Case series

Petals of rose: Application of rapid on-site evaluation in bronchoscopy

Sayan Bhowmik[1], J. Thanka[1], M. Aswin Manikandan[1], Sabarinath Ravichandar[2]

[1]Department of Pathology, [2]Department of Respiratory Medicine, Sree Balaji Medical College, and Hospital, Chromepet, Chennai, 600044, Tamil Nadu, India

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Corresponding author: **J. Thanka.** Email: thanka.path@bharathuniv.ac.in

ABSTRACT

In present day scenario, procedures that are minimally invasive like FNAs and Core needle biopsies are on the rise. Rapid on-site evaluation (ROSE) is a laboratory service that assesses the cytomorphologic features from FNA smears or biopsy contact imprints in the biopsy room and can provide on the spot input and suggestionsfor the clinician through immediate cytological examination of the biopsy sample. ROSE also allows for a preliminary diagnosis, allowing for the requirement of additional material for ancillary studies. We are presenting two cases which highlights the merits of ROSE in cytological diagnosis.

In the first case, a thirty four year old male patient came with complaints of productive cough, breathlessness and fever. Bronchoscopic needle aspiration and biopsy was done with Rapid Onsite Evaluation. ROSE revealed two non-caseating epithelioid granulomas on the 4th pass. Bronchoscopic lymph node biopsy was non-contributory. With other clinical and biochemical parameters, diagnosis of Sarcoidosis was made. This case study underscores the significance of ROSE in arriving at the diagnosis.

In the other case, a fifty seven year old male patient came to hospital with productivecough and breathlessness (MMRC grade II). CT chest revealed features suggestive ofbronchogenic carcinoma. ROSE was performed along with bronchial brush cytology in which presence of atypical cells with increased nuclear cytoplasmic ratio, nuclear hyperchromatism and nuclear molding was noted. On histopathological examination,it was diagnosed as a case of non-small cell carcinoma of lung – poorly differentiatedtype. This case proves the advantage of ROSE in avoiding repeated invasive procedures for the patient.

Keywords: Bronchoscopy; ROSE, diagnosis.

INTRODUCTION

For decades, transbronchial biopsies (TBB) have been used as a mode of investigation to diagnose sarcoidosis. TBB's diagnostic effectiveness has been observed to range between 40 and 90 percent in prior research and 68.7% in another investigation. The presence of non- caseating granulomas can be caused by a variety of etiological factors, and accurate clinical correlation can help determine the best treatment strategy (1). TBB was the most used method in the study of Kıter *et al.*, and Sarcoidosis Working Group of Turkish Thoracic Society, which showed a 48.8% success rate (2). In present day scenario, minimally invasive procedures such as FNAs and Core needle biopsies are on the rise. Fine needle aspiration (FNA) helps to establish a diagnosis whileavoiding more invasive procedures for the patient (3-5).

The increased use of biopsied material for accurate diagnosis and recommending customized treatment has increased the value of specimen collection with specific emphasis for sufficientspecimens. Rapid on-site evaluation (ROSE) includes quick and real time evaluation and guidance of cytological characteristics of fine needle aspiration smears or contact imprints of the biopsy material (6-10).

Fine needle aspiration has proven to be an effective method for diagnosing mediastinal lesions while avoiding more invasive procedures (3-5). The accessibility to rapid on-site assessment (ROSE) raises the diagnostic accuracy varying from 80% to 100%, with higherspecificity and sensitivity.

Case report 1

A 34 years' old male patient came to pulmonology unit with productive cough and breathlessness for 1 month and fever for 1 week. He also had history of fever for 1 week with body pain and generalized weakness. CECT chest revealed patchy areas of parenchymal consolidation in the posterobasal segment of left lower lobe and superior segment of right lower lobe. Subpleural consolidation in the

superior segment of lower lobe. Smooth irregular septal thickening in the central region of both lungs. Multiple enlarged mediastinal, bilateral hilar and paraesophageal lymph nodes. Based on the above findings provisional diagnosis was given with possibilities of 1. Tuberculosis, 2. Sarcoidosis, 3. Lymphoma.

Bronchoscopy needle aspiration and biopsy of the mediastinal lymph node was done with Rapid Onsite Evaluation. A total of 4 passes of needle aspiration was done. First 3 passes showed only bronchial epithelial cells. 4thpass showed two non-necrotizing granulomas withoccasional giant cells (Fig 1-A, B, C). Background showed mature lymphocytes and macrophages. Bronchoscopic biopsy of the lymph node was non-contributory.

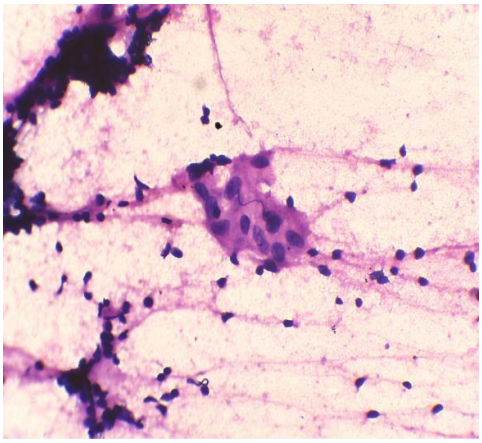

Fig. 1(A): Multinucleated giant cell

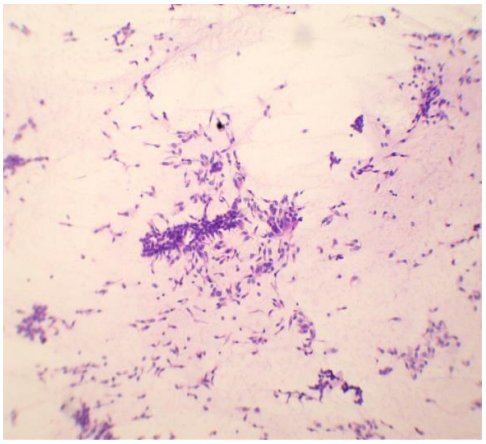

Fig.1 (B): Normal bronchialepithelial cells

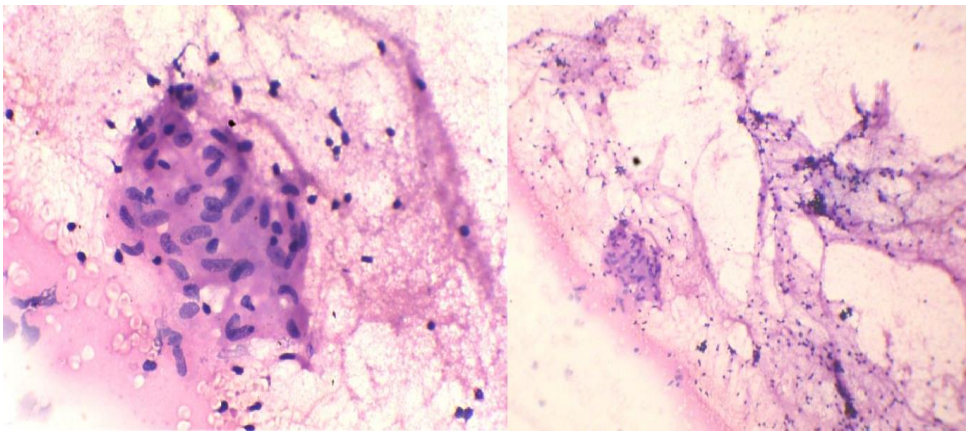

Fig. 1(C): High power and low power view of non-necrotizing granuloma

Case report 2

A 57 years' old male patient presented to the pulmonology department with complaints of productive cough for 8 months, which have aggravated since past 3 months. Patient also complaints of breathlessness (MMRC grade II) for 1 month. CT chest showed an irregular enhancing mass in right hilum causing mild obstruction/ narrowing of right main bronchus and anterior segmental bronchus – features suggestive of bronchogenic carcinoma. Bronchialbrush cytology was performed along with ROSE which showed large number of bronchial epithelial cells along with occasional atypical cells with increased nuclear cytoplasmic ratio, nuclear hyperchromatism and nuclear molding in fig 2(A) and 2(B). BAL fluid sent for cytology was negative for malignant cells and showed only bronchial epithelial cells and pigment laden macrophages. Bronchoscopic biopsy was done which revealed a malignant neoplasm with pleomorphic neoplastic cells showing hyperchromatism and moderate cytoplasm arranged in clusters (Fig.2 C). An impression of non-small cell carcinoma of lung-poorly differentiated type was given.

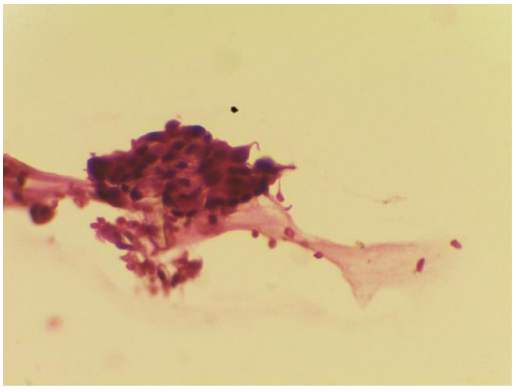

Fig.2(A): Atypical cells seen on bronchial brush cytology with ROSE

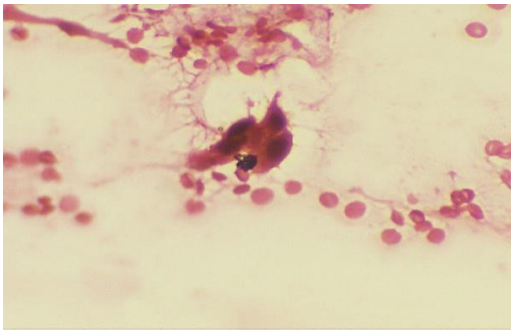

Fig.2(B): Atypical cells on bronchial brush cytology with ROSE

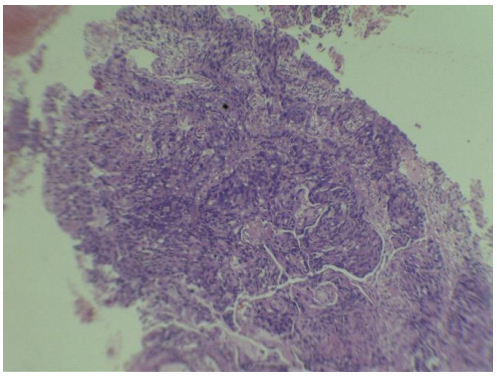

Fig.2(C): Histopathological picture of poorly differentiated non-small cell carcinoma

DISCUSSION

Case 1

Bronchial epithelial cells are normal components of a lung biopsy specimen. These are ciliated columnar epithelial cells, which may be present in singles or in clusters as picket fence formation. Individual cells are bipolar and have round or ovoid nuclei, vacuolated cytoplasm and uniform nuclear contour, and small nucleolus. In our first case, only bronchialepithelial cells were present in the first 3 passes indicating that pass was not taken from the lymph node (12).

The adequacy of a sample from lymph node must be interpreted based on the cytological findings along with the clinical impression as well. If we can identify a primary a metastatic cancer, or any granulomatous inflammation with or without infectious agents is present, the specimen is generally regarded adequate. If malignancy or granulomas are not detected, an adequate specimen should be comprised of abundant pigment-laden macrophages or more than 40 lymphocytes at X40 magnification, according to Alsharif *et al.*,(11). In our first case, the presence of abundant mature lymphocytes and macrophages in the background in the 4th pass suggested that the sample was obtained from the lymph node.

Infection with *Mycobacterium tuberculosis* causes granulomatous inflammation. Aggregates of epithelioid histiocytes, lymphocytes, and Langhans giant cells can be found in cytologic specimens. There may or may not be signs of necrosis (12-14). Sarcoidosis is another common condition with an unknown cause where noncaseating granulomas are seen in a variety of organs, most frequently the lung. Noncaseating granulomas comprised of epithelioid histiocytes with scattered lymphocytes and multinucleated giant cells are seen in microscopy (12). Presence non caseating granuloma and negative report for sputum AFB pointed towards Sarcoidosis in our first case.

The most common mediastinal lymphoma is Hodgkin's lymphoma. Presence of atypical mononuclear cells, Reed Sternberg cells, plasma cells, eosinophils, histiocytes with a background population of lymphocytes are the characteristic findings of Hodgkin's lymphoma (12,15). In our first case, these features were not present which ruled out thediagnosis of lymphoma.

Along with other clinical parameters and negative culture for *Mycobacterium tuberculosis*, the diagnosis of Sarcoidosis was made. The patient received treatment for the same and responded well to the treatment.

Case 2

The most prevalent type of lung malignancy is adenocarcinoma. Cytomorphological features include tumor cells in clusters or sheets and rare present in singles. The tumor cells are pleomorphic with vacuolated or granular cytoplasm, round nuclei, and prominent nucleolus. Focal areas show necrosis (10,14,15). Squamous cell carcinoma of lung presents as tumor cells arranged in cohesive cluster or singly. Individual cells are polygonal with increased N:C ratio, dense cytoplasm, and hyperchromatic nuclei. Small cell lung carcinoma has the typical characteristic cytomorphologic features of small to intermediate tumor cells with scant cytoplasm, round or oval nucleus with speckled chromatin and absence of nucleolus.

Abundant necrosis and apoptosis can also be seen (12,17,18). Another common lung malignancy – Carcinoid presents as single /dyscohesive group of uniform tumor cells with moderate cytoplasm and round or oval nucleus, with speckled chromatin, placed eccentrically (10,15).

Based on this we noticed few atypical cells on the bronchial brush cytology done along with ROSE and advised histopathological correlation which confirmed the diagnosis of non-small cell lung carcinoma. Thus, ROSE helped us arrive at an early pathological diagnosis and confirmed the clinical suspicion of bronchogenic carcinoma.

ROSE can improve the diagnostic outcome of biopsy procedures and aids in procuring enough sample for

ancillary research on numerous occasions (6-10). ROSE's scope involvesdetermining sample adequacy and specimen triage. ROSE also helps establish a preliminary diagnosis, allowing for the requirement of additional material for further studies including microbiology culture, flow cytometry, and molecular tests. The non-diagnostic rate in FNAsdone without ROSE is around 20%, whereas when ROSE is applied, it is 2-10% (18-22). In general, smaller nodules have higher non diagnostic rates and lower sensitivity for FNAC (18). ROSE improves the adequacy of the specimen, which lowers the nondiagnostic rate. ROSE also corresponds better with final report in general (5, 6, 24-26).

In our cases, results of the ROSE provided real-time input to the biopsy physician, allowing him to make multiple passes and change the target site to ensure appropriate specimens were collected. Therefore, ROSE could be able to assist in lowering the nondiagnostic rate and, as a result,lowering the need of repeated biopsies. It also establishes a tentative diagnosis that can be used to assess if further biopsies are necessary

CONCLUSION

ROSE has proven to be an outstanding method for diagnosing mediastinal lesions while avoiding more invasive operations. With Rapid on-site Evaluation (ROSE), we were able to determine the specimen adequacy and guide the clinician towards the accurate site oflesion in both the cases. In the second case, presence of atypical cells also prompted us towards the diagnosis and immediate treatment measures were taken. Clinicopathological correlation could be made with the microscopic findings which helped us arrive at an early diagnosis and the patient benefited greatly.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

REFERENCES

1. Ozbudak, I.H., Ozbilim, G., Ozbudak, O., Kovan, T.S. Diagnostic value of transbronchialneedle aspiration cytology in sarcoidosis. Turk Patoloji Derg. 2011 May; 27(2):149-153.
2. Kiter, G., Musellim, B., Cetinkaya, E., Turker, H., Uzaslan, E., Yentürk, E., *et al.*, Clinical presentations and diagnostic work-up in sarcoidosis: a series of Turkish cases (clinics and diagnosis of sarcoidosis). Tüberküloz ve toraks. 2011; 59: 248-258.
3. Sharma, A., Shepard, J.O. Lung cancer biopsies. Radiol Clin N Am. 2018;56(3):377-390.
4. Gonzalez, M.F., Akhtar, I., Manucha, V. Changing trends and practices in cytopathology.Acta Cytol. 2017;61(2):91-95.
5. DaCunha, S.G. ROSEs (rapid on-site evaluations) to our patients: the impact onlaboratory resources and patient care. Cancer Cytopathol. 2013;121(10):537-539.
6. Jain, D., Allen, T.C., Aisner, D.L., Beasley, M.B., Cagle, P.T., Capelozzi, V.L., *et al.*, Rapid on-site evaluation of endobronchial ultrasound-guided transbronchial needle aspirations for the diagnosis of lung cancer: a perspective frommembers of the Pulmonary Pathology Society. Arch Pathol Lab Med. 2018;142(2):253-262.
7. Mehmood, S., Jahan, A., Loya, A., Yusuf, M.A. Onsite cytopathology evaluation and ancillary studies beneficial in EUS-FNA of pancreatic, mediastinal, intra-abdominal, and submucosal lesions. Diagn Cytopathol. 2015;43(4):278-286.
8. Mohanty, S.K., Pradhan, D., Sharma, S., Sharma, A., Patnaik, N., Feuerman, M., *et al.*, Endoscopic ultrasound guided fine-needle aspiration: what variables influence diagnostic yield? Diagn Cytopathol. 2018;46(4):293-298.
9. Pearson, L.N, Layfield, L.J., Schmidt, R.L. Cost-effectiveness of rapid on-site evaluationof the adequacy of FNA cytology samples performed by non-pathologists. Cancer Cytopathol. 2018;126(10):839-845.
10. Stevenson, T., Powari, M., Bowles, C. Evolution of a rapid onsite evaluation (ROSE) service for endobronchial ultrasound guided (EBUS) fine needle aspiration (FNA) cytology in a UK Hospital: a 7-year audit. Diagn Cytopathol. 2018.
11. Alsharif, M., Andrade, R.S., Groth, S.S., Stelow, E.B., Pambuccian, S.E. Endobronchial ultrasound-guided transbronchial fine-needle aspiration: the University of Minnesota experience, with emphasis on usefulness, adequacy assessment, and diagnostic difficulties. Am J Clin Pathol. 2008;130(3):434-443.
12. Cibas, E.S. Cytology: diagnostic principles and clinical correlates. 3rd ed. London, England: Saunders; 2009. 59-104.
13. Bezabih, M., Mariam, D. and Selassie, S. Fine needle aspiration cytology ofsuspected tuberculous lymphadenitis. Cytopathology. 2002; 13: 284-290.
14. Rajwanshi, A., Bhambhani, S., Das, D.K. Fine-needle aspiration cytology diagnosis of tuberculosis. Diagn Cytopathol [Internet]. 1987;3(1):13-16.
15. Harris, N.L. Shades of gray between large B-cell lymphomas and Hodgkin lymphomas: differential diagnosis and biological implications. Modern Pathology. 2013 Jan;26(1): S57-S70.
16. Travis, W.D., Brambilla, E., Noguchi, M., Nicholson, A.G., Geisinger, K.R., Yatabe, Y., *et al.*,international association for the study of lung cancer/American thoracic society/European respiratory society international multidisciplinary classification of lung adenocarcinoma. J Thorac Oncol [Internet]. 2011;6(2):244-285.
17. Idowu, M.O., Powers, C.N. Lung cancer cytology: potential pitfalls and mimics - a review. Int J Clin Exp Pathol. 2010;3(4):367-385.
18. Sturgis, C.D., Nassar, D.L., D'Antonio, J.A., Raab, S.S. Cytologic features useful for distinguishing small cell from non–small cell carcinoma in bronchial brush and wash specimens. Am J Clin Pathol [Internet]. 2000;114(2):197-202.
19. Williams, D.B., Sahai, A.V., Aabakken, L., Penman, I.D., vanVelse, A., Webb, J., *et al.*, Endoscopic ultrasound guided fine needle aspiration biopsy:a large single centre experience. Gut. 1999;44(5):720-726.
20. Jhala, N.C., Jhala, D., Eltoum, I., Vickers, S.M., Wilcox, C.M., Chhieng, D.C., *et al.*, Endoscopic ultrasound-guided fine-needle aspiration biopsy: a powerful tool to obtain samples from small lesions. Cancer. 2004;102(4):239-246.
21. Gress, F.G., Hawes, R.H., Savides, T.J., Ikenberry, S.O., Lehman, G.A. Endoscopic ultrasound-guided fine-needle aspiration biopsy using linear array and radial scanning endosonography. Gastrointest Endosc. 1997;45(3):243-250.
22. Shin, H.J., Lahoti, S., Sneige, N. Endoscopic ultrasound-guided fine-needle aspiration in 179 cases: the M. D. Anderson Cancer Center experience. Cancer. 2002;296(3):174-180.
23. Klapman, J.B., Logrono, R., Dye, C.E., Waxman, I. Clinical impact of on-site cytopathology interpretation on endoscopic ultrasound-guided fine needle aspiration.Am J Gastroenterol. 2003;98(6):1289-1294.
24. Eloubeidi, M.A., Tamhane A., Jhala, N., Chhieng, D., Jhala,

D., Crowe, D.R., *et al.,* Agreement between rapid onsite and final cytologic interpretations of EUS-guided FNA specimens: implications for the endosonographer and patient management. Am JGastroenterol. 2006;101(12):2841-2847.
25. Anila, K.R., Nayak, N., Venugopal, M., Jayasree, K., Role of rapid on-site evaluation in CT-guided fine needle aspiration cytology of lung nodules. J Cytol. 2018;35(4):229-232.
26. Ali, S., Hawes, R.H., Kadkhodayan, K., Rafiq, E., Navaneethan, U., Bang, J.Y., *et al.*,Utility of rapid onsite evaluation of touch imprint cytology from endoscopic and cholangioscopic forceps biopsy sampling (with video). Gastrointest Endosc. 2019;89(2):340-344.