

Fine-Needle Aspiration Cytology of Non-Neoplastic Adrenal Pathology

Rajesh Kumar, M.D., and Pranab Dey, M.D., F.R.C.PATH*

Background: The incidence of many fungal and parasitic lesions are on the rise over the last few decades. In this study, we have analyzed the spectrum of non-malignant lesions in adrenal gland diagnosed on fine-needle aspiration biopsy (FNAB) in a tertiary health care center.

Methods: FNAB of the adrenal gland was done under CT (4 cases) and ultrasound guidance (11 cases). In six cases, the lesions were present in both the adrenal glands. Special stains were done whenever needed. No complications were encountered in any of the FNAB procedure. Detailed cytomorphological study was done along with clinical history.

Results: There were total of 15 cases comprising of 5 tuberculosis, 5 Histoplasma, 2 acute inflammation, 2 granulomatous inflammation, and 1 myelolipoma. Acid fast bacilli positive on Ziehl Neelsen stain were labeled as mycobacterial infection possibly tuberculosis. The capsule of Histoplasma was bright pink on Periodic Acid Schiff stain.

Conclusions: FNAB is an easy, reliable, and minimally invasive method to diagnose and categorize the various benign non-neoplastic diseases of adrenal gland. Diagn. Cytopathol. 2016;44:472–476. © 2016 Wiley Periodicals, Inc.

Key Words: adrenal gland; FNAB; cytology; histoplasma

Fine-needle aspiration biopsy (FNAB) of adrenal glands are rarely performed. There are studies that have demonstrated FNAB to be specific and sensitive procedures for adrenal lesions.^{1–3} Radiological guidance is practically always needed to ensure a representative sample. The

advantage of FNAB is its easiness-to-perform, cost-effectiveness, and time-saving procedure with lesser complications than biopsy.^{4,5} Although adrenal FNAB is considered to distinguish metastatic or hematology neoplasms from non-functioning primary adrenal lesions, quite a few times these lesions are due to an infectious disease (e.g., histoplasmosis and tuberculosis).

Materials and Methods

Written consent was taken before performing ultrasonography (USG) and CT scan guided FNAB. There was no ethical violence in this paper and the study is retrospective collection of cases diagnosed in last 10 years. The identity of the patients was kept in secret.

This retrospective study was carried out in the department of cytology, Post Graduate Institute of Medical Education and Research, Chandigarh, for the period May 2005 to May 2015. The study included non-neoplastic aspirations (15 cases) from adrenal glands. We have excluded all those cases where no diagnostic materials were aspirated. The clinical symptoms such as fever, weakness, cough along with bilateral involvement (six cases) in many cases raised the suspicion of infective lesion of the adrenal glands and prompted us to perform FNAB in these cases. In cases 4 and 14, no clinical history was available in our FNAB record. Detailed hormonal levels were not available at the time of FNAB except in one case (this case showed normal hormonal profile, case 1) where all aspirations were done under radiological guidance which included 4 cases of CT guided and 11 cases of USG-guided FNAB. Aspirations were done using a 22-gauge needle and 20-mL syringe. A verbal and also written consent were taken in all cases. We measured the initial blood pressure and other vital features of the patient before doing the FNAB and after the procedure. The emergency clinical team was ready at the time of FNAB to prevent any future complications. We did not encounter any complications during the FNAB procedure.

Department of Cytology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Ethical justification: Written consent was taken before performing USG and CT scan guided FNAB. There was no ethical violence in this paper and the study is retrospective collection of cases diagnosed in last 10 years. The identity of the patients were kept in secret.

*Correspondence to: Dr. Pranab Dey, MD, MIAC, FRCPath, Professor, Department of Cytology, Postgraduate Institute of Medical Education and Research, Chandigarh, India. E-mail: deypranab@hotmail.com

Received 1 November 2015; Revised 30 January 2016; Accepted 22 February 2016

DOI: 10.1002/dc.23467

Published online 9 March 2016 in Wiley Online Library (wileyonlinelibrary.com).

Table I. Summary of Non-Neoplastic Adrenal Lesions Diagnosed on FNAB.

Case number	Sex	Age	Laterality	Diagnosis	Special stain	Material aspirated	Necrosis	Modality	Clinical symptoms	Radiological findings	Clinical diagnosis	Hormones (prolactin and ACTH)
1.	M	23	L	TB	ZN	N	+	USG	Fever since 15 days, abdominal pain since 21 days	Heterogeneous enhancing lesion in left adrenal 3 cm × 3 cm × 3 cm	Adrenal adenoma?	normal
2.	F	21	R	TB	ZN/PAS	N	+	USG	Peripheral pigmentation	B/L Adrenal heterogeneous lesion with calcification: L-3.5 cm × 2 cm × 1.8 cm; R-2 × 1.8 cm × 1.5 cm	Addison's Disease? TB? Histoplasma?	NA
3.	M	37	B/L	H	PAS/ZN	N	+	USG	Septic shock	B/L Adrenal heterogeneous lesion with calcification: L-6 cm × 4 cm; R-6 cm × 3cm	Addison's Disease? TB? Histoplasma?	NA
4.	M	36	R	GI	ZN	N	+	USG	NA	NA	NA	NA
5.	M	56	R	H	-	P	-	USG	Fever, fatigue and cough with expectoration since 1 year	Right adrenal heterogeneous lesion with hepatosplenomegaly	NA	NA
6.	M	14	L	TB	ZN	N	+	USG	Fever, pain abdomen since 15 days	Heterogeneous lesion in left adrenal with foci of calcification	TB?	NA
7.	M	45	L	MY	-	BM	-	USG	Incidentally detected adrenal lesion	Heterogeneous lesion 7 cm × 6 cm × 6 cm	Myelolipoma?	NA
8.	M	38	L	TB	ZN	N	-	CT	Macroprolactinoma	B/L adrenal mass	Hematoma?	NA
9.	M	30	L	GI	ZN	BM	-	CT	Pain abdomen since 4 weeks	Heterogeneous mass with calcification in left adrenal	Addison's disease? TB?	Prolactin & ACTH raised, Cortisol normal
10.	M	70	R	H	PAS	N	+	USG	ATT 6 month back COPD with pleural based nodule	Left adrenal nodule 3 cm × 2 cm × 2 cm	TB?	NA
11.	M	38	R	GI	ZN	N	-	USG	Pain at right hypochondrium	Bilateral adrenal mass?metastasis	Malignancy?	NA
12.	M	74	R	AB	PAS	N	+	USG	Hemoptysis? Ca lung	Right adrenal mass	Malignancy?	NA
13.	M	48	L	H	ZN/PAS	N	+	USG	Type II DM, Fever, Loss of weight, Loss of appetite since 1 month	B/L adrenal heterogeneous lesion	Metastasis?	NA
14.	M	50	R	H	ZN/PAS	N	+	CT	NA	B/L adrenal hypodense lesion	TB? Histoplasma?	NA
15.	M	23	L	TB	ZN	N	+	CT	Weight loss	Heterogeneous lesion with areas of calcification 5x2cm	NA	NA
							+	CT	Pigmentation of hands		TB? Lymphoma?	NA

M = Male; F = Female; L = Left; R = Right; B/L = Bilateral; TB = Tuberculosis; H = Histoplasmosis; GI = Granulomatous inflammation; AB = Abscess, MY = Myelolipoma; ZN = Ziehl Neelsen stain; PAS = Periodic Acid Schiff; N = Necrosis; F = Fluid; BM = Blood mixed, CT = Computerised tomography, USG: Ultrasonography.

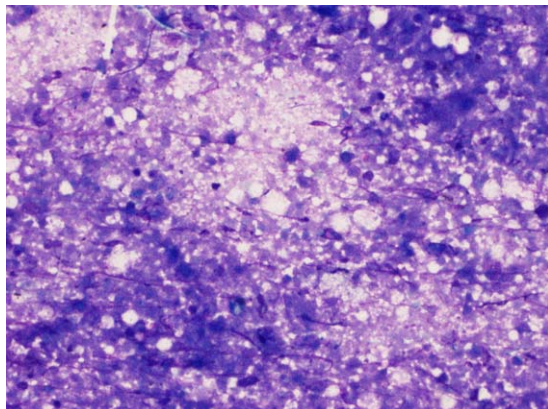


Fig. 1. Extensive necrosis. May–Grunwald–Giemsa (Giemsa stain 400×). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

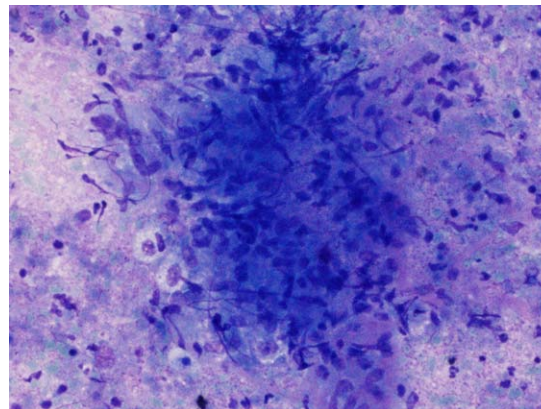


Fig. 2. Epithelioid cell granuloma in a necrotic background (Giemsa stain 400×). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Fourteen FNABs were unilateral with seven each done from left and right adrenal. Single FNAB was done from both the adrenals. In cases where necrotic material was aspirated, the syringes were sent for culture of mycobacteria. Total 4–6 slides were prepared and were stained with hematoxylin–eosin and May–Grunwald–Giemsa stains in equal proportions. In case of necrosis or granulomatous lesions, special stains like Ziehl Neelsen, Periodic acid Schiff's stains were done.

Results

Total of 160 adrenal FNABs were performed from June 2005 to May 2015. Table I summarizes the clinical features of these cases. Fifteen cases (9.3%) were diagnosed as non-neoplastic adrenal lesions. The mean age of these patients were 40.2 years (range = 14–74 year). All were male except one female. The average size of lesions undergoing FNABs under USG and CT guidance were 4.2 cm and 3.5 cm. Eleven patients had nonspecific constitutional symptoms, pyrexia, anorexia, and weight loss. In nine cases necrotic material were aspirated (Fig. 1). Special stains were simultaneously ordered in all cases in which either the aspirate was necrotic or Giemsa stained slides were destined in absolute alcohol and special stains were ordered if granulomas or any organism were identified on morphology (Fig. 2). In all necrotic aspirate, Ziehl Neelsen (ZN) stain were done for acid fast bacilli. ZN stain was positive in five cases which were reported as tuberculosis (TB). On ZN stain acid fast bacilli were seen as beaded organism bright pink in color (Fig. 3). In two cases even though epithelioid cell granulomas were sent, ZN stain could not reveal any acid fast bacilli even on extensive screening, these cases were reported as granulomatous inflammation. In five cases histoplasma were

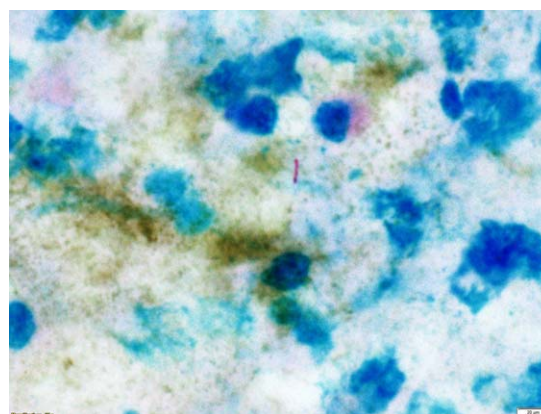


Fig. 3. Rod-shaped beaded acid fast bacilli (Ziehl Neelsen stain 1,200×). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

seen. Three of these cases yielded pus-like material on aspiration. ZN and Periodic Acid Schiff (PAS) stains were done in all of these necrotic cases. PAS stain was performed in all cases where histoplasma were identified morphologically. The capsule of histoplasma was bright pink on PAS stain. The histoplasma were also better highlighted on ZN stain, as the methylene blue stains the fungus.

In cases where histoplasma were seen the smears showed many histiocytes and giant cells along with epithelioid cell granuloma. Many intracellular and few extracellular 3–5 μm yeast-like fungal organism were seen. On PAS stain capsule was bright pink in color (Fig. 4). One of the patient diagnosed as histoplasmosis was human immune deficiency virus positive however, immune status of other patients were not known.

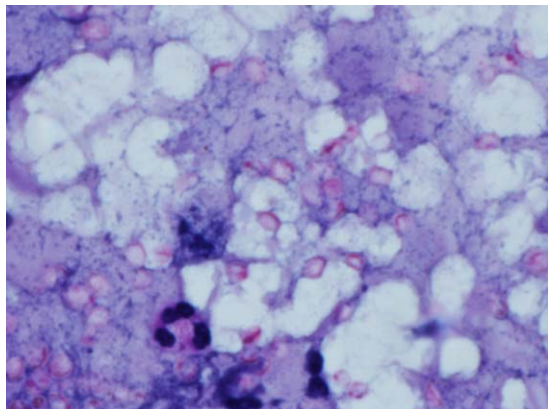


Fig. 4. Abundant histoplasma organism within the necrotic material. (Periodic Acid Schiff stain 1,200 \times). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

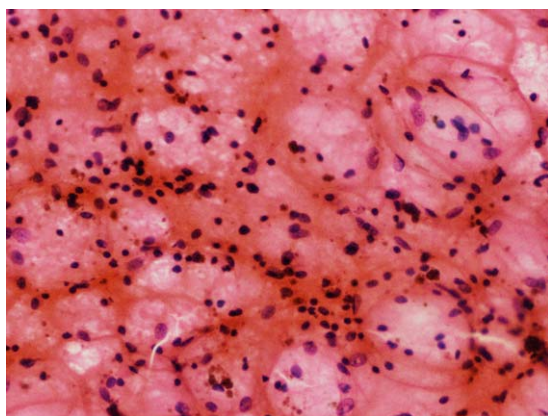


Fig. 5. Smears showing adipose tissue and bone marrow elements. (Hematoxyline and Eosin stain 400 \times). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

One case was diagnosed as myelolipoma, the smears showed adipose tissue and hematopoietic elements (Fig. 5).

Discussion

FNAB of adrenal gland is performed mostly in tertiary care center. Radiological guidance is required for precise localization of adrenal masses. FNAB being easy and economically cheap technique has become important diagnostic technique in the diagnosis of adrenal lesions. Clinical features along with bilateral involvement of adrenal glands and heterogeneous echotexture due to necrosis may indicate infection. However, only on the clinical and radiological basis exact nature of infection is not possible. Core biopsy of the adrenal gland should not be done as this may induce significant trauma and severe complications. Therefore, FNAB of the adrenal gland is a preferable and reliable technique in suspected non-functioning

and non-neoplastic adrenal gland lesions.^{1,2} In India, tuberculosis (TB) is the most common cause of adrenal insufficiency, and if we consider all cases of TB, adrenal involvement is seen in 46–56% of all cases.⁶

Histoplasmosis is another common infective adrenal lesion caused by *H. capsulatum* and needs to be differentiated from tuberculosis as their management is entirely different. The clinical manifestation of chronic disseminated histoplasmosis resemble those of other chronic infection such as TB. Usually these patients presents with low grade fever, weight loss, anorexia, night sweats, and with the features of adrenal insufficiency.⁷ In 99% cases infection is subclinical. Incidence is 2–5% in HIV patients. Only one case out of five histoplasma diagnosed cases was HIV positive. In 11 cases in this study presented with nonspecific complaints like fever, weight loss, and generalized weakness. Although histoplasma presents as bilateral adrenal masses in most of the cases, in our study only one case had bilateral presentation.

There is no reliable imaging feature to distinguish between various causes of bilateral adrenal masses. The radiological findings are not specific to histoplasmosis and may occur with other infections like TB, cryptococcosis, and in malignancy like metastases and lymphoma.⁸ Confirmatory diagnosis in all our cases were done on FNAB. A single case of myelolipoma was included which presented as adrenal mass incidentally detected. The patient presented with dull aching abdominal pain. There was no history of hypertension. Further workup revealed non-functioning adrenal mass. FNAB showed adipose tissue and hematopoietic elements. Myelolipoma is a rare adrenal lesion with few case reports in the literature. Incidence at autopsy reported in literature is 0.08–0.4%.⁹ With the use of non-invasive imaging its incidental detection has increased, reaching up to 7% of the adrenal masses.¹⁰

In conclusion, we have performed FNAB of 15 benign adrenal gland lesions by USG and CT scan guidance. We considered that FNAB is an easy, reliable, and minimally invasive method to diagnose and categorize the various benign non-neoplastic diseases of adrenal gland.

References

1. Fassina AS, Borsato S, Fedeli U. Fine needle aspiration cytology (FNAB) of adrenal masses. *Cytopathology* 2000;11:302–311.
2. Tirabassi G, Kola B, Ferretti M, et al. Fine-needle aspiration cytology of adrenal masses: A re-assessment with histological confirmation. *J Endocrinol Invest* 2012;35:590–594.
3. De Agustin P, Lopez-Rios F, Alberti N, Perez-Barrios A. Fine needle aspiration cytology of the adrenal glands: A ten-year experience. *Diagn Cytopathol* 1996;14:126–134.
4. Gangopadhyay M, Bhattacharyya NK, Ray S, Chakrabarty S, Pandit N. Guided fine needle aspiration cytology of retroperitoneal masses—Our experience. *J Cytol* 2011;28:20–24.
5. Mangal N, Sharma VK, Verma N, Agarwal AK, Sharma SP, Aneja S. Ultrasound guided fine needle aspiration cytology in the

- diagnosis of retroperitoneal masses: A study of 85 cases. *J Cytol* 2009;26:97–101.
6. Kochupillai N. Clinical endocrinology in India. *Curr Sci* 2000;79: 1061–1067.
 7. Dwivedi MK, Piparsania B, Issar P, Dewangan L. Disseminated histoplasmosis of adrenal gland. *Indian J Radiol Imaging* 2006;16: 651–652.
 8. Kumar N, Singh S, Govil S. Adrenal histoplasmosis: Clinical presentation and imaging features in nine cases. *Abdom Imaging* 2003; 28:703–708.
 9. Olsson CA, Kran RJ, Klugo RC, Selikowitz SM. Adrenal myelolipoma. *Surgery* 1973;73:665–670.
 10. Aso Y, Homma Y. A survey on incidental adrenal tumours in Japan. *J Urol* 1992;147:1478–1481.