Role of ultrasound guided biopsy (Fine needle aspiration cytology and core needle biopsy) in the diagnosis of advanced ovarian cancer, Khartoum-Sudan

Azza A Zulfu, MD*, Abdalla M Abdalla, MD**, Amar H Hussain, MSc***, Durria Rayis, MD****, Khalid YM Ahmed, MD MRCOG*****; Amir Elnahas, MD MRCOG******, Moawia E Hummeida, MD*******

Histopathology & Cytology Department*, Radiology Department**, Department of Obstetrics and Gynecology, Faculty of Medicine, University of Al-Neelain, Khartoum-Sudan

Abstract

Background
Ultrasound guided biopsy: fine needle aspiration cytology and core needle biopsy is being used increasingly in the diagnosis of advanced ovarian cancer. The aim of this study is to evaluate the efficiency and safety of ultra-sound guided biopsy in the diagnosis of advanced ovarian cancer.

Patients & Methods
The study was conducted on 51 female patients diagnosed as having advanced ovarian cancer based on clinical and imaging techniques: ultrasonography, computed tomography scan and magnetic resonance imaging. Both fine needle aspiration cytology and core needle biopsy were performed under ultrasound guidance.

Results
Fine needle aspiration was possible on the 51 patients, yielded 138 diagnostic aspirates, diagnostic accuracy was 89.7%, and diagnosis as malignant was made on 43 patients. Core needle biopsy was possible on 16 patients, eight patients gave diagnostic yield, eight patients gave non-diagnostic results, and diagnostic accuracy was 50%.

Conclusion
Ultrasound guided biopsy is efficient and safe in diagnosing advanced ovarian cancer, fine needle aspiration is superior to core needle biopsy.

Keywords: Ovarian cancer, ultrasound guided biopsy, fine needle aspiration cytology, core needle biopsy...
Introduction
Ovarian cancer is the 3rd common cancer and 3rd cause of cancer death in females worldwide and in Sudan; next only to breast cancer and cervical carcinoma\(^1\)\(^2\). Data from central Sudan showed that ovarian cancer is the commonest gynaecological malignancy, with malignant surface epithelial tumors being the commonest histological subtype (82.2%), followed by cervical cancer\(^3\). Most patients of ovarian cancer present with advanced disease\(^4\). Malignant surface epithelial tumors represent about 90% of ovarian cancers in the Western world\(^4\).

Histopathology of surgical specimens is the definitive diagnosis in ovarian cancer and other malignancies. Surgery in advanced cancer either for diagnosis (as an incisional biopsy) or excisional (debulking or cytoreductive) is associated with poor outcome. Initial neoadjuvant chemotherapy followed by interval cytoreduction may reduce the bulk of the disease in patients with advanced ovarian cancer, improving surgical operability and surgical outcome\(^5\). Image guided biopsy was studied and accepted as an alternative method for diagnosis\(^6\)\(^9\). There have been few publications on the use of image guided biopsy in the diagnosis of advanced ovarian cancer\(^5\). To the best of our knowledge; this is the first study on this topic in Sudan.

The aims of this study was to assess the efficiency of ultrasound guided biopsy: fine needle aspiration cytology (FNAC) and core needle biopsy (CNB) in the diagnosis of advanced ovarian cancer, to assess the safety of the procedure and to compare the efficiency and safety of FNAC to CNB.

Patients & Methods
This is a prospective study conducted on 51 female patients, during the period from January 2012 to August 2013 at Khartoum Teaching Hospital, which is the major tertiary and referral hospital in Sudan, located in Khartoum city, the capital of the country. Obstetrics & Gynaecology department was a major referral department at the time of the study. Radiology, laboratory & research unit, histopathology and cytology were active departments. Patients with ovarian cancer were seen within a context of an interdisciplinary clinic. Research ethics approval was obtained from the ethical committee at the Research department. Verbal informed consent was taken from all patients who agreed to participate in the study. Patients diagnosed as suspicious of having advanced ovarian cancer based on clinical and radiological evaluation were seen. Patients who agreed to participate in the study, and who were evaluated by gynaecological surgeons as inoperable were included in the study.

Ultrasound (U/S) and subsequent biopsy were performed in the U/S department using a Toshiba Apio machine (Toshiba Medical system). Colour Doppler U/S images were obtained to assess tumor vascularity and avoid major vessels.

Patient’s verbal informed consent was obtained prior to the biopsy. Biopsy sites were localized under ultrasound guidance. Biopsies were taken by a cytopathologist, histopathologist and radiologist with good experience in interventional radiology. Patients were planned to undergo both FNAC & CNB. Patients with abnormal bleeding profile (platelets count <40x10\(^9\)/L, INR of more than 1.5) were excluded from CNB biopsy but included in FNAC. The volume and site of intra-abdominal disease were first assessed on a staging computed tomography (CT) scan. All patients with gross ascitis underwent drainage prior to the procedure. The procedure was taken under possible aseptic conditions. For both biopsy modalities; direct visualization of the biopsy needle within the pathological tissue was confirmed before biopsy. FNAC was performed using a 20 gauge needle attached to a 20 ml syringe. For deep seated lesions, a
lumbar puncture needle size 20 was used. Tru-cut needle biopsy under local anaesthesia was performed when possible by size 18-20 core needle. Glass smears prepared from aspirates were stained with both May-Grunwald-Gimsa (MGG) and Papanicolaou (Pap) stains. Cell blocks and core biopsies were processed, sectioned and stained by haematoxylin and eosin (H&E) stain. Aspirate from ascitic and pleural fluids were H&E stain. Aspirate from ascitic and pleural fluids were done, peritoneal and liver deposits were biopsied. Surgical specimens were submitted for histopathology examination. Massive ascitis, abnormal bleeding profile, extensive tumor necrosis and poor patient tolerance were the major difficulties encountered.

Patients monitored for 2 hours after biopsy, no significant complications were observed. All biopsy materials were obtained; cytology smears, cell blocks, core biopsy and surgical specimens were examined and reported by two cytohistopathologists.

**Results**

Fifty-one patients were studied; the age range was from 4-85 years old. The main clinical presentations were abdominal swelling and pain. U/S showed solid cystic or complex pelviabdominal masses. Figure 1 shows aspiration needle within a complex ovarian mass, and Figure 2 shows needle within a solid mass. Omental, peritoneal and liver deposits were also seen.

Fine needle aspiration cytology under guidance was possible on all 51 patients (100%) yielding 145 aspirate sample (Table 1), cytological diagnosis as malignant was consistent in 130 samples belonging to 43 (84%) patients (Figs 3 & 4), and diagnostic accuracy for FNAC was 89.7%. Cell blocks were prepared from 18 FNAC samples (Fig 6). 15 FNAC aspirate belonging to 8 patients gave inconclusive/non-diagnostic results.

CNB (Fig 5) was possible on16 out of 51 patients (31%), histological diagnosis as malignant was consistent in 8 (50%) patients, and the remaining 8 patients gave inconclusive/non-diagnostic results. Diagnostic accuracy was 89.7% for FNAC compared to 50% for CNB. When both FNAC & CNB were combined in the same patient diagnostic accuracy was 85.7% (Table 2).
Table 1: Details of FNA samples & results:

<table>
<thead>
<tr>
<th>Site of FNA</th>
<th>Diagnostic sample</th>
<th>Non-diagnostic sample</th>
<th>Total</th>
<th>Diagnostic accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenexal mass</td>
<td>43</td>
<td>8</td>
<td>51</td>
<td>83%</td>
</tr>
<tr>
<td>Omental/peritoneal deposits</td>
<td>23</td>
<td>2</td>
<td>25</td>
<td>92%</td>
</tr>
<tr>
<td>Ascitic fluid</td>
<td>43</td>
<td>0</td>
<td>43</td>
<td>100%</td>
</tr>
<tr>
<td>Pleural fluid</td>
<td>3</td>
<td>2</td>
<td>5</td>
<td>60%</td>
</tr>
<tr>
<td>Liver deposits</td>
<td>3</td>
<td>0</td>
<td>3</td>
<td>100%</td>
</tr>
<tr>
<td>Cell block</td>
<td>15</td>
<td>3</td>
<td>18</td>
<td>83%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>130</strong></td>
<td><strong>15</strong></td>
<td><strong>145</strong></td>
<td><strong>89.7%</strong></td>
</tr>
</tbody>
</table>

Fig 2: FNAC smear stained with MGG, consistent with papillary serous carcinoma

Fig 3: FNAC smears stained with Pap from the same patient in Fig 3 (papillary carcinoma)

Fig 4: Cell block featuring tumor nests within loose inflamed stroma

Fig 5: CNB papillary serous carcinoma

Table 2: Combined results of FNA & CNB

<table>
<thead>
<tr>
<th></th>
<th>Diagnostic sample</th>
<th>Non-diagnostic sample</th>
<th>Total</th>
<th>Diagnostic accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNB (all were adenexal masses)</td>
<td>8</td>
<td>8</td>
<td>16</td>
<td>50%</td>
</tr>
<tr>
<td>FNA</td>
<td>130</td>
<td>15</td>
<td>145</td>
<td>89.7%</td>
</tr>
<tr>
<td>FNA+CNB</td>
<td>138</td>
<td>23</td>
<td>161</td>
<td>85.7%</td>
</tr>
</tbody>
</table>
Surgical specimens were available in 21 cases, eight of them belong to patients who gave inconclusive/non-diagnostic FNA results, thirteen surgical specimens belong to patients diagnosed as malignant by FNA after receiving neoadjuvant chemotherapy. Thirteen surgical specimens gave histological diagnosis concordant to cytological diagnosis.

The histological diagnoses of surgical specimens were as follows: 11 cases of papillary serous carcinoma, 2 cases of dysgerminoma, 3 cases of metastatic carcinoma (Fig 7) and 5 cases of poorly differentiated carcinomas (Fig 8).

Discussion
Ultrasound guidance was very helpful in assessing the nature of lesions (solid, cystic or complex). Doppler facility helped in identifying and avoiding blood vessels and differentiating cellular from necrotic areas. FNAC was possible in all patients. FNAC had the following advantages: it was easy, simple, enables multiple passes within the pathological tissue, less hazardous, can be performed in patients with abnormal coagulation profile, can be done in patients with ascitis, no need for local anaesthesia, cheap, possible on both solid and cystic areas, negative pressure enables good cellular yields and the possibility of preparing cell blocks. FNAC has the disadvantage of providing little tissue for immunohistochemistry and molecular studies. The cell block preparation was utilized yielding 18 samples with accurate diagnosis on 15 (85%) samples. Core needle biopsy was possible on 16 out of the 51 patients (mainly due to abnormal bleeding profile and massive ascitis). Diagnosis was possible on 8 patients, compared to FNAC, CNB had the advantage of providing enough tissue for immunohistochemistry and molecular studies. Disadvantages of CNB include: the need for local anaesthesia, the prerequisite for normal coagulation profile and solid areas within the pathological tissue, the limited number of needle passes within lesions, technically more difficult than FNAC, CNB requires more skill, more hazardous, the tru-cut needle is expensive and manufacturer dependent.

Other researchers studied the value of image guided biopsy in diagnosing ovarian masses: Mehdi et al evaluated both benign and malignant lesions using FNAC with an overall accuracy of 80.9% (6), with higher accuracy in malignant tumors 88.2% (6). Khan et al
achieved diagnostic accuracy with FNAC of 89%\(^7\). Moran et al 96%\(^8\). The diagnostic accuracy of FNAC in this study was 89.7%, it is within keeping with other similar studies. Stewart et al compared the accuracy of FNA to CNB in diagnosing radiologically detected abdominal lesions, FNAC identified 86% of the lesions compared to 80% for CNB. When both FNAC and CNB were combined in the same patient the sensitivity increases to 90%, Stewart et al. concluded that FNAC is more sensitive and accurate than CNB\(^{14}\). Naguib et al studied the accuracy of combined tru-cut and FNAC in pre-operative sampling of ovarian tumors reporting diagnostic accuracy of 95% for FNAC and 95.7% for CNB, when both modalities were combined accuracy was 95.5%\(^{15}\), despite these results were higher than ours, these findings were consistent with the results of this study\(^{16}\) Spencer et al. in their review, reviewed a number of large studies on image guided core biopsy of the omentum and peritoneum, they concluded that this modality is safe and efficient, special concern was focused on women suspected to have advanced peritoneal carcinomatosis from ovarian or primary peritoneal cancer, the initial management of many of these women is primary chemotherapy. With current clinical trials for ovarian cancer directed to specific morphologic subtypes of the disease, image guided core biopsy offers a rapid and well tolerated non-surgical means of providing this information\(^{16}\).

There are some limitations in this study: most patients presented with extensive ascitis and abnormal coagulation profile, so were unfit for CNB. Extensive tumor necrosis seen during U/S and poor patient compliance limited the diagnostic yield for FNA; so these factors may have contributed to lowering diagnostic accuracy in this study. Patients were supposed to receive neoadjuvant chemotherapy and surgical specimens following debulking were supposed to be sent to our laboratory, but from the 51 patients studied, only 21 came back with surgical specimens.

In conclusion, ultrasound guided biopsy is efficient and safe in diagnosing advanced ovarian cancer. FNAC is superior to CNB. Clinical examination, pelvic imaging and U/S guided biopsy are complementary and none of the methods is diagnostic by itself. Patients can confidently receive neoadjuvant chemotherapy based on the cytological and or histological diagnosis of U/S guided biopsy. A multidisciplinary team is essential for the management of advanced ovarian cancer.

References
1. Hamad HMA. Cancer initiatives in Sudan: annals of Oncol 2006;17( suppl 8):viii32-36