Immunohistochemical expression of endocan, as a marker of assessment of angiogenic potential in benign vascular lesions (hemangioma, lymphangioma and lobular capillary hemangioma) of head and neck region

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ABSTRACT

BACKGROUND: Vascular tumors are a heterogeneous group of diseases with biological behavior ranging from a hamartomatous growth to frank malignant. The pathophysiology of lymphangioma, vascular malformation and hemangioma is interconnected, blood vessels known to be the site of origin of hamartomas, venous malformations and some neoplasms as benign, tumor-like growth of vessels (hemangiomas). Angiogenesis is the process of formation of new blood vessels from an existing structure.

Aims of study: Assessment of angiogenic potential in benign vascular lesions (hemangioma, lymphangioma and lobular capillary hemangioma) of head and neck region.

Materials and Methods: Twenty-two formalin-fixed paraffin-embedded tissue blocks of Hemangioma/vascular malformation, thirty of lobular capillary hemangioma and another twenty of lymphangioma to be stained with Endothelial cell-Specific Molecule-1 (ESM-1) monoclonal antibody.

Results: Microvessel density expressed by Endothelial cell-Specific Molecule-1 (ESM-1) immunomarker was found in all cases with mean density of (37.44±23.16) for lobular capillary hemangioma and (25.02±13.89) for hemangioma and (6.34±3.52) for lymphangioma. According to post hoc test ESM-1 marker expression showed a high significant difference between (hemangioma and lymphangioma=0.001), (lymphangioma, pyogenic granuloma=0.000), and it was significantly different between (hemangioma, pyogenic granuloma=0.011)

Conclusions: The obvious capillary growth in lobular capillary hemangioma revealed that lobular capillary hemangioma showed the highest activity of angiogenic potential in comparison to hemangioma and lymphangioma.

Keywords: Endocan, vascular tumor, angiogenic potential.

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INTRODUCTION:

The vascular system is non-uniform organ system and a highly heterogeneous, therefore to make a decision whether the whole lesion is composed of only lymphatic channels or whether there is a venous component cannot be easy (1).

Angiogenesis is the process of formation of new blood vessels, which means that the human body grows new blood vessels from an existing structure to increase the flow of blood to ischemic tissue (2). The vascular development begins by the meeting of a vessel plexus from single cell precursors, this plexus then undergoes adjustment by sprouting growth and remodeling (angiogenesis), followed by recruitment of vessels into target tissues, lastly new vessels differentiate according to the specific needs of the tissue (3).

Endocan also known as Endothelial cell-Specific Molecule-1 (ESM-1) has appeared since its discovery as a dermatan sulfate proteoglycan, with unique structural and functional properties. ESM-1 naturally expressed by endothelial cells, a highly regulated in presence of proinflammatory and proangiogenic molecules, binds to growth factors, integrin, matrix proteins and cells, and considered as an accurate marker of endothelial activation (4).

MATERIALS AND METHODS

The sample is consisted of twenty-two formalin fixed paraffin embedded tissue blocks of Hemangioma/vascular malformation, twenty of lymphangioma and another thirty of lobular capillary hemangioma. The samples obtained from the archives of the department of Oral & Maxillofacial Pathology/College of Dentistry/University of Baghdad & Al-Shaheed Ghazi Hospital/ Medical City / Baghdad dated from (1979 till 2015).

After histopathological reassessment of haematoxylin and eosin stained sections for each block, an immunohisto-chemical staining was
performed using endocan, assessment MVD based on the criteria of weidner (5).

RESULTS
ESM-1 Expression
The immunostaining method of ESM-1 was applied to lymphangioma, hemangioma and pyogenic granuloma, where the endothelial cells of blood vessel were stained with brown coloration as seen in (Figures 1, 2, 3, 4 and 5).

In (Table 1), the mean±Sd of MVD evaluated by ESM-1 immunomarker expression, according to ANOVA test imploded between samples groups. There was a high statistical significant difference in the mean of expression of ESM-1 in pyogenic granuloma in comparison to lymphangioma and hemangioma (p=0.000).

Table (1): Description of statistics obtained by immunohistochemistry of ESM-1:

<table>
<thead>
<tr>
<th>ESM-1</th>
<th>N</th>
<th>mean</th>
<th>SD</th>
<th>Min.</th>
<th>Max.</th>
<th>F</th>
<th>SIG.</th>
</tr>
</thead>
<tbody>
<tr>
<td>hemangioma</td>
<td>22</td>
<td>25.0182</td>
<td>13.89151</td>
<td>10.00</td>
<td>62.60</td>
<td>20.17</td>
<td>0.000</td>
</tr>
<tr>
<td>lymphangioma</td>
<td>20</td>
<td>6.3400</td>
<td>3.51604</td>
<td>2.30</td>
<td>15.60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pyogenic</td>
<td>30</td>
<td>37.4400</td>
<td>23.16239</td>
<td>8.60</td>
<td>95.30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>granuloma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>72</td>
<td>25.0056</td>
<td>21.04732</td>
<td>2.30</td>
<td>95.30</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

According to post hoc test, whereas multiple comparisons were made between hemangioma, lymphangioma and pyogenic granuloma with different markers, a highly significant difference was found between ESM-1 expression in hemangioma and in lymphangioma (0.001), and it was significantly different between pyogenic granuloma and lymphangioma (0.011) (Table 2).

Table (2): multiple statistical comparisons by post hoc test

<table>
<thead>
<tr>
<th>ESM-1</th>
<th>Dependent variable</th>
<th>Mean difference</th>
<th>Std. Error</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>hemangioma</td>
<td>Lymphangioma</td>
<td>18.67</td>
<td>5.24</td>
<td>.001**</td>
</tr>
<tr>
<td>Pyogenic</td>
<td></td>
<td>-12.42</td>
<td>4.76</td>
<td>.011*</td>
</tr>
<tr>
<td>Lymphangioma</td>
<td>Pyogenic</td>
<td>-31.10</td>
<td>4.89</td>
<td>.000**</td>
</tr>
</tbody>
</table>

Figure (1) A: Photomicrograph showing ESM-1 immunostaining - positive blood vessels and negative stain lymphatic vessels in lymphangioma X100) B: Positive blood vessels X400) (thin arrow for lymphatic while, thick arrow for blood vessels
DISCUSSION

This study showed the highest positive expression of ESM-1 in lobular capillary hemangioma which is in accordance with previous studies which determined ESM1 as a critical proangiogenic molecule (7), also it agrees with Chen LY et al. (8) whom found in vitro that endocan being over-expressed during angiogenesis. This can be explained at the molecular level by understanding the pathogenesis of lobular capillary hemangioma that considered as the imbalance between angiogenesis enhancers and inhibitors, that is overexpression of bFGF and VEGF and decreased quantity of angiostatin direct to the development of pyogenic granuloma (9).

In this study, ESM-1 was positively expressed in lymphangioma and that agrees with Shin JW et al. (10) whom explained that ESM-1 was a potential target for the inhibition of VEGF-C–or VEGF-A–induced pathologic lymphatic vessel growth and activation and considered it as a novel mediator of lymphangiogenesis. The obvious capillary growth (hyperplastic granulation tissue) in lobular capillary hemangioma suggests that there should be a strong activity of angiogenic potential (9). This agree with the findings of the present study, which found that ESM-1 expression being higher in lobular capillary hemangioma, which explains the proliferative nature of this lesion.

REFERENCES:

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الخلاصة

الخلفية: إن مصطلح الأورام الوعائية يستخدم عادة لشرح مجموعة من أورام الأوعية الدموية والتشوهات الخلقية. الأورام الوعائية والأورام اللمفية هي أورام مرتبطة بالعفونات. تهدف هذه الدراسة لتقييم قابلية تكون الأوعية الدموية في الأورام الوعائية والأورام اللمفية في منطقة الرأس والعنق. المواد وطرق الدراسة: في هذه الدراسة، تم جمع 22 عينة من الأورام الوعائية المعالجة بالفورمالين والمغمورة بالبارافين، و30 عينة من الأورام الوعائية الشعرية المتضمنة. الاختبارات المخبرية: كتلة الأوعية الدموية الموضحة من خلال الأجسام المناعية ESM-1. الاستنتاجات: التطور الوعائي الواضح للأورام الوعائية الشعرية الموضحة تظهر نسبة عالية من الأوعية الدموية بالإضافة إلى الأورام الوعائية والأورام اللمفية.