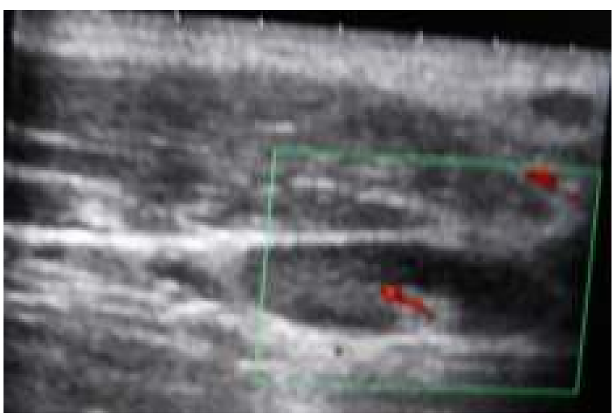

Figure 1: Colour Doppler of a reactive node showing single hilar vessel

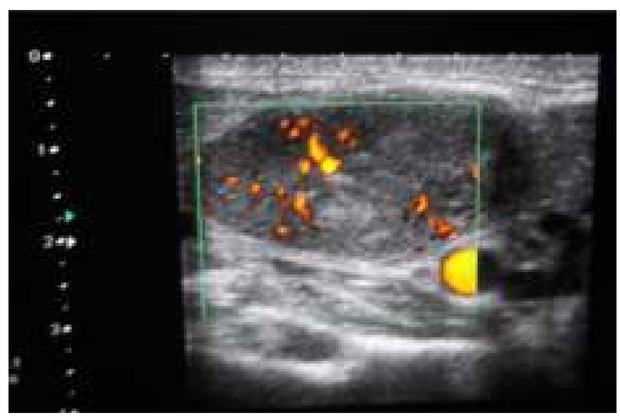

Figure 3: Power Doppler of a Metastatic node with multicentric and peripheral vascularity

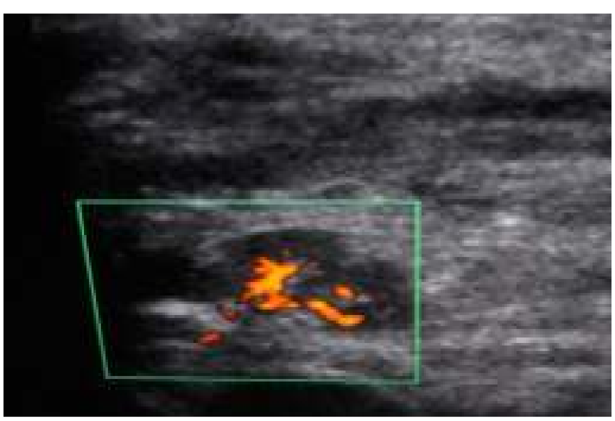

Figure 2: Power Doppler of a lymphomatous node with activated hilar vascularity

Figure 4: Spectral trace of a reactive node showing low RI, PI

Figure 5: spectral Doppler of lymphomatous node seen in Figure 2 shows high RI and PI

Figure 6: spectral doppler of Metastatic node (Figure 3) shows high RI, PI and low EDV

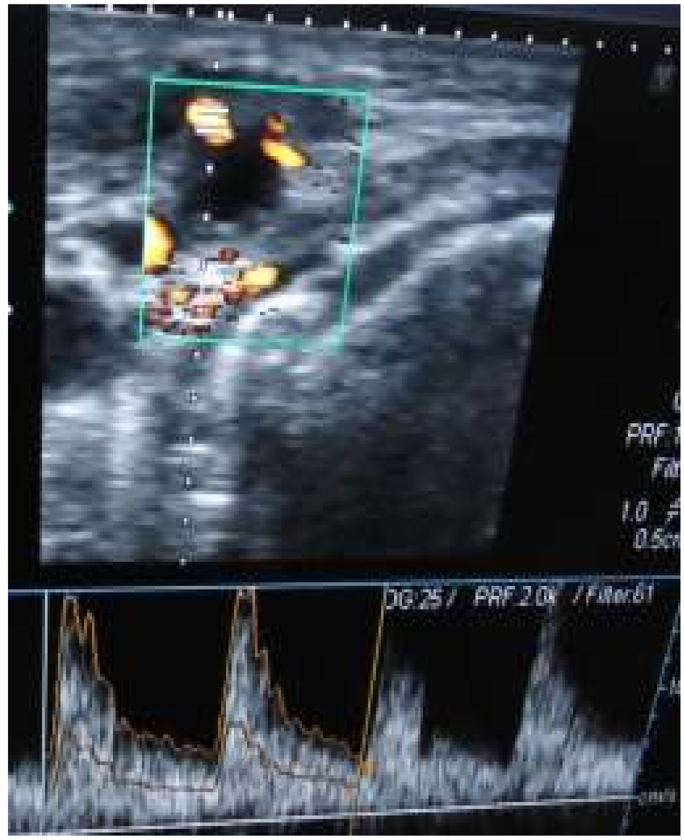

Figure 7: Doppler of a tubercular node with necrosis and multifocal vascularity and spectral trace also being indeterminate

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