Effects of inflammation on the accuracy of ultrasound diagnosis of epidermoid cysts

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Abstract

Aims: Ultrasound (US) findings of epidermoid cyst (EC) are complex and diverse. Cases of misdiagnoses are high when EC is accompanied by inflammation. The aim of this study was to analyze the features of US diagnosis of EC with inflammation and explore the characteristic images which can improve the accuracy of ultrasound diagnosis. Material and methods: A total of 241 cases were included and retrospectively analyzed. Complete clinical data of all cases were available. Lesions were examined by US before operation and the diagnosis was confirmed by histopathological examination. Based on pathological results ECs with/without acute and chronic inflammation and/or granuloma, all cases were divided into two groups: inflammation and non-inflammation group. The difference of clinical data and US features between groups was analyzed by univariate and multivariate logistic regression. Results: Analysis of skin color, length/thickness, shape, boundary, CDFI and US diagnosis accuracy showed statistical differences between the two groups (p<0.05). Multivariate logistic regression model showed that indistinct boundaries and color Doppler signal were more frequent than those in ECs without inflammation (OR=4.72, 5.89, p<0.05). Conclusion: Indistinct boundaries and color Doppler signal are important features for US diagnosis of EC with inflammation, which can help in improving the accuracy of diagnosis.

Keywords: epidermal cyst; inflammation; subcutaneous tissues; ultrasound

Introduction

Epidermoid cysts (ECs), also known as sebaceous cysts or keratinous cysts, are common tumor-like skin lesions [1-4]. Conventionally, due to its non-invasive nature and high diagnostic specificity, the ultrasound (US) approach is suitable for preoperative examination of superficial skin tumors [5]. Although EC is referred to as a cyst, it does not present as a typical anechoic nodule on the US examination. Due to the different content of keratin in ECs, US features are complex and diverse. When accompanied by inflammation, ECs show special US features, which may result in a misdiagnosis [2,6-9].

A search conducted on PubMed and SpringerLink did not find any report on the effects of inflammation of ECs on US diagnosis. We aimed to evaluate the effects of inflammation on the accuracy and reliability of US for the diagnosis of EC by comparing clinical and ultrasonic features between inflammation and non-inflammation groups.

Materials and methods

General information

A total of 241 patients admitted to the Second Hospital of Shandong University from December 2015 to October 2020 were enrolled in this study. Each patient only had one lesion, which was surgically removed during the inpatient/outpatient period. Pathological analysis (golden standard) showed that all lesions were ECs. Based on the pathological results, ECs with acute and chronic in-
flammation and/or granuloma were classified into the inflammatory group (group A), while the rest of the lesions without acute and chronic inflammation and/or granuloma were classified into the non-inflammatory group (group B). A flowchart showing patient selection protocol is presented in figure 1. This study was approved by the Ethical Committee of the Second Hospital of Shandong University (KYLL-2021(LW)055). The current study was retrospective, therefore informed consent from patients was not required.

Ultrasound examination

All patients were examined using the LOGIQ E9 US diagnostic apparatus (GE Healthcare, Wauwatosa, WI, USA) with a linear array probe (6-15MHz frequency). US examination included grayscale and color Doppler flow imaging (CDFI). The examination of the lesion comprised multi-section and multi-angle observation, analysis, and recording of related data. Images obtained from all cases were analyzed by two sonographers with more than five years of experience. The two sonographers were blind to pathological results. The variables were assessed, including locations, sizes, shapes, boundaries, internal echo, parenchyma echo and rear echo changes, calcification characteristics, halos around the lesions, special signs as well as blood flow signals (fig 1, fig 2,3). In cases where the two sonographers did not agree, a third sonographer, with more than ten years of experience made the final decision. This was a double-blind study of pathological and sonographic results.

Statistical analysis

Statistical analyses were performed using SPSS statistical software (IBM Corp. Released 2016. IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp.). Normally distributed data were expressed as mean ± standard deviation () while data that were not normally distributed were expressed as the median (quartile). Univariate analysis was used to evaluate the characteristics of ECs with inflammation. The independent sample t-test was used to compare the means for normally distributed data, whereas the non-parametric test (Mann-Whitney U test) was used to compare the medians for non-normally distributed. The Pearson’s chi-square or Fisher’s exact tests were used for comparisons of categorical variables. Variables with statistical significance in univariate analysis (p<0.05) were included in the logistic regression model for multivariate analysis. p<0.05 was considered to be statistically significant.
Results

Clinical features
Group A comprised 130 cases (87 males), whereas group B, the control group, comprised 111 cases (74 males). The average age was 43.38±1.67 years for group A and 40.59±1.69 years for group B. The average onset time was 60.82±7.48 months for group A and 60.75±7.96 months for group B. Abnormal skin colors included red, dark red, bruise, and blackhead, was in 33 (25.4%) cases, 1 (0.8%) case, 2 (1.5%) cases, and 6 (4.6%) cases, respectively, in group A and 15 (13.5%) cases, 2 (1.8%) cases, 1 (0.9%) case, and none in group B. Differences in skin colors between the two groups were significant (p<0.05), whereas differences in other clinical features were not significant (p>0.05) (Table I).

Ultrasound analysis
The average length (L), width, thickness (T), and volume of ECs in group A were 3.14±0.24 cm, 2.51±0.21 cm, 1.50±0.15 cm, 43.76±314.55 cm³, whereas those of the control group were 2.58±0.22 cm, 2.13±0.20 cm 1.25±0.07 cm, 12.38±60.27 cm³, respectively. In group A, 70 (53.8%) of ECs were hypoechoic, 4 (3.1%) hyperechoic, 1 (0.8%) isoechoic, 47 (36.2%) anechoic, and 8 (6.2%) mixed echo. In group B, 56 (50.5%) of ECs were hypoechoic, 6 (5.4%) hyperechoic, 3 (2.7%) isoechoic, 43 (38.7%) anechoic, and 3 (2.7%) with mixed echo. In group A 35 (26.9%) cases were homogenous, whereas in group B 27 (24.3%) cases were homogenous. US findings for ECs, including shape, boundaries, calcification, CDFI, rear echo, special signs, and hypoechoic halo are presented in Table II. Analysis showed significant differ-

<table>
<thead>
<tr>
<th>Factors</th>
<th>Group A (n=130)</th>
<th>Group B (n=111)</th>
<th>T/χ²</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical reasons</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mass</td>
<td>117 (90.0%)</td>
<td>103 (92.8%)</td>
<td>0.587</td>
<td>0.498</td>
</tr>
<tr>
<td>Redness and pain</td>
<td>13 (10.0%)</td>
<td>8 (7.2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin color</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>88 (67.7%)</td>
<td>93 (83.8%)</td>
<td>8.292</td>
<td>0.004</td>
</tr>
<tr>
<td>Abnormal</td>
<td>42 (32.3%)</td>
<td>18 (16.2%)</td>
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<td></td>
</tr>
<tr>
<td>Skin damage</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presence</td>
<td>17 (13.1%)</td>
<td>9 (8.1%)</td>
<td>1.536</td>
<td>0.298</td>
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<tr>
<td>Absence</td>
<td>113 (86.9%)</td>
<td>102 (91.9%)</td>
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<td></td>
</tr>
<tr>
<td>Skin adhesion</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presence</td>
<td>19 (14.6%)</td>
<td>11 (9.9%)</td>
<td>1.216</td>
<td>0.329</td>
</tr>
<tr>
<td>Absence</td>
<td>111 (85.4%)</td>
<td>100 (90.1%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Location</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Head and neck</td>
<td>35 (26.9%)</td>
<td>37 (33.4%)</td>
<td>3.587</td>
<td>0.732</td>
</tr>
<tr>
<td>Trunk</td>
<td>63 (48.4%)</td>
<td>45 (40.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Limbs</td>
<td>24 (18.5%)</td>
<td>20 (18.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Armpit and groin</td>
<td>8 (6.2%)</td>
<td>9 (8.1%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Factors</th>
<th>Group A (n=130)</th>
<th>Group B (n=111)</th>
<th>T/U/χ²</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>L/T</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posterior echo</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enhancement</td>
<td>98 (75.4%)</td>
<td>94 (84.7%)</td>
<td>3.619</td>
<td>0.164</td>
</tr>
<tr>
<td>Shadowing</td>
<td>5 (3.8%)</td>
<td>4 (3.6%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absence</td>
<td>27 (20.8%)</td>
<td>13 (11.7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shape</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Round or oval</td>
<td>115 (88.5%)</td>
<td>108 (97.3%)</td>
<td>6.764</td>
<td>0.009</td>
</tr>
<tr>
<td>Lobulated</td>
<td>15 (11.5%)</td>
<td>3 (2.7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boundary</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distinct</td>
<td>104 (80.0%)</td>
<td>106 (95.5%)</td>
<td>12.827</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Indistinct</td>
<td>26 (20.0%)</td>
<td>5 (4.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcification</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absence</td>
<td>105 (80.8%)</td>
<td>99 (89.2%)</td>
<td>3.266</td>
<td>0.076</td>
</tr>
<tr>
<td>Presence</td>
<td>25 (19.2%)</td>
<td>12 (10.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDFI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absence</td>
<td>73 (56.2%)</td>
<td>98 (88.3%)</td>
<td>30.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Presence</td>
<td>57 (43.8%)</td>
<td>13 (11.7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Special signs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absence</td>
<td>70 (53.8%)</td>
<td>54 (48.7%)</td>
<td>0.648</td>
<td>0.440</td>
</tr>
<tr>
<td>Presence</td>
<td>60 (46.2%)</td>
<td>57 (51.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypoechoic halo</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absence</td>
<td>109 (83.8%)</td>
<td>96 (86.5%)</td>
<td>0.329</td>
<td>0.592</td>
</tr>
<tr>
<td>Presence</td>
<td>21 (16.2%)</td>
<td>15 (13.5%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
ences in L/T, shape, and blood flow signals between the two groups (p<0.05).

**Comparison between ultrasound and pathological results**

In group A, 93 (71.5%) out of 130 cases were accurately diagnosed, whereas 37 (28.5%) cases, which had a different diagnosis for US examination and pathological results, were misdiagnosed. In comparison, 95 (85.6%) out of 111 cases in group B were accurately diagnosed, while 16 (14.4%) cases were misdiagnosed. Further analysis revealed a statistical difference in consistency between US diagnosis and pathological results for the two groups (p=0.012; Table III).

**Multivariate logistic regression analysis of epidermoid cysts with inflammation**

The significant variables in univariate analysis (skin color, L/T, shape, boundary, CDFI) were included as independent variables in the multivariate logistic regression model. The results showed that the model was statistically significant ($\chi^2=1.441$, p<0.001, $R^2=0.837$). Therefore, CDFI and indistinct boundaries in ECs with inflammation were more frequent than those in ECs without inflammation ($OR=5.89, 4.72$, p<0.05; Table IV).

**Discussion**

We established that the presence of inflammation in EC significantly influences the US diagnosis. The accuracy of US diagnosis in all patients was 78%, in the inflammatory group 71.5%, and in non-inflammatory group 85.6% (p<0.05). Hung et al reported that the sensitivity and specificity for US diagnosis of EC were 80% and 95.4%, respectively [8]. After considering all differential diagnoses, the accuracy of US in evaluating superficial soft tissue masses was reported to be 79% [9-11].

### Table III. Comparison between pathological and US results

<table>
<thead>
<tr>
<th>US results</th>
<th>Pathological results</th>
<th>Group B (n=111)</th>
<th>T/U/$\chi^2$</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>EC</td>
<td>92 (70.8%)</td>
<td>97 (87.4%)</td>
<td>23.627</td>
<td>0.014</td>
</tr>
<tr>
<td>Others</td>
<td>38 (29.2%)</td>
<td>14 (12.6%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcifying epithelioma</td>
<td>3 (2.3%)</td>
<td>1 (0.9%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Undiagnosed</td>
<td>5 (3.8%)</td>
<td>2 (1.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lipomyoma</td>
<td>5 (3.8%)</td>
<td>2 (1.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyst</td>
<td>2 (1.6%)</td>
<td>2 (1.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Giant cell tumor of tendon sheath</td>
<td>0 (0.0%)</td>
<td>1 (0.9%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inflammatory nodules</td>
<td>12 (9.2%)</td>
<td>2 (1.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thyrohyoid cyst</td>
<td>3 (2.3%)</td>
<td>2 (1.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abscess</td>
<td>6 (4.6%)</td>
<td>1 (0.9%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemangioma</td>
<td>2 (1.6%)</td>
<td>1 (0.9%)</td>
<td></td>
<td></td>
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</tbody>
</table>

### Table IV. Results of multivariate analysis of ECs

<table>
<thead>
<tr>
<th>OR (95%CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boundary</td>
<td></td>
</tr>
<tr>
<td>Distinct</td>
<td>1.00</td>
</tr>
<tr>
<td>Indistinct</td>
<td>4.72 (1.68-13.25)</td>
</tr>
<tr>
<td>CDFI</td>
<td></td>
</tr>
<tr>
<td>Absence</td>
<td>1.00</td>
</tr>
<tr>
<td>Presence</td>
<td>5.89 (3.00-11.55)</td>
</tr>
</tbody>
</table>

$\chi^2=1.441$, p<0.001, $R^2=0.837$

Our diagnostic accuracy for group A was lower than that reported by Hung et al [11] but multivariate analysis revealed that boundary and CDFI were features of EC with inflammation. ECs with inflammation were 5.89 and 4.72 times more likely to have blood flow signals and indistinct boundaries than those without inflammation, which improved the diagnostic accuracy.

Blood flow signals act as a double-edged sword in ECs with inflammation. Previous studies indicated that inflammation of EC caused by inner layer ruptures and the keratin scales could spread to the surrounding soft tissues [12,13] to lead to acute foreign body granuloma reaction [11-14]. Blood flow signals may be present around or inside the cysts with low blood flow [11,14]. However, in addition to ECs, blood flow signals may be present in other superficial tissue lesions, such as inflammatory nodules, abscesses, and hemangiomas [6,14,15]. If a lesion has an abundant flow signal but no characteristic appearance of EC on two-dimensional images, the nodule is more likely to be misdiagnosed. Notably, 12 (9.2%) cases in group A were diagnosed as inflammatory nodules, while 6 (4.6%) cases were diagnosed as abscesses. Moreover, 2 (1.6%) cases were misdiagnosed as hemangioma, and rich blood flow signals were observed in the lesions.

The boundary is an important factor for the diagnosis of ECs with inflammation. Although boundaries for
most ECs in our study were distinct, the number of ECs with indistinct boundaries in group A (26/130) was significantly higher relative to group B (5/111). Hoang et al suggested that infection of the cyst may lead to chronic infiltration of inflammatory cells outside the cyst wall [14]. Keratin scales can cause acute foreign body granuloma response resulting in unclear boundaries in ECs. Waralee et al found that the EC associated with infection is likely to have unclear boundaries, which hampers the diagnostic accuracy [16]. In our study, 3 cases were misdiagnosed due to unclear boundaries: two cases as abscesses and one as a branchial cleft cyst.

Although calcification is not a useful characteristic during the diagnosis of EC with inflammation, it may interfere with US diagnosis and this could be related to two reasons. First, inflammation is associated with calcification. Yi et al demonstrated that calcification inside lesions may be caused by calcium salt deposition or internal connective tissue hyperplasia, accompanied by calcification in the late stages of infection [17]. Second, US features of these lesions with calcification are all hypoechoic nodules associated with acoustic shadow and blood flows inside nodules, which can be misdiagnosed as calcified epithelioma [18,19]. In group A, 3 (2.3%) cases were misdiagnosed as calcified epithelioma. In group B 25 (19.2%) lesions with inflammation and 12 (10.8%) without inflammation showed calcification inside the nodules. Differences in internal calcification between the two groups were insignificant. However, the proportion of calcification in group A was slightly higher than in the control group. These inconsistent findings imply that the correlation between calcification and inflammation will need to be further studied.

Inflammation may cause changes in skin color. Park et al reported that the black spots on the skin surface are key characteristics of EC [5,20]. Hoang et al suggested that EC with inflammation can cause redness and swelling of the skin surface [14], which is consistent with our findings. In our analysis, 33 (25.4%) cases with inflammation in group A had red skin surfaces, while 6 (4.6%) cases had black spots on their skin, which were significantly higher than in group B. To date, only a few studies have explored the relationship between color abnormality and inflammation in EC [5,14,21]. Therefore, further clinical studies should be conducted to explore the relationship between skin color abnormality and inflammation in EC.

In the univariate analysis, there was a statistically significant difference in the L/T ratio between the two groups. If lesions had a greater L/T value, there was a possibility of inflammation. These findings imply that lesions with inflammation are more likely to extend to the surrounding tissues. Specific effects of inflammation on various diameters of the lesion have not been fully elucidated. Some studies have revealed that the aspect ratio of some malignant tumors is greater compared to that of benign tumors [22]. This is because malignant tumors infiltratively and aggressively grow and may thus break through the capsule [22]. Contrastingly, benign tumors are swellings that grow parallel to the skin because the dense surrounding capsule limit their growth in the direction perpendicular to the skin [22,23]. This may be explained by the fact that EC is a benign lesion with a similar growth pattern as a benign tumor. However, in this study, the growth rate of the lesion in the same layer is fast when accompanied by inflammation. Perpendicular growth to the skin is inhibited by the dense surrounding capsule, resulting in an increased L/T ratio.

This study has some limitations. First, it is a retrospective study. US information was reanalyzed; however, retention of nodule images depends on the experience level of the operator. Some important information may be inadvertently lost in the process of taking the pictures. Second, this was a single-center study with a small sample size. Third, internal components of the cyst may have been cleaned during surgery or pathology, and thus US characteristics may not be directly related to the distribution of substances inside the cyst.

In conclusion, in addition to typical characteristics of EC, US imaging of EC with inflammation exhibits unique features, such as blood flow signals, indistinct boundaries, calcifications, abnormal skin surface colors, and larger L/T ratios. Blood flow signals and indistinct boundaries may improve the diagnostic accuracy of US for EC with inflammation.

**Conflict of interest:** None.

**References**


