ABSTRACT

Background: Image-guided fine-needle aspiration cytology (FNAC) serves as first-line diagnostic modalities for the assessment of mural thickening of the gallbladder (GB).

Aim: The main objective of the present study was to correlate the diagnostic accuracy of preoperative image-guided FNAC of the thickened GB wall based on imaging findings to arrive at a final diagnosis in a tertiary care center.

Materials and Methods: Fifty-seven image-guided fine-needle aspirations (FNAs) were performed from mural thickening of the GB over a period of 4 years and the smears prepared were stained with Leishman and Papanicolaou (Pap) stain. Out of 57 cases, 51 were included in the study for which follow-up histopathology was performed.

Result: Out of 51 aspirations, 43 (84.3%) were adequate, 5 (9.8%) were inconclusive, and 3 (5.9%) were inadequate. Among the adequate aspirations, the most common was adenocarcinoma—36 (70.5%). The correlation between confirmatory cytological diagnosis and adequacy was significantly high (\( p = 0.0001 \)). The overall diagnostic accuracy for adequate aspiration was 95.3%. The common diagnostic pitfalls were necrotic areas, aspiration of reactive hepatocytes adjacent to the GB mass, and mucus islands. No procedural complication was observed in any patient.

Conclusions: Image-guided FNAC can be used as a safe, rapid, and successful diagnostic procedure with high sensitivity, specifically for supporting and confirming ultrasonography (USG)/computed tomography (CT) diagnosis of GB mass or mural thickening of the wall.

Key words: Carcinoma of the gallbladder (Ca GB); gallbladder (GB) mass; image-guided fine-needle aspiration cytology (FNAC); mural thickening

Introduction

Carcinoma of the gallbladder (Ca GB) is the most common malignancy of the biliary tract. It has high incidence in certain populations in the world.\(^1\) It is eight times more common in North India than in South India.\(^2\) It affects women 2-6 times more commonly than men and its incidence steadily increases with age.\(^3\) Rarely it is discovered at a dissectible stage and the mean 5-year survival is about 1% despite surgical intervention.\(^4\) A quick and cost effective fine-needle
aspiration cytology (FNAC) procedure of mass lesion of the gallbladder (GB) discovered by imaging techniques speeds up the diagnosis and thus, avoids the unresectable stage of tumor. In the present study, we have evaluated the accuracy of FNAC with imaging findings for GB mass.

**Materials and Methods**

In this prospective study of 57 image-guided fine-needle aspirations (FNAs) were performed from mural thickening of the GB in a tertiary care hospital over a period of 4 years. Out of 57 cases, 51 were included in the study for which follow-up histopathology was performed.

All 57 cases were advised ultrasonography (USG)/computed tomography (CT) scan of the hepatobiliary tract for their chronic complaints of upper abdominal pain, jaundice, dyspepsia, nausea, or vomiting. These cases were subjected to imaging and on discovery of mural thickening of the GB wall, FNAC was performed under image guidance.

After obtaining written consent, the patients were scanned to identify the lesion and access site. Once a suitable access was selected, the overlying skin was marked and sterilized. Percutaneous transhepatic aspiration was performed using 23-27G needle and 10 mL disposable syringe. Air-dried smears were stained with Leishman Geimsa and alcohol-fixed smears were stained with Papanicolaou (Pap) stain. Diagnostic criteria laid down by G. Kocjan et al.,[5] 2010 were utilized while analyzing smears. Multiple passes were made under radiological guidance to increase the adequacy rate of the sample. The presence of five or six groups of cells deemed to represent the lesion was considered as adequate for reporting.

**Statistical analysis**

The results are presented in percentages. The chi-square test was used to compare dichotomous/categorical variables. The sensitivity, specificity, and diagnostic accuracy of adequate aspiration were calculated. P value <0.05 was considered to be significant. All the analyses were carried out by using STATA 8.0 version (StataCorp LP, USA).

**Results**

A total of 51 cases were included in this study. Out of 51 cases, 38 (74.5%) were females and 13 (25.5%) males. The maximum number of cases (51.2%) was in the age group of 61-70 years. USG and CT revealed GB mass or mural thickening with or without hepatic and distant metastasis suggestive of Ca GB. The aspirations were categorized into three groups on the basis of adequacy as shown in Table 1:

- **Group I**: Adequate aspiration where definitive cytological diagnosis was offered.
- **Group II**: Inconclusive, due to insufficient number of epithelial cells or necrosis was predominant.
- **Group III**: Inadequate, due to predominance of mucus or hemorrhage and absence of epithelial cells.

Overall, 84.3% adequate aspirates including neoplastic (72.5%) and nonneoplastic (11.8%) were obtained. The probability of adequacy of aspirated samples was highly significant ($P = 0.0001$). The identification of neoplastic etiology was significantly high with $P = 0.0001$. The statistical distribution of nonneoplastic lesions is nonsignificant due to very small number of cases ($n = 6$).

Cytological diagnosis offered in adequate fine-needle (FN) aspirate is shown in Table 2. Adenocarcinoma contributed to the majority of neoplastic lesions — 36 of 51 cases (70.5%). It showed cells in clusters, disorganized sheets, small acini, and single pleomorphic cells. Marked nuclear enlargement, nuclear crowding, molding, irregular nuclear membranes, and high nuclear-cytoplasmic (N:C) ratio permit a definitive diagnosis of malignancy when there is adequate well-preserved material[5] [Figure 1]. Adenomatous lesion had papillary configuration with fibrovascular stalk lined by columnar epithelial cells without any of the abovementioned cytological features of adenocarcinoma.

**Table 1: Categories of aspiration**

| Category       | No. of aspirates | Percentage (%) | Statistics       |
|----------------|------------------|----------------|-----------------|
| Adequate       | 43               | 84.3           | Probability of adequacy |
| Inconclusive   | 5                | 9.8            | $P$ value*: 0.0001* |
| Inadequate     | 3                | 5.9            |                 |
| Total          | 51               | 100            |                 |

1Chi-square test, *Significant

**Table 2: Cytological diagnosis offered in adequate aspiration ($n = 43$)**

| Cytological diagnosis          | Number (%) | Histological confirmation |
|--------------------------------|------------|--------------------------|
| Nonneoplastic ($n = 06$)       |            |                          |
| Chronic cholecystitis          | 03 (6.9)   | 03                       |
| Xanthogranulomatous change     | 02 (4.7)   | 02                       |
| Adenoma                        | 01 (2.3)   | 01                       |
| Neoplastic ($n = 37$)          |            |                          |
| Mucinous adenocarcinoma        | 32 (74.5)  | 32                       |
| Poorly differentiated carcinoma| 02 (4.7)   | 02                       |
| Suspicious of malignancy       | 03 (6.9)   | 02                       |

(adenocarcinoma)
Xanthogranulomatous cholecystitis at times mimic well-differentiated adenocarcinoma but cytological features, which clinch the diagnosis include regular arrangement of epithelial cells in sheets and mixed inflammatory cell component with a large number of foamy histiocytes and surrounding capillary blood vessels.[6] Chronic cholecystitis demonstrate scant epithelial cells to sheets of tall columnar cells, nuclei oval and basal with fine nuclear chromatin and inconspicuous nucleoli in Pap stain, often described as “matchstick” cells in cytotology textbooks.[7]

The correlative study was conducted between cytological findings and histopathology [Table 3]. Thirty-six cases out of a total of 37 neoplastic cases diagnosed as malignant on cytology had a concordant histopathological diagnosis. The only case, which was reported as suspicious of malignancy, turned out to be xanthogranulomatous cholecystitis on histopathology. The study revealed an overall sensitivity and specificity of 94.7% and 98.6%, respectively, and diagnostic accuracy for adequate aspiration of 95.3%.

**Discussion**

FNAC, being a safe, superior to open biopsy, rapid, cost-effective, and nonsurgical intervention and a daycare investigation procedure, is gaining popularity as a diagnostic modality for GB mass lesions and intraabdominal lesions.[8] Diffuse mural thickening and single/multiple lesions detected by USG and CT scan are primary indications for FNAC.[9,10]

Precise radiological localization with novel techniques, multiple passes, and well-defined cytological criteria increases the sensitivity of the test to arrive at a definitive diagnosis. Krishnani et al.[11] have reported an adequacy rate of 62.7% from a single puncture. Repeat aspirations performed by experienced hands and better angle on imaging after initial report of inconclusive or inadequate aspiration increases the sensitivity of the test.[12] In the present study, repeat aspiration was performed in 11 cases to obtain adequate material. Four of these aspirations were repeated thrice, three aspirations were repeated four times, and single aspiration was repeated five times. The overall adequacy rate was 84.3 %. USG/CT-guided percutaneous FNA of mural thickening of the GBs is a safe procedure and no major complication was reported in any of the 57 cases, which is comparable with other studies.[13]

The overall diagnostic accuracy of preoperative USG-guided FNA of the GB lesion has been reported to be up to 97%,[11,14] In our study, the accuracy for adequate aspiration in relation to USG and CT findings was 95.3%, which is comparable with other studies. In a prospective study of cytopathological diagnosis of xanthogranulomatous cholecystitis of 31 cases by Krishnani et al.,[11] the overall possibility of missing carcinoma was 12.01%, whereas in our study two cases showed adenocarcinoma of the GB, which was inadequate or insufficient for reporting on cytology. However, sensitivity for the adequate aspirations was 100% in this study and no case was missed on cytology.

The diagnostic pitfalls of this study included necrotic material, hemorrhage, inadequate epithelial cells, and the predominance of mucus flakes. In two cases, reactive hepatocytes were of diagnostic dilemma but repeat aspirate with better precision and angle on imaging confirmed adenocarcinoma on cytology.

**Conclusions**

In the present study, we reported our experience of FNAC of mass lesion or mural thickening of GB wall as a diagnostic adjunct to medical imaging in the preoperative evaluation and management of patients. Cytological smears interpreted with clinicoinaging findings and reliable diagnostic criteria with repeated aspirations, whenever indicated, will increase the sensitivity and diagnostic accuracy of the test. Preoperative
USG-guided FNAC will offer a speedy diagnosis and urgency of treatment and thus, reduce the incidence of unresectable tumors.

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Conflicts of interest
There are no conflicts of interest.

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