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Review Article

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Rapid On-site Evaluation (ROSE) for Diagnosing Bone Pathologies: A Narrative Review

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Abstract

Infective or neoplastic bone lesion needs radiological and histological correlation for the diagnosis. Bone needs to be decalcified so the process is time-consuming. The quality and quantity of biopsy material taken need evaluation in order to avoid false-negative results and delay in diagnosis. This study aims to study the utility of ROSE, its background, process, and interpretation for different bone lesions.

ROSE can be considered a useful tool to identify false negative benign cases and true positive malignant cases. The use of this technique can save the turnaround time for the bone biopsy report and help in treating patients with malignant bone tumors more aggressively and appropriately. This in turn will benefit the outcome of the patients in terms of morbidity and mortality in rapidly growing lesions and the overall survival of the patients.

Key Words : Rapid Diagnostic test, Neoplasm, Tuberculosis, Sample adequacy, Histology

Introduction

To reach the final diagnosis for definitive management of the patient with an infective lesion or tumor of the bone an algorithm needs to be followed which includes a detailed history, examination, radiographs, and blood parameters before carrying out a biopsy. (figure 1) [1-3].

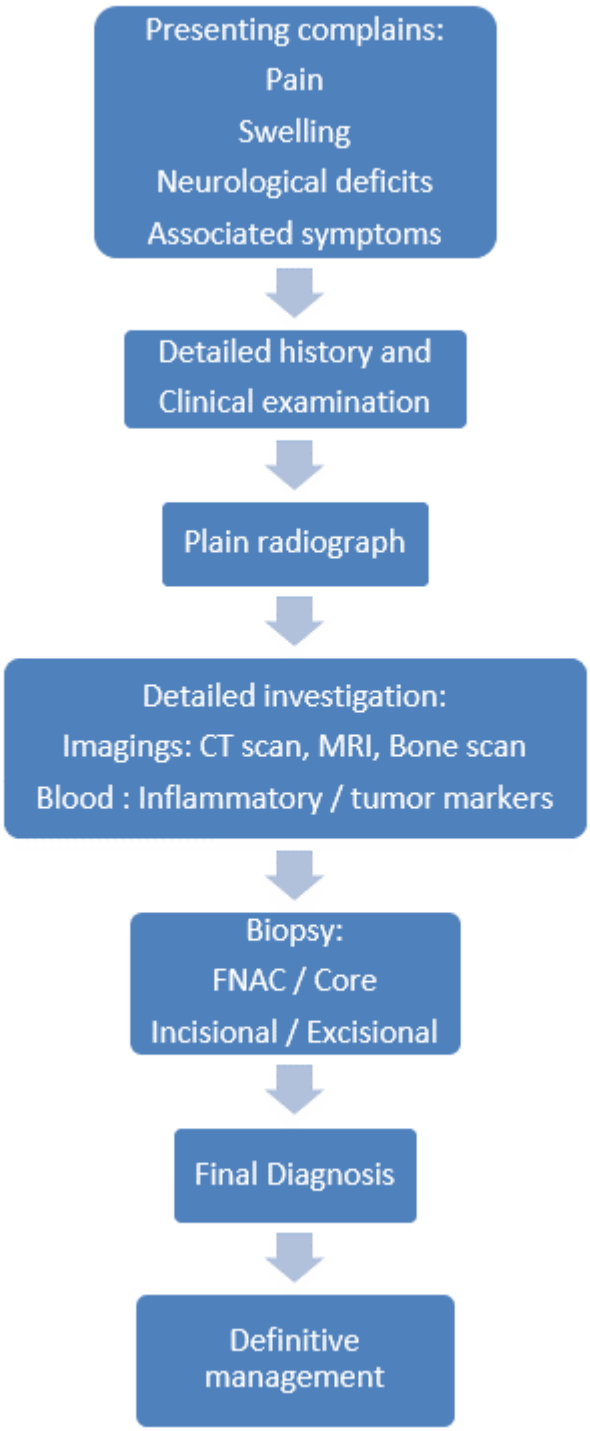

Figure 1: Algorithm for an approach to bony lesion

Biopsy from a bone can either fine-needle aspiration cytology (FNAC), core biopsy, incisional, or excisional as shown in figure 2 [4-5]. Biopsy often involves technical skills and meticulous judgments. If the biopsy is performed in a suboptimal manner and the specimen obtained is inadequate which may jeopardize the diagnosis [6].

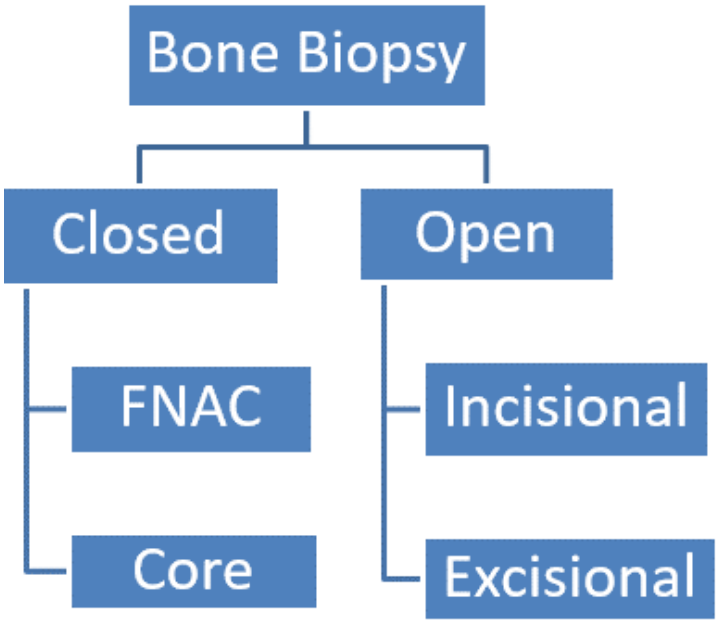

Figure 2: Types of bone biopsy

Most of the musculoskeletal lesions can be diagnosed with a well-done core needle biopsy with a diagnostic accuracy of up to 94% for non-image guided biopsies and up to 98% for image-guided biopsies [7, 8]. It is even lower in spine lesions, infectious illness, benign lesions, and low-grade malignancies in contrast with malignant tumors [9]. For lytic lesions, large targets, the diagnostic yield improves when several specimens/samples are obtained[10]. However, in FNAC only cells rather than tissue architecture are evaluated hence, its accuracy at determining specific tumor type is much lower [11]. Open biopsy is the gold standard for biopsy of bone and soft-tissue tumors, but complications are greater with incisional biopsy when compared with needle biopsy, like; bleeding, infection, tissue contamination [12-14].

As bone tissue contains calcium which needs to be decalcified to make it soft for sectioning before the examination, interpretation of bone biopsy takes a longer time than biopsy of other soft tissues [15]. This adds to the turnaround time (TAT) and the treatment/staging decisions essential for time management are delayed [16]. Delay in the diagnosis and repeat biopsies if not adequate and not taken from the representative areas may change the outcome both in terms of morbidity and mortality, especially important in rapidly growing malignant bone tumors such as osteosarcoma and Ewings sarcoma where limb salvage surgery is planned [17-19].

For the above-mentioned concerns, primary information in terms of quality and adequacy of material collected to make a provisional diagnosis can be done by rapid onsite evaluation (ROSE) [20, 21]. ROSE of cytology smears/imprints allows to combine the radiological findings, treating physicians' opinion, and pathological expertise simultaneously to direct the needle to the best possible location for sampling and withdraw the biopsy sample in an adequate amount from the correct position [22]. This is ul-

timately helpful for the patient as it likely reduces the need for repeat testing, hence reaching to correct diagnosis early and timely management. It also allows several passes (number of trials needle is passed on to a site) to give immediate feedback on the quality of the sample [23].

To assess the role of ROSE on the adequacy of FNAC samples taken in settings of image-guided aspirates from several sites many studies had been performed [21]. Though the absolute benefits are contested, ROSE limited the number of passes needed for endobronchial ultrasound (EBUS) guided FNA samples in several studies [24, 25]. Meta-analysis on the effect of ROSE on sample adequacy revealed up to 12% overall augmentation when ROSE was utilized, but the extent of initial adequacy varied without ROSE [26].

In most organs where FNAC and cytology form an important part of patient management, such as thyroid, salivary glands, cervix, and breast, the diagnostic ability of these tests have appropriate validation. There are no such established reporting systems for FNAC of bone and soft tissue other than isolated studies proposing adequacy criteria [27, 28]. As per recent literature search, there haven't been studies published on ROSE for bony lesions, despite some centers using it and recommending its use in routine practice, which could partly be attributed to ROSE being a relatively new terminology or due to the reason that ROSE requires timing and coordination of various specialties at the operation site [29].

This article aims to present the rapid onsite evaluation useful in bone pathologies. Use of which is ultimately helpful for the surgeon, pathologist and for patients aslo as it reduces the need for repeat testing, hence reaching to correct diagnosis early and timely management.

The Procedure of ROSE

The biopsy region is sterilized with the sterile solution, the area needs to be covered with a sterile drape. Local anesthetic injected into the skin, soft tissues, and periosteum. After local anesthesia had taken effect, an incision was given on the skin surface, underlying soft tissue, and a Jamshedi biopsy needle is inserted into the lesion along with the stylet to the desired depth, sometimes in a clockwise manner. The stylet is then withdrawn and the biopsy needle is rotated in semi-circular, clockwise, and anti-clockwise positions, which yields a cylindrical sample of bone.

The fresh sample without any added fixative or formalin is immediately given to the pathologist. Material given is then expressed onto glass slides where either touch imprints or smeared tissue are taken.

The slides are then air-dried and dipped a few times for 10-30 seconds in a Coplin jar with toluidine blue before being rinsed or dipped in tap water several times for ROSE. Excess water and stain are wiped from the bottom of the slides and the slide is then examined under the microscope and its cellularity was assessed (figure 3).

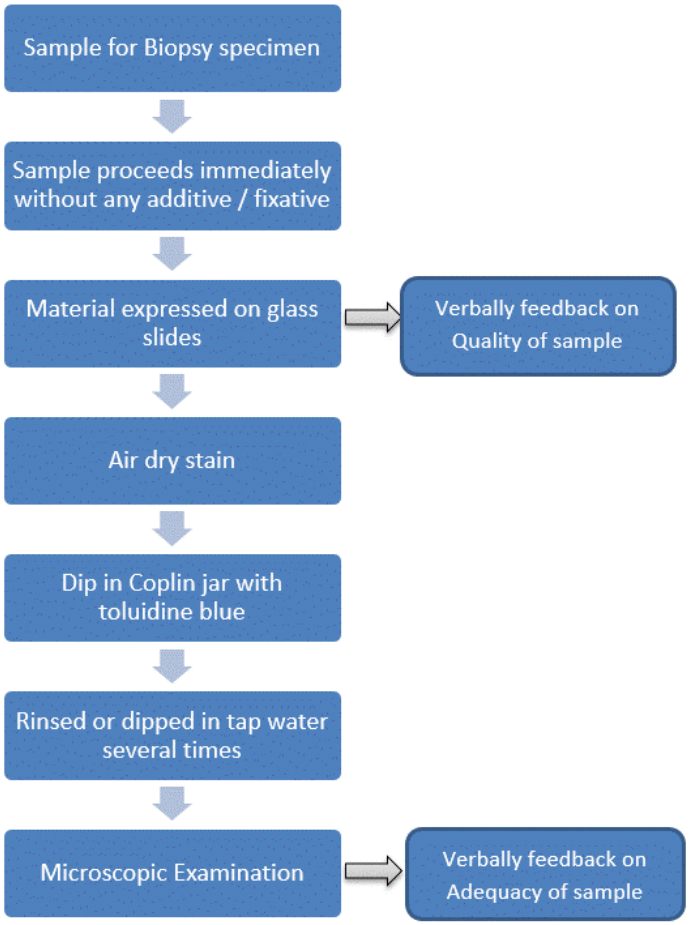

Figure 3: Procedure to perform ROSE

In the clinically suspicious lesions, sampling should continue until diagnostic adequacy is obtained or unless the procedure is stopped for clinical reasons. The clinician should be informed whether the sample is adequate or not and whether a repeat is required. Adequacy is based on a combination of the cellularity and adequacy microscopically and the amount of material obtain macroscopically. A second pass is not obtained if the aspirated material was deemed enough for making a diagnosis. Additional passes were taken if the ROSE slide did not contain enough material to make a histopathological diagnosis. (figure 4)

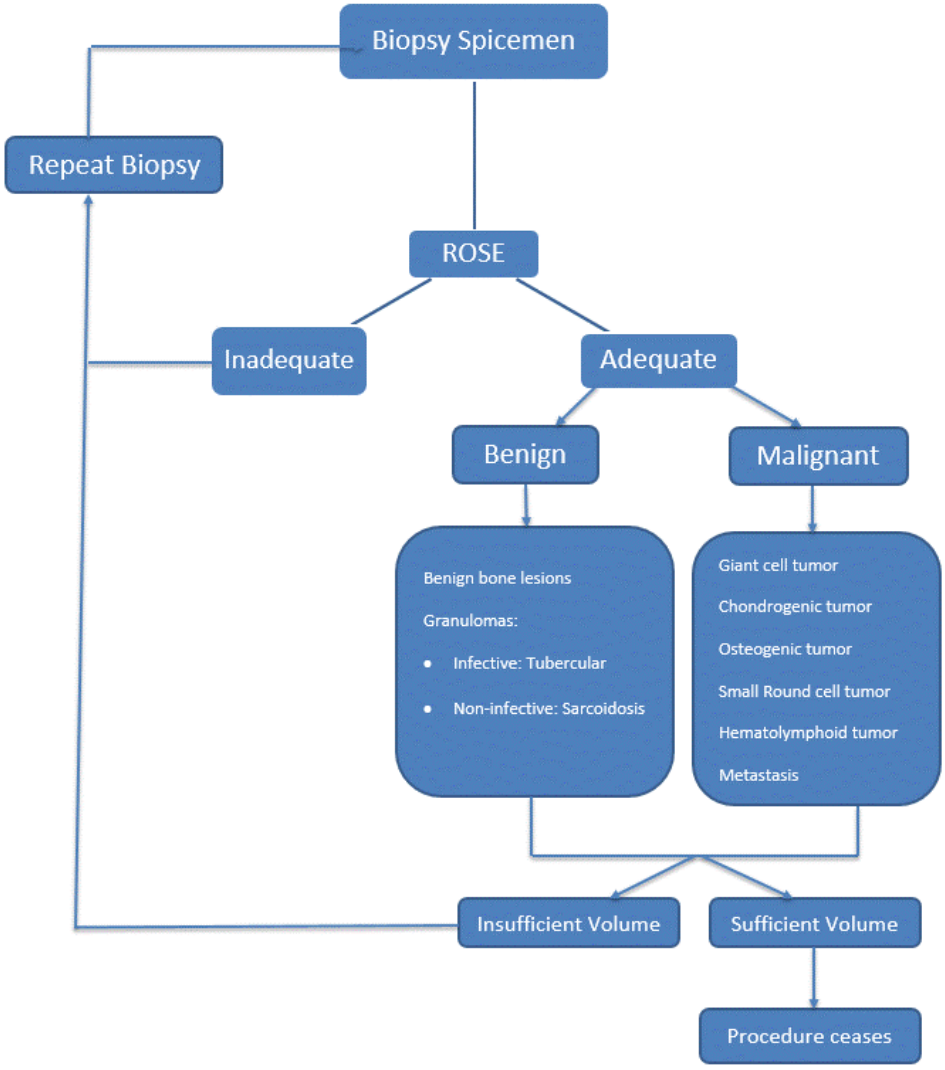

Figure 4: Flowchart for the interventions during the ROSE test

To look for the adequacy of the sample, Choi et al. constructed an algorithm to improve the diagnostic accuracy of ROSE on lymph node specimens from endobronchial ultrasound-guided transbronchial needle aspiration. Where they set core size more than 2 cm, presence of malignant cells, presence of microscopic anthracotic pigment (MAP), and mean lymphocyte density (LD) more than 40 cells/field in the sequential order to evaluate for the adequacy of the specimen, as shown in figure 5. The accuracy for adequacy of the specimen only using the first criteria was 64.7%, which was increased to 97.0% using all four sequential criteria. Also, the sensitivity for adequacy of the specimen using only the first criteria was 64.4%, which was increased to 98% using all four sequential criteria [30].

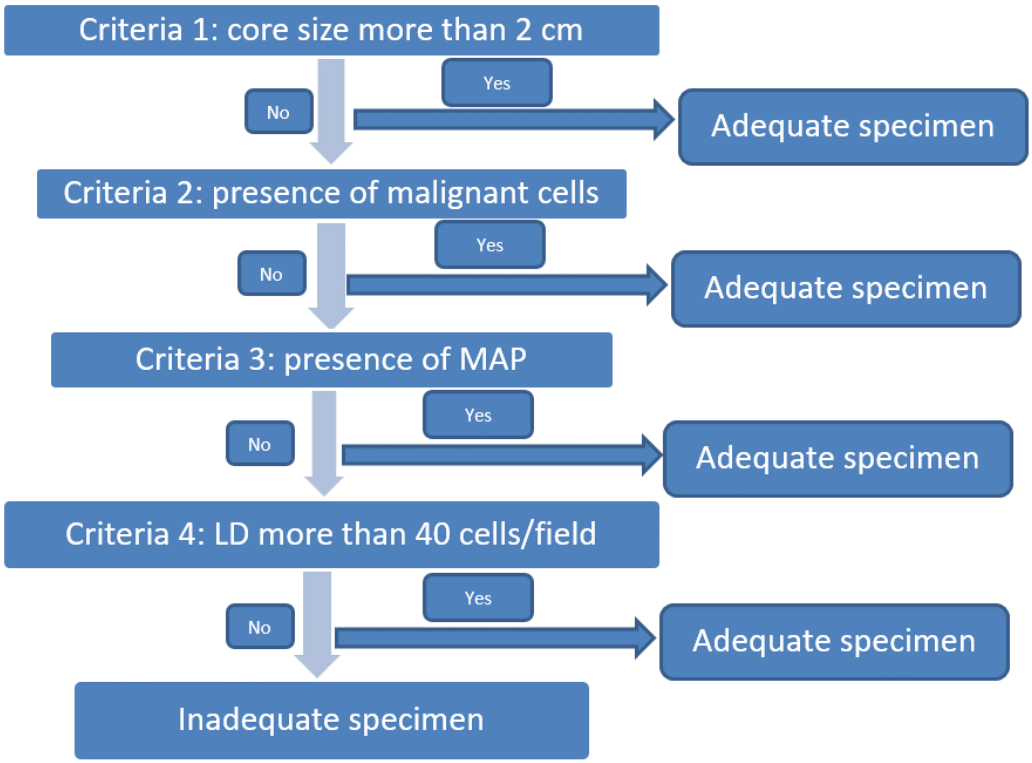

Figure 5: Algorithm to Evaluate the Adequacy of ROSE purposed by Choi et al. 2015; Abbreviations: MAP: microscopic anthracotic pigments (MAP); LD: mean lymphocyte density (redrawn from an original article by Choi et al. 2015)

Interpretation of ROSE

There were no criteria set for adequacy as no literature is available on this. Diagnostic categories were assigned as Inadequate, benign, suspicious probably benign, suspicious probably malignant, and malignant as shown in figure 6.

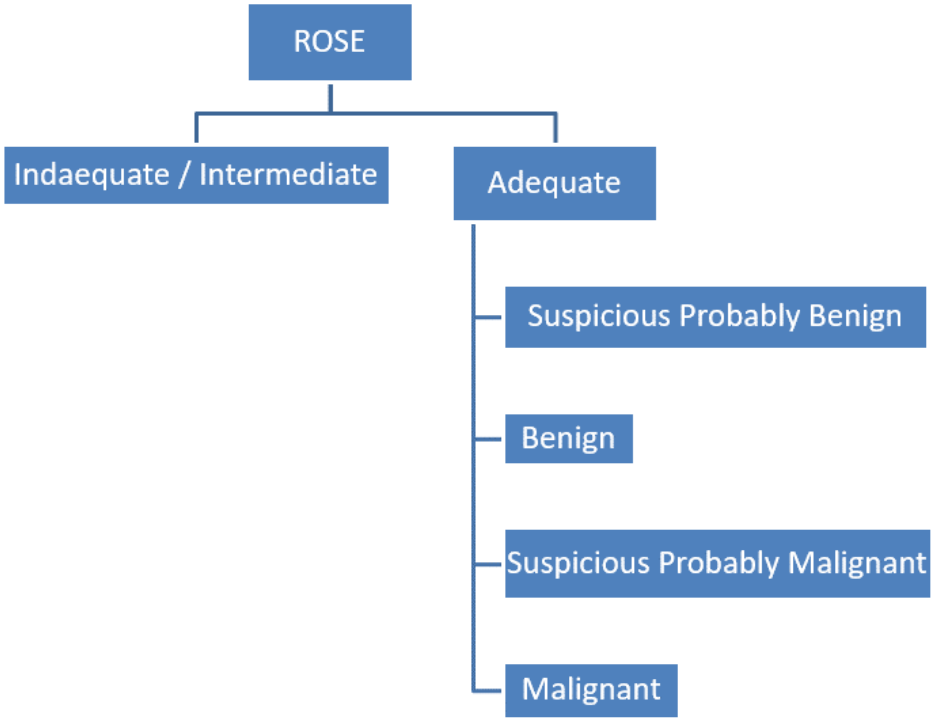

Figure 6: Interpretation of ROSE

Microscopy features of the prepared smear were assigned as a giant cell in giant cell tumor, chondrogenic picture in enchondroma, osteogenic picture in osteosarcoma, small round blue cell picture in Ewing's sarcoma, hematolymphoid picture in lymphoma, highly pleomorphic atypical cells in metastatic lesions (figure 7). Marked benign microscopic features of the lesion assigned as epithelioid cell granulomas in tuberculosis, scattered hooklets, and membrane in hydatidosis (figure 8).

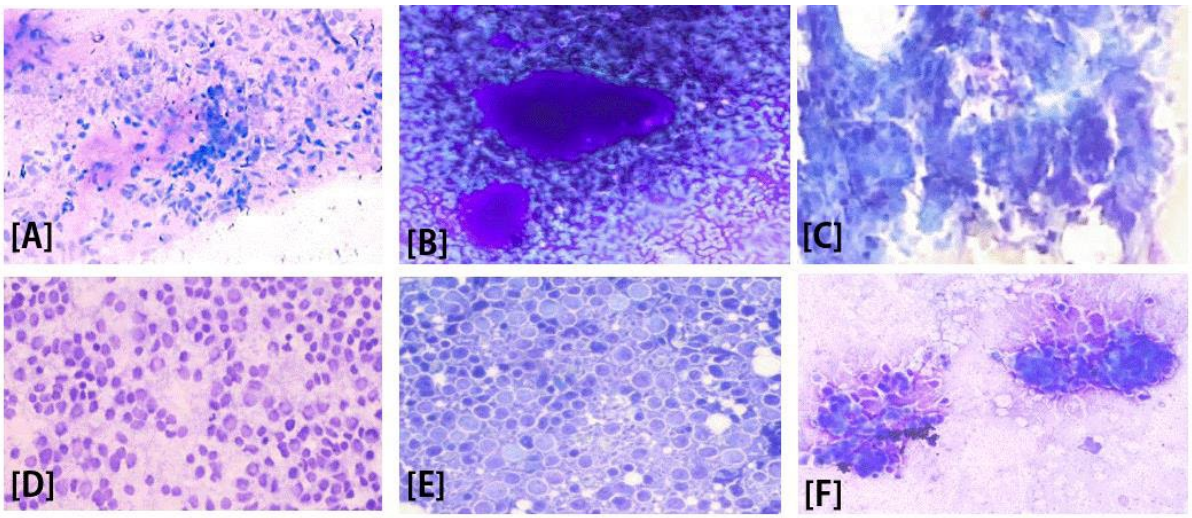

Figure: 7: Toluidine blue stained smears showing malignant features; A: fragments and clusters of pleomorphic spindle cells with pink intercellular material consistent with osteoid, consistent with osteosarcoma; B: large fragments of paucicellular chondroid material, consistent with enchondroma; C: large fragments and sheets of cohesive round to oval cells with mild to moderate pleomorphic nuclei along with numerous scattered giant cells, consistent with giant cell tumor; D: sheets, clusters and dissociated cells with round to oval nuclei and scant to moderate cytoplasm, consistent with Ewing's Sarcoma; E: scattered monomorphic population of large, atypical lymphocytes with background lymphoglandular bodies, consistent with Lymphoma; F: large clusters, and fragments of highly pleomorphic atypical cells, a moderate amount of cytoplasm, consistent with the metastatic lesion.

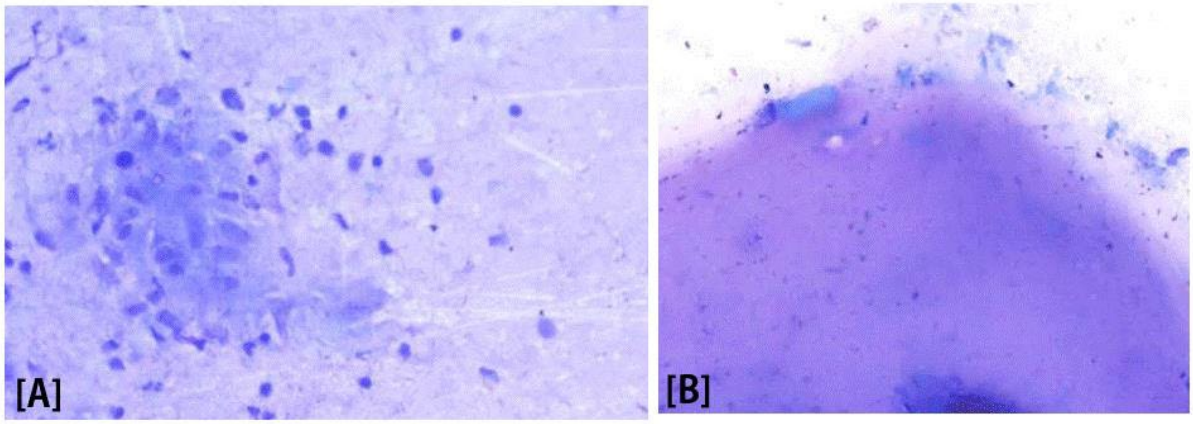

Figure 8: Toluidine blue stained smears showing benign features; A: epithelioid cell granulomas with elongated polygonal cells with pale cytoplasm and indistinct cell borders in a necrotic background, consistent with tuberculosis; B: scattered hooklets and membrane fragments in a necrotic background, consistent with hydatidosis

Even the beautiful flower rose always has thorns with it, ROSE has its advantages like its cost-effectiveness, it reduces the need for multiple sampling, improves the adequacy rate, decreases the number of passes for adequate sampling, assists further diagnostic triage, stores fresh cells for molecular sampling, improves overall diagnostic yield and sensitivity. Besides beautiful petal, thorns aspect of ROSE includes that, it needs optimal staining quality, need a longer procedure for repeated sampling, discrepancy on the result as it relies solely on morphology, need of experienced on-site cytopathologist, need extra time for cytopathologist, financial under-compensation of pathologist's time, and it needs optimal clinical-pathologist communication which maybe not feasible on all hospital setting [21, 31].

There are only a few pieces of literature, where authors discussed the ROSE, even fewer studies on bone. Literature published by P.

W. Shield et al. did a review of 3032 specimens where, the adequacy rate for the 3032 specimens was 94%, and the confirmation of a ROSE of adequacy at reporting was uniformly high ranging from 98% to 100%. The inadequacy rate for thyroid FNAs with ROSE was 6%, which was significantly lower than for non-ROSE thyroid FNAs. A significantly higher proportion of adequate ROSE thyroid specimens was reported with abnormalities, compared with non-ROSE thyroid collections [23].

In the Meta-analysis done by Robert L. Schmidt, et al. authors concluded that ROSE was associated with a 12% improvement in the adequacy rate. Studies on lung, soft tissue, head and neck, thyroid, and lymph nodes all showed statistically significant improvement in the adequacy after implementation of ROSE. In the studies on breast, pancreas, and mediastinum or in studies reporting results aggregated from several different anatomic locations, ROSE was not associated with improvement [32].

Literature available on ROSE study of the spine lesions by Israh Akhtar et al. concluded that the overall sensitivity of the procedure in spinal and vertebral lesions has been reported to be 96%, where the sensitivity of soft tissue study was 97% and bone 93%, and overall specificity was 98%, where the specificity of soft tissue study was 98% and bone 100%. However, the accuracy rate depends on the skill of the radiologist in deciding the optimal route of approach at various anatomic levels [33].

Overall, ROSE improves the adequacy rate of almost all tissue samples including the bone. Non-ROSE adequacy varies significantly among the anatomical site of tissue, way of sampling, the experience of clinician and pathologist, and the performed institutions.

Limitations

Although ROSE reduces the need for repeat testing while taking the biopsy specimen for histopathological examination, which helps in reaching to correct diagnosis early and timely management, it has liminations like: the need of more manpower in the procedure room, availability of pathologists nearby procedure field, availability of staining materials and microscope nearby procedure field which may not be available in all hospital setting.

Conclusion

On-site triaging of tissue for further investigations has the potential to improve the logistics of patient care in several ways. Although, the material collected in ROSE preparation is invaluable for molecular testing, especially in the setting of bone lesions. However, we can conclude that ROSE is a good investigating tool to decrease the turnaround time and false-negative results for the biopsy, increasing the outcome both in terms of morbidity and mortality by early diagnosis and timely management of the disease.

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Conflict of interest

None of the investigators has any conflict of interest whatsoever with the research and its outcome.

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