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Original Research Article

Ultrasound guided fine needle aspiration cytology of gall bladder mass and mural thickening: a radio-pathological correlation

Geetanjali Barman[1], Kabita Bujarbaruah[1]*, Binoy Kumar Choudhury[1], Shiraj Ahmed[2], Jagannath Dev Sharma[2], Amal Chandra Kataki[3]

[1]Department of Radiology, [2]Department of Pathology, [3]Department of Gynecologic Oncology, Dr. B. Borooah Cancer Institute, Guwahati, Assam, India

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***Correspondence:**
Dr. Kabita Bujarbaruah,
E-mail: drkabitabb@gmail.com

ABSTRACT

Background: Carcinoma of the gall bladder (GB) is the commonest malignancy of the biliary tract. Ultrasound (US) guided Fine Needle Aspiration Cytology (FNAC) plays a major role in early detection of malignancy in a suspicious GB lesion. The aim of this study was to evaluate the safety and diagnostic accuracy of US guided FNAC in detection of GB malignancy, to find the association of gall stones with GB malignancy, to study the ultrasound pattern of GB malignant mass and demographic profile of the disease in North eastern India.
Methods: The study was conducted retrospectively in Dr. B. Borooah Cancer Institute, Guwahati from January 2016 to December 2017. A total number of 173 patients suspected to have GB malignancy were subjected to US guided FNAC.
Results: Total 161 patients were positive for malignancy with significant female majority. There were 124 female (77.02%) and 37 males (22.98%) in the range of 29 to 82 years. Male female ratio was 1:3.5. One was diagnosed as xanthogranulomatous cholecystitis and another was chronic cholecystitis. FNAC remained inconclusive in 2 patients. There was no major procedure related complication. Adenocarcinoma was the most common malignancy found in 146 patients (98.68%). Cholelithiasis was associated in 88.19% of malignant lesions.
Conclusions: US-guided FNAC is a safe, highly accurate and reliable procedure for early detection of GB malignancy.

Keywords: Cytology, Gallbladder, Malignancy, Mural thickening, North East India, Ultrasound

INTRODUCTION

Carcinoma of the GB is the most frequent neoplasm of the biliary tract.[1,2] Early symptoms of this disease are vague. Patient usually presents late when the disease is well established or reaches an inoperable state.[3] So it is a highly fatal cancer with high morbidity and mortality rate. While surgery may well be curative at early stages, both surgical and nonsurgical treatments remain largely unsuccessful in patients with more advanced disease. Clinical examination alone is not sufficient to make an accurate diagnosis in most of the cases.[4] US is an easily available, quick, cost effective and also reliable modality for examination of GB pathologies. However, at times it may fail to detect the GB mass because of the associated inflammatory changes that obscures the underlying malignancy.[5] US guided biopsy from any suspicious lesion of the GB helps in quick and early detection of malignancy and planning of treatment accordingly.[6]

According to epidemiology, GB cancer shows a notable difference in incidence by geography and ethnic background. It has 10 times more common incidence in North India than in South India.[1] Incidence of GB cancer shows an increasing trend in North eastern part of India. Dr. B. Borooah Cancer Institute Guwahati being the tertiary level cancer centre in this region it caters most of the patients from North eastern India. According to the Hospital based cancer registry of our Institute, in 2015-2016 and 2016-2017 GB carcinoma is the 2nd commonest malignancy in female (13.1%) and the 7th commonest malignancy in male (4.8%). Patients coming to our hospital with the suspicion of GB mass are subjected to US guided FNAC. So, a study was carried out in the department of radiology and imaging in collaboration with the department of pathology of this institute with the following aims and objectives:

- To discuss the technique, along with safety and accuracy of ultrasound guided FNAC of GB malignancy.
- Detection of malignancy in isolated mural thickening of GB without any separately demonstrable focal mass.
- Incidence of GB mass with coexisting cholelithiasis.
- US pattern of GB malignancy in North eastern part of India.
- Demographic profile of GB malignancy in North eastern part of India.

METHODS

It was a retrospective study conducted between January 2016 to December 2017. A total of 173 patients with the suspicion of GB malignancy referred to Radiology department for US guided FNAC were enrolled in the study. Before the FNAC was performed, the patients' coagulation parameters including platelet count, prothrombin time, INR (International Normalized Ratio**)** were investigated to exclude any underlying bleeding disorder so as to avoid the risk of significant intraprocedural hemorrhage. A diagnostic ultrasound was done in all cases to localize and characterize the mass and also to mark the suitable access site for FNAC. Ultrasound and US-guided FNAC were done in GE ultrasound machine (Logic E9) using 1-6 MHz convex transducer. FNAC was performed using 20/22 G spinal needle or Chiba needle depending on the depth of the mass. Either transhepatic or transperitoneal route was taken whichever was necessary to avoid injury to major vessels or vital structures. The skin over the site for FNAC was thoroughly scrubbed with spirit swab and cleaned with betadine solution so as to maintain proper asepsis. Using free hand technique, the needle was inserted into the abdomen at the appropriate site followed by constant monitoring of the needle tip under real time ultrasound guidance. Effort was taken to avoid the cystic/necrotic areas as much as possible. Once the needle tip hit the target area a 20 ml syringe was mounted on the needle. The needle was quickly moved back and forth for multiple times in different direction with continuous suction of the syringe until the sample was collected. After withdrawing of the needle, the aspirated material was smeared on pre-cleaned glass slides. The procedure was repeated if necessary, to increase the adequacy of the sample. Post procedure scan was performed to look for any immediate complication. The patient was then kept under observation for 1 hour. If there was no symptom of any complication, the patient was discharged with necessary instructions and information to contact the concerned doctor at any time if he or she becomes symptomatic.

Few smears were put in 90% ethanol in Koplin jars for wet fixation and subsequent staining by Papanicolaou method. Rest of the smears were air dried for staining with May-Grunwald-Giemsa (MGG) stain. For our study we have categorized the microscopic findings into:

- Diagnostic-Where malignancy was found.
- Non-diagnostic-Where suspicious and/or non-malignant finding was detected.

RESULTS

Out of 173 cases included in the study, 137 aspirates were diagnostic for malignancy in the initial biopsy and 36 aspirates were non-diagnostic. Cases with initially negative (non-diagnostic) aspirates were subjected to repeat FNAC once or several times out of which 24 showed malignancy. So, total number of cases positive for malignancy in this study was 161 (137 from initial FNAC and 24 from repeat FNAC).

Out of the remaining 12 repeat cases, 7 cases showed benign glandular cells with no atypia. One case was suspicious for malignancy. Two cases showed inconclusive reports even after multiple repeat FNAC. Rest 2 cases with advice of repeat FNAC were lost for follow up. On post cholecystectomy biopsy of the 7 cases with benign glandular cells with no atypia, 6 came out to be chronic cholecystitis and one adenocarcinoma. The remaining case that was suspicious for malignancy on cytology was confirmed as xanthogranulomatous cholecystitis on post cholecystectomy biopsy on the basis of multinucleated giant cells, foamy macrophages and mixed inflammatory cell infiltrate.

In this study adenocarcinoma was found to be the most common malignancy. Out of 161 cases positive for malignancy 146 were adenocarcinoma where smears showed clusters of atypical glandular cells with moderate to marked nuclear pleomorphism, vesicular nuclei, prominent nucleoli and moderate to abundant cytoplasm. 8 cases were diagnosed as squamous cell carcinoma where smear showed dispersed and few sheets of atypical squamous cells with variable amount of keratinisation. Next in order were poorly differentiated and adenosquamous carcinoma with 5 and 2 patients respectively. Smear from poorly differentiated carcinoma

showed dispersed sheets and occasional clusters of moderately pleomorphic cells with irregular, hyperchromatic to vesicular nuclei, inconspicuous nucleoli and scanty cytoplasm. No definite glandular or squamous cells seen. Adenosquamous carcinoma showed sheets and clusters of glandular cells (with vesicular nuclei, prominent nucleoli and moderate amount of cytoplasm) admixed with few discrete and occasional sheets of malignant squamous cells showing keratinisation.

Diagnostic ultrasound was performed in all cases prior to US guided FNAC. The different ultrasonographic pattern in favour of GB mass included in present study along with their incidence are shown in table below.

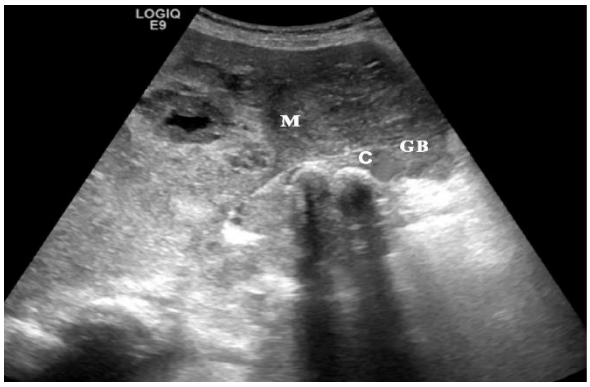

Figure 1: USG abdomen showing mixed echoic mass replacing the GB lumen with impacted calculi and hepatic infiltration (M-mass, C-calculi, GB-gall bladder).

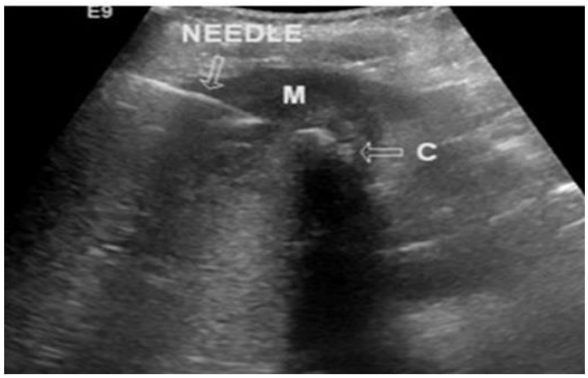

Figure 2: USG showing mass (M) replacing GB lumen associated with cholelithiasis (C) and FNAC needle in situ.

In this study, author have found that mass replacing the GB fossa (Figure 1 and 2) was the most common pattern (53.75 %), followed by focal or diffuse wall thickening (27.16 %) (Figure 1-6) and polypoidal intraluminal mass (19.07 %).

Other associated findings were infiltration of liver (Figure 1), hepatic metastases, involvement of surrounding organs and porta, abdominal lymphadenopathy, ascites and peritoneal deposits. Out of 48 cases with diffuse wall thickening 38 came out to be positive for malignancy on US guided FNAC.

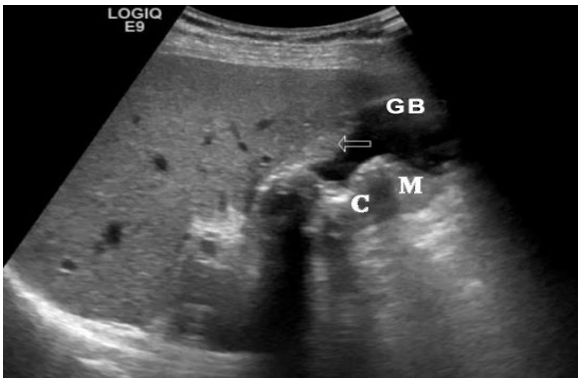

Figure 3: USG showing focal irregular thickening of GB wall and polypoidal growth involving body and neck region of the GB with associated cholelithiasis. (M-mass, C-calculus, GB-Gall bladder, Arrow-Focal irregular thickening of GB wall).

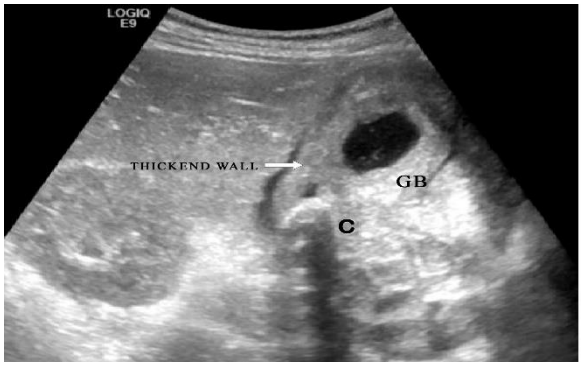

Figure 4: USG showing diffuse gallbladder wall thickening with cholelithiasis and pericholecystic fluid (GB-Gall bladder, C-calculus).

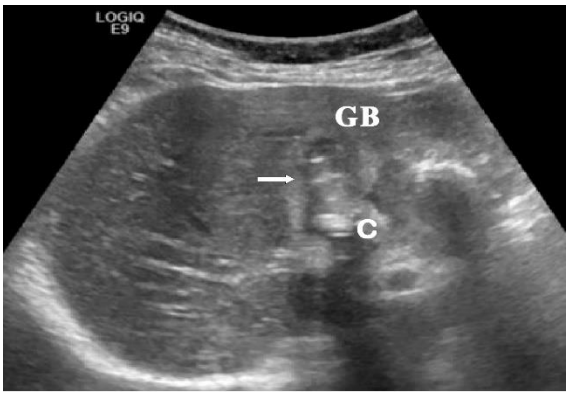

Figure 5: USG showing irregular mural thickening of the gallbladder associated with cholelithiasis and hepatic infiltration (GB-Gall bladder, C-calculus, Arrow-Irregular thickened GB wall with hepatic infiltration).

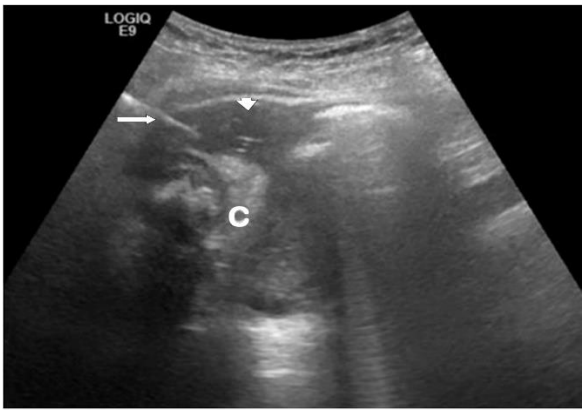

Figure 6: US guided FNAC in a 60 year old male patient with gall bladder wall thickening associated with calculus and needle in situ. (C-calculus, Arrow head- Thickened GB wall, Arrow-Needle tip in thickened GB wall).

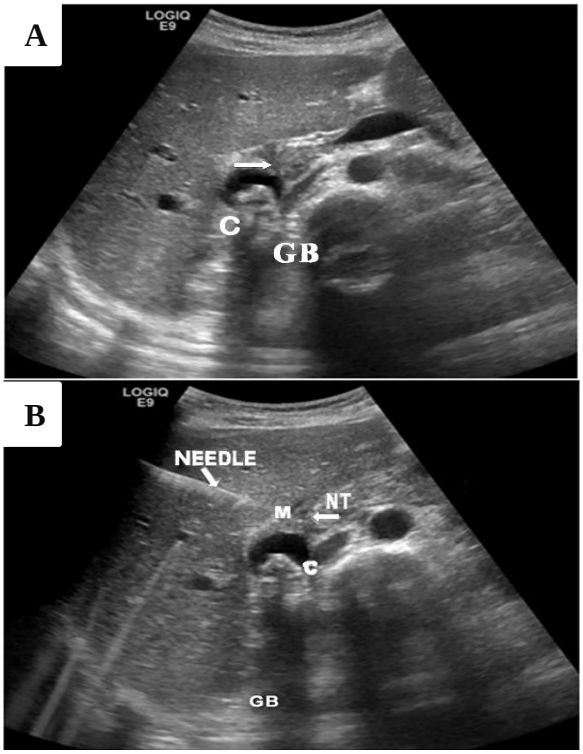

Figure 7: (A) USG showing Gallbladder wall thickening at fundus associated with cholelithiasis (GB-Gall bladder, Arrow-Thickened GB wall at fundus, C-calculus), (B) US guided FNAC from thickened GB wall at fundus (NT-Needle tip at thickened GB wall at fundus, C-Calculus).

Cholelithiasis was associated with 142 (8.19 %) cases out of total 161 cases positive for malignancy on FNAC (Figure 1-7). In our study we found 124 female and 37 males out of 161 malignant cases. Incidence of GB malignancy was 3.35 times more in female than in male population. The highest numbers of cases (106) were found in the age group of 4th to 6th decades (Table 1).

Table 1: Age and sex distribution of gall bladder malignancy.

Age group	Total (161)	Male patients (37)	Female patients (124)
<30 years	01	01	0
31-40 years	20	05	15
41-50 years	4	08	46
51-60 years	52	10	42
61-70 years	21	07	14
71-80 years	12	05	07
Above 80	01	01	0

DISCUSSION

US-guided FNAC allows real time monitoring of the needle tract and the needle tip. Biopsy from the solid part of the lesion can be taken avoiding the necrotic or cystic areas. It is an outdoor procedure and patient does not require hospital stay. It also precludes the need for surgery and hence no risk of general anesthesia and post-operative complications.

Out of 173 cases included at the beginning of our study, 137 cases were diagnostic for malignancy in the initial biopsy and 36 cases were non-diagnostic. Out of these 36 initials non-diagnostic aspirates 24 cases showed malignancy in subsequent FNAC/FNACs. Seven cases where no malignant cell was seen on initial cytology were subjected to cholecystectomy. Chronic cholecystitis was the histopathological diagnosis in 6 of them and adenocarcinoma in the remaining case. Another case reported as suspicious for malignancy on cytology was later on confirmed to be xanthogranulomatous cholecystitis following histopathology. All these 8 cases showed diffuse wall thickening on ultrasound. There was one false negative case in our study where cytology report showed no malignant cell, but histopathology confirmed malignancy. This discordance of FNAC and histology reports may be due to sampling from inappropriate area like fibrosed, inflamed areas. Inflammatory changes can simulate or mask the signs of malignancy.[5] We also had one false positive case in our study where cytology report was in favour of malignancy but histopathologically came out to be xanthogranulomatous cholecystitis. Xanthogranulomatous cholecystitis is a chronic inflammatory disease of the GB associated with inflammatory polyps and may cause thickening of the GB wall creating confusion with neoplastic process.[7] The single case of xanthogranulomatous cholecystitis in our study presented with diffuse wall thickening and infiltration of the surrounding liver parenchyma. Xanthogranulomatous cholecystitis at times mimic well differentiatiated adenocarcinoma but cytological features which clinch the diagnosis include regular arrangement of epithelial sheets and mixed inflammatory cell component with a large number of foamy histiocytes and surrounding capillary blood vessels.[2] Pleomorphism in

reactive histiocytes can occasionally raise the suspicion of malignancy.[8] Two cases were persistently inconclusive even after repeated FNAC and showed hemorrhage and scanty material.

Ultrasound done prior to FNAC revealed diffuse mural thickening in all 8 cases undergoing cholecystectomy as well as in the 2 cases showing repeatedly inconclusive cytological report.

Author found in this study that out of the total number of 48 cases with isolated mural thickening, 38 were diagnosed to be malignant, six showed chronic cholecystitis, one case showed false negative, one patient showed false positive result on cytology. Rest 2 cases with mural thickening remained inconclusive.

Single FNAC may not yield a conclusive diagnosis in all cases. In our study malignancy was diagnosed in 80.1% of cases in initial biopsy. (137 out of 171, excluding the 2 cases lost for follow up). By performing repeat FNAC, malignancy could be confirmed in 94.1% of cases (161 out of 171). Barbhuiya M et al, reported that the chance that a single puncture would procure a representative sample is 72.3%.[9]

Overall sensitivity of US guided FNAC in this study is 99.38%. Author found specificity of 85.71%, accuracy 98.81%, false negative rate of 0.61%. Singh et al, reported a sensitivity of 93.5% in FNAC of GB masses.[4] In another study by Kumar et al, in 2015, revealed an overall sensitivity and specificity of 94.7% and 98.6% respectively and diagnostic accuracy of 95.3% in GB malignancy.[2] Yadav et al, in 2013 found a sensitivity of 96.8%.[6] The findings are comparable to other studies. Literature have shown that the incidence of false negative results varies by 11% to 41%.[6,10] The study had a very low false negative rate which may be attributed to repeat FNAC in cases where initial result of FNAC was negative. While doing repeat FNAC another site different from the previous one was selected with alteration of angle.

Some of the reported complications of GB FNAC are hemorrhage, vasovagal syncope, hypotension, biliary peritonitis, bacterial infection and hemobilia.[6] In our study no such major complication was observed except for mild abdominal pain for which analgesic tablets were prescribed.

In this series, authors found adenocarcinoma to be the most common malignancy (90.6%). The observation was in accordance with studies of Yadav et al, in 2013 where they found 86.7% to be adenocarcinoma.[6] Venkataramu et al in 2010 found 89.7 %, and Kumar et al 2017 found 96% of adenocarcinoma in their study of GB masses.[3,11]

Cholelithiasis is a common association of GB malignancy. Gall stone causes chronic irritation of the GB wall which leads to production of secondary bile acids. This triggers epithelial metaplasia, subsequent dysplasia, carcinoma in situ and finally invasive carcinoma.[12] We have found that 88.19% of our patients had coexisting gall stones. Multiple moderate to large size calculi were seen impacted within the mass or within a contracted GB with diffusely thickened wall. The results are comparable to studies conducted by Iqbal et al in 2008 where they found 90% associated cholelithisis with GB malignancy.[13]

Author also studied the demography and the age distribution of GB malignancy in this study. The youngest patient was 29 years old and the oldest was 82 years old. Both of them were male. Majority of the patients were in the age group of 41 to 60 years. Our findings are comparable to the study conducted by Tandon et al, 2017.[14] They found the disease to be most common in 5th and 6th decades of life.

The disease shows a female predominance. Author also observed that 37 (22.98%) patients were male and 124 (77%) were female with a male to female ratio of 1:3.5. Similar results have been documented in the series conducted by Handa et al, in 2010 which showed the male to female ratio was 1:3.4.[15] Das et al, in 1997 reported a male female ratio of 1:3.8.[5] Hence, the findings are comparable to previous studies.

CONCLUSION

Ultrasound guided FNAC is a safe, non-surgical, quick and accurate modality in diagnosing GB malignancy. One diagnostic pitfall of this procedure that is of concern is false negative results. However, this can be significantly reduced by taking repeat aspirations. Since there a rising incidence of GB malignancy in North eastern India and majority of patients present in late stage of the disease, US guided FNAC can be used as safe and effective tool for early detection of malignancy so as to achieve a satisfactory outcome.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Bhartiya R, Mallick S, Mallik M, Agrawal P, Singh R, Singh RV. Ultrasound-guided fine needle aspiration cytology diagnosis of gall bladder lesions with application of WHO histological classification of tumors on cytoaspirate material. Ann Trop Med Pub Heal. 2017;10:138-42.
2. Kumar N, Singhal P, Agarwal A, Khan MA. Cytopathological diagnosis of gallbladder mass and mural thickening based on imaging findings: A prospective study of 51 cases. J Cytol. 2015;32:234-7.

3. Venkataramu NK, Sood BP, Gupta S, Gulati M, Khandelwal N, Suri S. Ultrasound-guided fine needle aspiration biopsy of gall bladder malignancy. Acta Radiol. 1999;40:4:436-9.
4. Singh P, Jaiswal VK, Singh G. Diagnostic accuracy of usg-guided FNAC in gall bladder mass. Rec Adv Path Lab Med. 2017;3:1-3.
5. Das DK, Tripathi RP, Bhambhani S, Chachra KL, Sodhani P, Malhotra V. Ultrasound guided fine needle aspiration cytology diagnosis of gall bladder lesions: a study of 82 cases. Diag Cytopathol. 1998;18:258-64.
6. Yadav R, Jain D, Mathur SR, Sharma A, Iyer VK. Gall bladder Carcinoma: An attempt of WHO histological classification of fine needle aspiration material. Cytol J. 2013;10:12.
7. Rammohan A, Cherukuri SD, Sathyanesan J, Palaniappan R, Govindan M. Xanthogranulomatous cholecystitis masquerading as gallbladder cancer: can it be diagnosed preoperatively? Gasteroenterol Res Pract. 2014:253645
8. Shukla S, Krishnani N, Jain M, Pandey R, Gupta RK. Xanthogranulomatous Cholecystitis. Fine needle aspiration cytology in 17 cases. Acta Cytol. 1997;41:413-8.
9. Barbhuiya M, Bhunia S, Kakkar M, Shrivastava B, Tiwari PK, Gupta S. Fine needle aspiration cytology of lesions of liver and gall bladder: An analysis of 400 consecutive aspirations. J Cytol. 2014;31:20-4.
10. Shukla VK, Pandey M, Kumar M, Sood BP, Gupta A, Aryya NC, et al. Ultrasound-guided fine needle aspiration cytology of malignant gallbladder masses. Acta Cytol. 1997;41:1654-8.
11. Kumar R, Srinivasan R, Gupta N, Dey P, Rajwanshi A, Nijhawan R, et al. Spectrum of gallbladder malignancies on fine-needle aspiration cytology: 5 years retrospective single institutional study with emphasis on uncommon variants Diag Cytopathol. 2017;45:36-42.
12. Gupta P, Agarwal A, Gupta V, Singh PK, Pantola C, Amit S. Expression and clinicopathological significance of estrogen and progesterone receptors in gallbladder cancer. Gastrointest Cancer Res. 2012;5:41-7.
13. Iqbal M, Gondal KM, Qureshi AU, Tayyab M. Comparative study of ultrasound guided fine needle aspiration cytology with open/laparoscopic biopsy for diagnosis of carcinoma gallbladder. J Coll Physicians Surg Pak. 2009;19:17-20.
14. Tandan P, Gautam W. Fine needle aspiration cytology in lesions of gall bladder-experience in a primary care setting. Int J Trop Disease Heal. 2017;21:1-7.
15. Handa U, Nanda A, Mohan H, Kochhar S, Sachdev A. Cytological diagnosis of gallbladder lesions-A study of 150 cases. Ind J Surg. 2010;72:181-4.

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