Original Research

Results of Percutaneous Computed Tomography-Guided Biopsy of Adrenal Lesions and Spectrum of Computed Tomography Findings

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INTRODUCTION

The adrenal glands may be affected in a variety of conditions, including benign neoplasms, primary malignant neoplasms, metastasis, and infections. Tissue sampling is needed in cases where a diagnosis cannot be made on biochemical grounds and imaging. Percutaneous computed tomography (CT)-guided adrenal biopsy is a safe method for obtaining tissue specimen from adrenal lesions. Tuberculosis is common in developing countries and it affects the adrenal gland.

ABSTRACT

Objective: Adrenal enlargement occurs in various conditions such as infections, benign, and malignant neoplasms. Percutaneous computed tomography (CT)-guided adrenal biopsy is a safe method for obtaining tissue specimen in cases where diagnosis cannot be established on imaging and biochemical grounds. The study aims to evaluate diagnostic yield, accuracy, and complications of percutaneous CT-guided adrenal biopsies. Furthermore, CT findings of various adrenal lesions have been described.

Materials and Methods: Data of CT-guided adrenal biopsies performed from September 2009 to May 2019 were analyzed. Biopsies were performed on a 64-slice or a 128-slice multidetector CT scanner using a coaxial technique. Pathological and microbiological reports were retrieved from the hospital information system. Clinical details were obtained from clinical case records.

Results: CT-guided adrenal biopsies were performed in 48 patients, 37 males and 11 females. Adrenal insufficiency was present in 31 (64%) cases and bilateral adrenal glands were affected in 35 (73%). Biopsy yielded a diagnosis in 35 cases (72.9%). The final diagnosis was achieved in 43 (90%) cases. Combined accuracy of CT-guided biopsy for identifying malignancy and infection was 88.3%. Adrenal histoplasmosis (AH) was the most common entity diagnosed (44%). After combining histopathology and microbiology results, the sensitivity for diagnosing AH was 100%. One (2%) patient had a major complication in the form of intra-abdominal hemorrhage requiring transfusion. Local hematoma and mild stable pneumothorax were noted in one patient each.

Conclusion: Percutaneous CT-guided biopsy is a safe procedure for the diagnosis of adrenal lesions. It has good accuracy for diagnosing adrenal conditions such as infections and malignancies. However, the specific diagnosis of benign adrenal lesions was difficult to make. AH, tuberculosis, and metastasis have overlapping imaging findings.

Keywords: Adrenal, Computed tomography-guided biopsy, Histoplasmosis, Lymphoma, Tuberculosis
adrenal gland is also affected in disseminated histoplasmosis. More recently, adrenal histoplasmosis (AH) is being increasingly reported in our region. This retrospective study was conducted to evaluate the diagnostic yield, accuracy, and complications of percutaneous CT-guided adrenal biopsy. In addition, the spectrum of CT findings of various adrenal diseases including histoplasmosis has been described.

**MATERIALS AND METHODS**

Data of percutaneous CT-guided adrenal biopsies performed from September 2009 to May 2019 were retrospectively evaluated. Procedure details and CT images were retrieved from the radiology records. Pathological and microbiological reports were obtained from the hospital information system. Clinical details of the patient were obtained from clinical case records. Ethical approval was obtained from the Institute Ethics Committee with a waiver of consent. In most of cases, biochemical workup and imaging evaluation were done before the biopsy to rule out lesion such as pheochromocytoma, myelolipoma, and lipid-rich adenoma. Pediatric adrenal biopsies were not included in this study. All biopsies were performed on a 64-slice multidetector CT (MDCT) scanner (Brilliance CT, Philips Medical Systems, Cleveland, OH) or a 128-slice MDCT scanner (Somatom Definition AS; Siemens, Forchheim, Germany). In bilateral disease, biopsy was taken from the side, where lesion was larger, a direct straight approach was possible without injuring lung, pleura, or kidneys, and no major vessel was near the needle path. An 18G or 20G coaxial quick core biopsy needle set (Cook, Bloomington, Indiana, USA) or Bard Mission Core Biopsy Instrument (BARD, Arizona, USA) was used. A 20G needle was preferred as it is less traumatic.

The biopsy technique used is similar to that described in earlier studies. A short admission is done for all biopsy procedures and coagulation profile is obtained. Six to eight hours fasting is advised; however, necessary medications like antihypertensive drugs are allowed 5–6 h earlier with small amount of water. After obtaining informed consent, mostly patient is placed in prone position on CT table for a direct posterior approach or oblique posterior approach. A needle path that avoids diaphragm, kidney, aorta, and splenic vessels is chosen. Oblique posterior approach with CT gantry angulation avoids injury to the posterior costophrenic sulcus and superior pole of kidney. However, sometimes, a transpulmonary or transpleural route is the only option. The right adrenal gland biopsy can also be done in right decubitus position from posterior approach or in supine position by a transhepatic approach. Similarly, the left adrenal gland biopsy can be done in left decubitus position from posterior approach or supine position by a transgastric approach. Many authors prefer the target site down decubitus approach as it moves the diaphragm higher and reduces respiratory motion. The patient comfort is important to ensure that patient can tolerate the procedure for longer duration if needed.

After positioning the patient, a diagnostic contrast-enhanced CT is done if the adrenal lesion has a vessel in vicinity; otherwise, a non-contrast CT is enough for planning needle trajectory (tube voltage, 120 kV; tube current, 100–250 mAs depending on body habitus, slice thickness 1–2 mm). The patient should be trained to hold breath consistently, preferably in mid-inspiration during diagnostic scan and subsequent needle manipulations as it reduced the effect of respiration. In general, the biopsy is performed under local anesthesia. The introducer needle is advanced in small increments toward the lesion and frequent check scans are taken. The check scans should be taken in sequential mode, low-dose setting (100–120 kV, 30–50 mA) and covering just enough to visualize the needle and few extra slices above and below it. This reduces the radiation dose significantly. A useful tip for holding the introducer needle in desired position is using a sterile cloth drape as needle holder. For neoplastic lesions, it is important to target the solid viable portion which can be delineated using contrast agent; however, it does not matter much for infective lesions. After satisfactory needle placement, multiple cores are obtained by gentle tilting the needle so as to sample slightly different areas each time. Adequate specimen should be obtained for histopathology, microbiology, and immunohistochemistry depending on clinical suspicion.

In addition to histopathology, microbiological results for tubercular and fungal microscopy/culture were also available in cases where an infection was suspected. Since 2017, cartridge-based nucleic acid amplification test for tuberculosis became available at our institute and was performed for rapid results in addition to tubercular culture. A biopsy procedure was considered diagnostic if a definite diagnosis could be made from histopathology or microbiology, or the result helped in clinical decision-making and no further tissue sampling was needed. Diagnostic yield was calculated by dividing the number of biopsies that were diagnostic divided by the total number of cases. Cases with non-specific histopathology diagnosis such as adrenal cortical neoplasm, unremarkable adrenal cortical cells, predominant necrosis, and inconclusive or inadequate results were considered non-diagnostic, if no diagnosis was achieved with microbiological examination as well. Two cases of granulomatous lesion (microscopy/culture negative for tuberculosis, CB-NAAT not performed) were considered diagnostic and treated as tuberculosis as no fungal elements were seen on histopathology and fungal microscopy/culture results were negative. A biopsy procedure was classified as accurate if the pathological or microbiological results were concordant with the final diagnosis based on surgical excision, treatment response, or follow-up. Accuracy was determined for exact diagnosis as well as for
detecting malignancy and infection. Procedures that were non-diagnostic on biopsy and had no final diagnosis were excluded from the calculation of accuracy. Complications associated with the biopsy procedure were also recorded. CT findings in different types of adrenal lesions were evaluated. The longest dimension of the lesion on axial CT image, short-axis dimension, and laterality of lesions were recorded. The contour of the affected adrenal gland, presence of calcification, contrast enhancement pattern, and other associated findings were recorded.

RESULTS

CT-guided adrenal biopsies were performed in 48 patients, including 37 males and 11 females. In one patient, the biopsy procedure was repeated as the initial procedure was inconclusive. The mean age of patients was 55.3 years (SD 16.06, range 21–78 years). Out of 48 patients, 31 had adrenal insufficiency, 9 had normal plasma cortisol, and no workup for adrenal insufficiency was available in 8 patients. In patients without adrenal insufficiency or without adrenal workup, adrenal lesions were detected during workup for fever, abdominal pain, weight loss, generalized edema, recurrent urinary tract inflammation, inflammatory arthritis, staging, or follow-up for malignancy elsewhere in the body. Following comorbidities were noted: coronary artery disease in 2, chronic obstructive pulmonary disease in 1, diabetes mellitus in 12, diabetes mellitus with chronic liver disease in 1, diabetes mellitus with hypertension in 2, hypertension in 2, hepatitis B in 1, and no comorbidities in 27 patients.

The site of biopsy was left adrenal gland in 28 and right in 20 patients. Mostly, a posterior oblique approach was used in 21 patients. A straight posterior approach without transgressing lung or pleura was possible in 20 patients. A transhepatic route was used in 4, transpleural in 2, and translumbar in 1 patient. Minor complications were noted in 2 patients; small local hematoma in 1 and mild stable pneumothorax in 1. In one patient, intra-abdominal hemorrhage and shock requiring blood transfusion were noted. This was a case of large right adrenal mass infiltrating inferior vena cava, diagnosed as lymphoma on histopathology.

Results of histopathology and microbiology are described in Table 1. Diagnostic yield was 72.9% as biopsy results were classified as diagnostic in 35 and non-diagnostic in 13 cases. Final diagnosis was achieved in 43 cases and 5 cases lost to follow up [Table 2]. The final diagnosis was histoplasmosis in 19, tuberculosis in 8, metastasis in 6, lymphoma in 4, myelolipoma in 2, benign adrenal cortical neoplasm in 2, and adrenal cortical carcinoma in 2 patients. Five lost to follow up cases were excluded for calculation of accuracy. The diagnostic accuracy of CT-guided biopsy was 76.7% for the exact diagnosis (33/43), whereas combined diagnostic accuracy for detecting adrenal malignancy and infection was 88.3% (38/43), with 87% sensitivity and 100% specificity. In the non-diagnostic category (n = 13), final diagnosis was obtained in 8 cases only as 5 were lost to follow up; adrenal cortical carcinoma in 1, benign adrenal neoplasm in 2, metastasis in 2, tuberculosis in 2, and myelolipoma in 1. In lost to follow up cases, 3 cases were reported inadequate/inconclusive, 1 adrenal cortical neoplasm, and 1 as unremarkable lobulated adrenal cortical tissue.

The adrenal lesions were bilateral in 35 and unilateral in 13 patients, with mean longest diameter on axial image of

| Histopathology diagnosis                                      | Number of cases microbiological examination performed | Result of microbiological examination |
|---------------------------------------------------------------|------------------------------------------------------|---------------------------------------|
| Adrenal cortical malignancy (1)                               | 1                                                    | Negative                              |
| Adrenal cortical neoplasm (2)                                 | 1                                                    | Negative                              |
| Granulomatous lesion (2)                                      | 2                                                    | Negative*                             |
| Fungal infection (1)                                          | 1                                                    | Histoplasmosis (1)                    |
| Histoplasmosis (16)                                          | 16                                                   | Histoplasmosis (14), negative (2)     |
| Lymphoma (4)                                                 | 3                                                    | Negative                              |
| Myelolipoma (1)                                              | 1                                                    | Negative                              |
| Metastasis (4)                                               | 1                                                    | Negative                              |
| Difficult to differentiate between primary adrenal neoplasm and normal adrenal tissue (1) | 3 | Negative (2), tuberculosis (1)* |
| Unremarkable adrenal cortical tissue (4)                     | 3                                                    | Negative (2), tuberculosis (1)*      |
| Inconclusive/inadequate (7)                                   | 5                                                    | Negative (3), histoplasmosis (1), tuberculosis (1)* |
| Predominant necrosis (5)                                     | 4                                                    | Negative (1), histoplasmosis (1), tuberculosis (2)* |

*CB-NAAT not performed. Microscopy and culture negative for tuberculosis as well as fungus, *tubercular culture positive, *microscopy and CB-NAAT positive for tuberculosis, rifampicin sensitive, whereas culture negative, both cases culture negative, in one case, microscopy was positive and CB-NAAT positive, rifampicin sensitive, and in another case, microscopy negative and CB-NAAT positive, rifampicin resistant. Numbers in parentheses are number of patients. CB-NAAT: Cartridge-based nucleic acid amplification test.
53.1 mm. Internal hemorrhagic areas were noted in 1 adrenal
lesion. Associated findings on CT scan were observed in
18 patients; cirrhosis in 1, enhancing liver lesions in 1,
lung mass in 2, lung nodules in 1, mediastinal mass in
1, myelolipoma opposite adrenal gland in 1, pericardial
effusion and thickening in 1, pleural effusion in 4, renal
scarring in 1 [Figure 1], retroperitoneal lymphadenopathy
in 1, multiple splenic lesions in 2, and splenomegaly
without focal lesion in 2 patients. The most common lesion
was AH with all cases having adrenal insufficiency and
bilateral disease [Figures 2-5]. Two cases of AH also had
multiple hypoenhancing splenic lesions [Figures 2 and 3].
Six cases were finally proven to have adrenal metastasis
and 4 of them had an obvious primary malignancy [Figures 6
and 7]. Four cases were histopathologically proven to be large
B-cell lymphoma and 3 of them were bilateral [Figures 8
and 9]. In 3 cases of lymphoma, the adrenal was thought to
be primarily affected. The average gland size was much larger
in lymphoma cases compared to other conditions. One case
had an irregular outline with contiguous involvement of
inferior vena cava and multiple lung nodules [Figure 9]. The
spectrum of radiology findings in different adrenal diseases
is described in Table 3.

**DISCUSSION**

Biochemical workup and imaging helps in the confident
diagnosis of many adrenal lesions and biopsy is not
required.67 Most of lipid-rich adenomas, myelolipomas,
pheochromocytomas, hormone-producing adrenal lesions,
and operable adrenal cortical carcinomas are not subjected
to adrenal biopsy. However, in equivocal cases, a biopsy
is required for further management. Percutaneous CT-
guided biopsy is a safe and accurate procedure for the
diagnosis of adrenal lesions. Welch et al. have reported 90%
accuracy, 81% sensitivity, and 99% specificity of adrenal
biopsy.1 In our series, the accuracy rate for exact diagnosis
was 76.7%, whereas combined accuracy for detecting
adrenal malignancy and infection was 88.3%. In none of
the cases, a false-positive result was obtained, suggesting a
high specificity and negative predictive value. However, the
major limitation was the confident diagnosis of primary
adrenal neoplasms mainly benign ones. In 12% of cases of
our series, the pathological diagnosis was unremarkable
cortical adrenal tissue or adrenal cortical neoplasm, rather
than a specific diagnosis. Similar observations have been
reported by Paulsen et al. and Mazzaglia et al.68,9 Most of the
non-diagnostic cases in our series were either benign adrenal
neoplasms or tuberculosis. We believe many cases which
were lost to follow up were benign neoplasms and patient
stopped seeking medical attention due to lack of symptoms.
The reason for missing the diagnosis of tuberculosis before
2017 was probably poor detection of acid-fast bacilli on
microscopy and culture; however, since the introduction of
the nucleic acid amplification test, the diagnosis of adrenal
tuberculosis has improved.

The most common complication of adrenal biopsy is
hematoma formation.1,2 Sometimes, a pneumothorax may
also occur if the lung is transgressed. Complications are
reported in 0–12% of cases; however, most of them are minor
and need no intervention.1,2 Complications necessitating
further treatment are reported in 0.4–2% of cases. In
our series, two patients developed minor self-limiting
complications while one patient developed abdominal
hematoma requiring active management.

| Table 2: Comparison of result obtained from computed tomography-guided biopsy specimens with final diagnosis. |
|---------------------------------------------------------------|
| **Result obtained from CT-guided biopsy specimens**        | **Final diagnosis**                        |
| Diagnostic (35)                                             | Adrenal cortical carcinoma (1)             |
| Adrenal cortical malignancy (1)                             |                                    |
| Granulomatous (2)                                           | Tuberculosis (2)                         |
| Histoplasmosis (19)                                         | Histoplasmosis (19)                      |
| Lymphoma (4)                                                | Lymphoma (4)                            |
| Metastasis (4)                                              | Metastasis (4)                          |
| Myelolipoma (1)                                             | Myelolipoma (1)                         |
| Tuberculosis (4)                                            | Tuberculosis (4)                        |
| Non-diagnostic (13)                                         | Adrenal cortical carcinoma (1), lost to follow up (1) |
| Adrenal cortical neoplasm (2)                               | Benign adrenal neoplasm (1)              |
| Difficult to differentiate between primary adrenal neoplasm | Lost to follow up (1)                    |
| and normal adrenal tissue (1)                              | Metastasis (1), tuberculosis (1), lost to follow up (2) |
| Inadequate (1)                                              | Metastasis (1), tuberculosis (1)         |
| Inconclusive (4)                                            |                                    |
| Necrosis (2)                                                |                                    |
| Unremarkable adrenal cortical cells (3)                     | Myelolipoma (1), benign adrenal neoplasm (1), lost to follow up (1) |

CT: Computed tomography
In our series, bilateral adrenal glands were affected in 73% of cases. Common causes of bilateral adrenal masses, especially in the setting of adrenal insufficiency, are tuberculosis, histoplasmosis, and lymphoma. In addition to these diseases, we have also observed adrenal insufficiency in a case of adrenal metastasis where both adrenals were affected. CT finding of AH has been reported in many studies. The usual finding is bilateral symmetrically enlarged glands with peripheral enhancement and hypodense center. Calcification has been reported in some cases of AH. In our series, the AH cases showed preserved gland contour in 4 and oval contour in 15 cases. We believe that in the initial course of disease, the shape of adrenal gland is preserved despite of enlargement due to diffuse involvement, while later on it becomes oval. Regarding the contrast enhancement pattern, we have observed peripheral enhancing rim with central hypoenhancing component in 26% of cases of AH. This rim was uniformly thick in one case with small central hypoenhancing area and in 4 cases, it was thin with large hypoenhancing core, representing a varying degree of necrotic changes. In 5 cases of AH, the glands were diffusely hypoenhancing likely due to an advanced disease with near-complete necrosis. However, in 26% of AH cases rather than a central hypoenhancing pattern, multiple hypoenhancing
areas or heterogeneous enhancement was seen. On histopathology, out of 19, a confident diagnosis of AH was made in 16 cases, whereas 1 case was reported as fungal disease. Fungal microscopy and culture were performed in all these cases with positive results in 17 cases (89%). However, combination of histopathology and microbiology detected all cases of AH.

CT findings of adrenal tuberculosis are similar to those of AH. Adrenal tuberculosis is also reported to cause bilateral adrenal involvement with peripheral rim enhancement.\textsuperscript{[13-15]}

In our study, a thin peripheral enhancing rim was noted in 50% of cases of adrenal metastasis (3/6) and in 2 cases, a thick irregular enhancing rim was noted. Imaging wise these cases mimic infective etiology; however, usually, an associated lesion was present in lung, mediastinum, or liver.

Four cases were diagnosed as adrenal lymphoma with bilateral disease in three. These lesions were much larger in size in 3 cases, rounded in contour in 1, and irregular outer margin in 1 infiltrating IVC. Lesions were either showing homogenous or heterogeneous enhancement. A thin peripheral enhancing rim was not seen in any lymphoma case. Adrenal glands may be primarily or secondarily involved in lymphoma.\textsuperscript{[16-19]} Primary adrenal lymphoma is relatively rare, though cases have been
reported in the literature. Bilateral adrenal gland involvement, large soft-tissue masses, homogeneous or inhomogeneous enhancement, and tendency to infiltrate adjacent structure are well documented in primary adrenal lymphoma.\textsuperscript{[16,17]}

The role of an adrenal biopsy in a region with frequent granulomatous infections is not well documented. The results of this study suggest that a CT-guided adrenal biopsy is an excellent tool for the diagnosis of infectious disorders such as histoplasmosis and tuberculosis of the adrenal glands. The study has some limitations as it was a retrospective study and investigations were conducted by different radiologists, pathologists, and microbiologists. All diagnostic tools were not available in each case.

**CONCLUSION**

Percutaneous CT-guided biopsy is a safe and reliable technique for adrenal lesions, especially if histoplasmosis,
tuberculosis, lymphoma, or metastasis are suspected. It is less reliable for diagnosing benign adrenal neoplasms. AH occurs more commonly than tuberculosis in our setting, mostly presenting with bilateral adrenal masses and adrenal insufficiency. Lymphoma and metastasis are less common but should be included in differential diagnosis of bilateral adrenal masses. CT finding in AH and tuberculosis varies with the degree of the necrotic component; however, a peripheral enhancing rim with hypoenhancing core is a common picture. A biopsy is needed to differentiate between these conditions as radiological findings are often overlapping.

Declaration of patient consent

Institute Ethics Committee (IEC) permission obtained for the study.

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Conflicts of interest

There are no conflicts of interest.

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