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Review Article

FINE NEEDLE ASPIRATION CYTOLOGY OF THE BREAST, COMPONENT OF A TRIPLE TEST: A REVIEW.

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Abstract:

Background: Fine needle aspiration cytology (FNAC) is a type of interventional cytology. It is a clinicopathological procedure involving the collection of cells from a lesion using a fine needle and syringe. The breast/mammary gland is one of the commonest organs in the body which may develop lesions/lumps requiring fine needle aspiration cytology. This test is ideally done as part of a triple test following clinical examination and imaging studies. Therefore the approach in fine needle aspiration cytology is multidisciplinary. This procedure has a high sensitivity and specificity in addition to several other advantages including the good turn round time, minimal side effect and cost of the procedure when compared to histology. It has proven to be a really effective method in the diagnosis of breast cancer when used as part of the triple test. The result is more accurate when it is done by an experienced cytopathologist. The complications from this procedure are rare and include infection, hematoma, pneumothorax and dissemination of the tumor.

Aim/Objective: To do a literature review on fine needle aspiration cytology as part of a triple test

Conclusion: Fine needle aspiration cytology has been an effective tool for screening for breast cancer for many years and it is very accurate when combined with clinical finding and imaging.

Keywords: Fine needle, aspiration, cytology, triples test, breast, and cytopathologist.

Background

Fine needle aspiration cytology (FNAC) is a type of interventional cytology. It is a Clinicopathological procedure involving the collection of cells from a lesion using a fine needle and syringe. Fine needle aspiration cytology (FNAC) of the breast is a rapid, relatively non-traumatic, safe, accurate method for the diagnosis of breast disease with a good turnaround time and may not require anesthesia.[(1)(2)] It has been used for the diagnosis of breast lesions over the years.[(3)(4)] FNAC biopsy is not a substitute for conventional surgical histopathology. Instead, it should be regarded as being complementary to it.[(5)] Best practice requires

that fine needle aspiration cytology is always interpreted in correlation with clinical and imaging findings, thus forming part of a triple test. It should be done for a patient after a thorough clinical and radiological imaging investigations have been done for both breast.[6] Van Rijk et al[7] and MacNeill et al[8] in their studies showed a significantly better outcome of the result when radiologic findings are combined with clinical examination and FNAC compared with when clinical examination and FNAC is used alone.[7][8] Also, Patel et al in their study showed that unsatisfactory aspiration cytology rate was significantly reduced by ultrasound localization of breast lesions.[9] The factors that determine the outcome of a FNAC include, the site and type of lesion, the experience of the aspirator, the quality of the specimen preparation and the diagnostic skills of the cytopathologist.[5][10] The accuracy of fine needle aspiration cytology is best when the same person examines the breast, collects the sample, stains and interprets the slide.[10]

Fine needle aspiration cytology of the breast is indicated for breast lesions/tumors to screen for breast malignancies.

Anatomy of the human breast

The breast rests on a bed that extends transversely from the lateral border of the sternum to the midaxillary line and vertically from the 2nd through 6th ribs. Two-thirds of the bed of the breast is formed by the pectoral fascia overlying the pectoralis major; the other third, by the fascia covering the serratus anterior. The breast consists of glandular tissue and fibrous and adipose tissue between the lobes and lobules of glandular tissue, together with blood vessels, lymphatic vessels, and nerves.[11] The histology of the breast varies according to gender, age, menopausal status, the phase of the menstrual cycle, pregnancy, and lactation, among other factors. Thus, whether a given breast specimen is normal or shows pathologic alterations must take these variables into consideration. The adult female breast consists of a series of ducts, ductules, and lobular acinar units embedded within a stroma that is composed of varying amounts of fibrous and adipose tissue in contrast to the epithelial elements of the male breast which consist of branching ducts without lobule formation.[12] Most lymph (> 75%) from the breast, especially from the lateral quadrants, drains to the axillary lymph nodes, initially to the anterior nodes and some lymph may drain directly to other axillary nodes or even to interpectoral, deltopectoral, supraclavicular, or inferior deep cervical nodes.[11][12]

The disadvantages of FNA cytology

It requires training in the preparation of quality smears, considerable cytology expertise is required to interpret FNAC. It is inappropriate for assessment of microcalcifications in the breast. FNAC does not enable the pathologist to distinguish ductal carcinoma in situ from invasive ductal carcinoma. There is difficulty in making diagnosis with FNAC in some lesions such as sclerotic fibroadenomas, infiltrating lobular carcinoma and sclerosing ductal carcinoma which is relatively hypocellular and yields scanty epithelial material.[6]

Patient Preparation/communication

Effective communication with a woman undergoing FNAC is extremely important. Information should be provided to the patient about the nature of the procedure and its interpretation, benefits, limitations, complications, and implications, in a reassuring and appropriate manner that is understandable to the patient. She should be informed on how and when she will be given the results, which should be provided in a timely fashion.[13][14]

FNAC and Clinical or Imaging guidance:

The pathologist should make up his mind on what guidance method he is to use. Clinical guidance for palpable lesions, ultrasound and stereotactic mammographic guidance

for any lesions that can be visualized by the imaging technique.

Concerning lesions that are easy to palpate, clinical guidance is the method of choice. For lesions that are difficult to palpate or when the breast has a prosthesis, imaging guidance should be used to ensure adequate sampling. Imaging guidance may also be preferred for palpable lesions, as it can reduce sampling errors and avoid complications. Some lesions are only visible on either mammography or ultrasound. If a lesion is visible on both mammography and ultrasound, ultrasound guidance is preferred to stereotactic mammographic guidance, as it is more convenient and faster.

The Procedure

FNAC of the breast is usually done transcutaneously with or without anesthesia. The patient is asked to lie down to best expose the area where the lesion is. The firmest portion of the lesion is located by palpation. The overlying skin is swabbed alcohol pad and the lesion is held steadily by the operators palpating hand. The needle is inserted to reach the lesion then the plunger of the syringe is pulled to create at least 2ml suction. The needle is moved back and forth with a change in angle and direction when necessary. This continues until blood is visible at the hub of the needle than the suction pressure relieved before removing the needle. Pressure is applied to the site of puncture for 2-3minutes.(15)

Following fine needle aspiration, detach the needle and syringe, draw air into the syringe and reconnect the needle and syringe. Express aspirate into the labeled glass slides place one slide face down on the other side and let the specimen slowly spread out between the two sides. Separate the two slides quickly like you are opening a book. Immediately following this, half the number of smears is immersed in 95% ethanol and transported to the laboratory in the fixative. The remaining smears are air – dried. Then dispose of the needle in an appropriate sharp disposal container.(16)(15)

Staining smears

The smears that are wet fixed could be stained using a Pap stain or modified hematoxylin and eosin stain which involves the use of Harri's hematoxylin nuclear stain and eosin, a cytoplasmic counterstain. The air- dried slide is stained with Romanowsky stains such May Grunwald Giemsa stain or Leishman's stain.(13)

Special/ancillary studies that can be done in FNA cytology to improve the accuracy of the diagnosis. They include:

- Immunocytochemical studies- This can be done for smears or cell blocks involves the use of immunocytochemical stain requiring the use of antibodies selected based on the differential diagnosis made from routine examination of the morphology of the smear. Immunocytochemistry for estrogen and progesterone receptor are commonly done.(13)
- Flow cytometry – This can be done to determine the ploidy status and S phase fraction of the tumor cells.(17)
- Electron microscopy- Transmission and scanning electron microscopy could be done for FNAC samples.
- Image analysis and morphometry – This technique is employed to determine parameters in the cellular morphology. They include nuclei to cytoplasm ratio, shape/size of nuclei and nucleoli and nuclear area.
- Molecular biologic technique – This includes Fluorescence in situ hybridization, DNA sequence analysis, and gene expression profile.(18)
- Microbiological studies – Aspirates could be submitted for viral, bacterial, mycobacterial and fungal culture when infection is suspected.
- Special stain – This could be done to aid the cytopathologist in making a diagnosis depending on the smear morphology. (13)

Interpreting the cytological smear requires a trained pathologist or cytopathologist. The more experienced the cytopathologist the better the accuracy of the report.[10] the interpretation could be done using the 5-tier system which includes: C1 (inadequate), C2 (benign), C3 (suspicious, probably benign), C4(suspicious, probably malignant) and C5 (malignant). A preliminary diagnosis can be available within one hour of the FNAC procedure. The report would include cellularity of smear, cell arrangement, nuclear and cytoplasmic features. This also includes comment on the background morphology.[19]

Limitations of FNAC

Limitations of FNAC are mainly due to the small population of the cells sampled with associated problems of the adequacy of the sample.[20][16] Orrell et al in his study noted that the diagnostic difficulties which are usually related to deviations from common cytological criteria that may occur in some lesions and others are due to the effects of the sampling procedure or of the preparation of samples.[16]

Quality assurance in FNAC

The quality assurance for FNAC results was obtained by comparing the histology with the cytology using United Kingdom NHS Breast Screening Programme Guideline(NHSBSP).[15][21] A study by Daramola et al[22] in 2015 on the correlation between fine needle aspiration cytology and histology for palpable breast masses at the Lagos University Teaching Hospital, Lagos, Nigeria show that the absolute sensitivity, complete sensitivity, full specificity and positive predictive value of the FNAC results to be within acceptable range. However, a similar study by Ebughe et al[23] in 2016 at the University of Calabar teaching hospital show the absolute sensitivity and complete sensitivity were higher than the minimum expected value while positive predictive value was below minimum expected value from the UK, NHSBSP.

Complications of FNAC

The complications of FNAC include hematoma, infection, pneumothorax and dissemination of tumor.(24) (25)

Breaking the bad news

The provision of results with a diagnosis of malignancy should be coordinated by the managing clinician.[6] As much as one can the various options for treatment should be communicated effectively to the patient and she should be encouraged to ask questions.[26] Though most doctors are not experienced in breaking bad news, it is required that doctors break this news with understanding or compassion. A study done by Konstantinos et al show that over 60% of doctors have not had specific training on breaking bad news and over 65% of the doctors have not heard of the SPIKES protocol for breaking bad news.[14] [27]

Breaking the bad news of a diagnosis of malignancy requires the use of SPIKES protocol involving the following six steps:

- S – **Setting up** the interview: include a mental rehearsal of what to say, arranging for some privacy, having someone else (of the patient's choice) present, sitting down, making a connection with the patient and managing time constraints.
- P – Assessing patient's **perception**: The patient should be made to understand the condition.
- I - Obtaining the patient's invitation: The doctor should first obtain a permit from the patient if he would want to be given details of all aspect of the illness before going ahead to do so.[28]
- K – Giving **Knowledge** and information to the patient: Warn the patient that bad news is coming e.g. "I got some bad news to tell you", use vocabularies the patient would understand, avoid excessive bluntness, give information in small bits and check for patient understanding periodically.

- E – Address patient's **emotions with empathic responses**: First observe the emotion whether tearfulness, sadness, shock or silence. Identify the emotional reaction; if not sure confirm from the patient then give an empathic response to acknowledge patient's response.
- S – **Strategy and Summary**: Patient should be made to understand various options for treatment, his role in the treatment process and prognosis of the disease.[28][26][29][30][14]

Conclusion

Fine needle aspiration cytology has been used for many years all over the world as part of the triple test to make screening/diagnosis of breast lesions especially malignancies. It is expected that in low resource settings as in sub-Saharan Africa, imaging facilities are not readily available making the triple test such a herculean task for doctors. However fine needle aspiration cytology when performed optimally (after a clinical examination and imaging studies) by a trained cytopathologist would immensely improve patient care in our environment.

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