Are CT and US imaging-guided percutaneous FNAs and/or spleen and focal splenic lesion tissue core biopsies safe and effective?

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ABSTRACT
The aim of this study was to evaluate the safety and effectiveness of computed tomography (CT) and ultrasound (US) imaging-guided percutaneous fine needle aspirations (FNAs) and/or spleen and focal splenic lesion tissue core biopsies in patients with splenomegaly and/or focal splenic focal lesions. The vascular interventional radiology records, clinical charts, laboratory and histopathology results of patients who underwent splenic FNAs and tissue core biopsies between January of 2016 and June of 2019 were retrospectively analyzed. These procedures success rate in making specific diagnoses and the frequency of related complications were documented. After conducting imaging-guided FNAs and tissue core biopsies, the diagnosis reached in 18 (90%) of the 20 (100%) patients. Of the 18 (90%) patients, tumoral and non-tumoral diagnoses were made in 10 (55%) and 8 (45%) patients, respectively. All procedures were achieved without major complications. In conclusion, CT and US imaging-guided percutaneous FNAs and tissue core biopsies are safe and effective for diagnosing the causes of splenomegaly and the nature of focal splenic lesions.

1. Introduction
The spleen is a vascular lymphoid organ located in the left upper side of the peritoneal cavity. The spleen participates in the body’s immune response against antigens and the removal of damaged blood cells (Lieberman, Libson, Sella, Lebensart, & Sosna, 2007). Splenomegaly and focal splenic lesions are encountered frequently in clinical practice. These conditions are often noted when imaging immuno-compromised patients, particularly while these patients are undergoing immunosuppressive therapy or harboring malignancies with metastatic splenic deposits (Schön, Görg, Ramaswamy, & Barth, 2006).

However, when metastatic deposits or infectious foci are seen in the spleen, other organs, particularly the liver and lymph nodes, tend to be involved. Occasionally, metastatic deposits are unexpectedly seen while working with patients with various clinical symptoms, such as patients with abdominal pain, fever, or generalized fatigue and weakness. Making a specific diagnosis of the cause of splenomegaly and focal splenic lesions is of paramount importance in treatment decisions and successful therapy. Therefore, several procedures have been established to obtain splenic tissues for laboratory and histopathology assessments. These procedures range from surgical splenectomy to splenic tissue sampling, either through surgical laparoscopy or under imaging guidance. Imaging guidance includes fine-needle aspirations (FNAs) and tissue core biopsies. Typically, imaging guidance is performed with either computed tomography (CT) or ultrasound (US) guidance (Lieberman et al., 2007).

Acquiring tissues reverse a number of purposes, including cytology evaluation, culture and sensitivity, or histopathology diagnosis, which is an everyday practice in interventional radiology. Tissues and samples were obtained from different body parts, including lung, bones, pancreas, liver, lymph node and many other organs under imaging guidance (Kang et al., 2007). Imaging guided percutaneous tissue sampling of the spleen dates back to 1916, when it was used to diagnose splenic involvement with visceral leishmaniasis (Lieberman et al., 2007). A relatively several clinical studies addressing the effectiveness and safety of obtaining tissue samples from the splenic parenchyma under imaging guidance (Kang et al., 2007; Lieberman et al., 2007; Muraca, Chait, Connolly, Baskin, & Temple, 2001). A publication has reported much lower complication rates with smaller needle diameters (≤18 gauge) (Gómez-Rubio et al., 2009). Diseases that commonly affect the spleen can pose a diagnostic challenge for the clinician, radiologist and pathologist and the reported diagnostic accuracy of splenic biopsy varies, ranging between 84% and 90% (Friedlander, Wei, Iyengar, & Moreira, 2008). More-recent series of percutaneous splenic biopsy have shown consistently low overall complication rates while maintaining relatively high diagnostic utility (Gómez-Rubio et al., 2009; Lucey et al., 2002;
McInnes, Kielar, & Macdonald, 2011). However, these studies have examined pooled data from both FNAs and core needle biopsies; in most instances, the total number of core needle biopsy performed was relatively small (Gómez-Rubio et al., 2009; Tam et al., 2008).

To the best of our knowledge, few large studies have focused exclusively on the diagnostic efficacy and complication rates associated with percutaneous image-guided core needle biopsy of the spleen. In addition, percutaneous image guided biopsies can lead to the preservation of the spleen, particularly in patients of the pediatric age group, where preservation of splenic functions becomes crucial (Muraca et al., 2001). For these reasons, we retrospectively analyzed the records of our institutions for specific patients who had undergone guided percutaneous FNAs and tissue core biopsies for splenomegalaly and/or splenic focal lesions. Consequently, the aim of this study was to evaluate the safety and effectiveness of CT and US imaging-guided percutaneous FNAs and/or spleen and focal splenic lesion tissue core biopsies in patients with splenomegaly and/or focal splenic focal lesions.

2. Material and methods

2.1. Selection and description of participants

The authors retrospectively reviewed interventional radiology records of King Fahad Medical City and King Khalid University Hospital between January 2016 and June 2019 to extract the number of patients who underwent imaging-guided percutaneous FNAs and/or tissue core biopsies of enlarged spleens and splenic lesions. The yield of the search was 20 patients. Their diagnostic imaging, interventional radiology, clinical, laboratory findings and pathology data were collected. Ethical approval was obtained from the local ethics committee of the two hospitals. Informed consent was acquired in all procedures after explaining the nature of the procedure, its alternatives and possible complications to the patient himself or his/her guardians in the case of pediatric patients. The authors confirmed that all medical devices used in this study were subjected to periodic quality control tests before use to avoid any error in the results obtained.

This study consisting of 20 patients; 12 (60%) females and 8 (40%) males. Study sample includes 7 (35%) pediatric patients (ranging in age from 2 to 10 years, with a mean age of 5 years) and 13 (65%) adult patients (ranging in age from 21 to 57 years with a mean age of 41 years). Clinical presentations include a fever for investigation in seven patients (all had focal splenic lesion, one patient known to have leukemia and one patient known to have lymphoma before the onset of fever). Five patients had splenomegaly without focal lesion (the diagnosis of splenomegaly occurred during the follow-up of Langerhans cell histiocytosis (LCH) disease in one patient, during an investigation of abdominal pain in three patients and during the work up of thrombocytopenia in one patient). Three patients were incidentally diagnosed with focal splenic lesions (during imaging for other purposes) and five patients were diagnosed with focal spleen lesions during periodic follow-up of their previously known malignant lesions (lymphoma in one patient, colon cancer in two patients, non-small lung cancer in one patient, and breast cancer in one patient too) (Table 1).

2.2. Patient preparation prior to percutaneous FNAs and/or spleen and focal splenic lesion tissue core biopsies

Patient preparation prior to percutaneous FNAs and/or spleen and focal splenic lesion tissue core biopsies closely resemble pre biopsy preparation for the other organs biopsy. Platelet counts normal range of 130–350 to

| No. | Patient age; gender | Clinical presentation | Availability of splenomegaly | Number of lesions | Size of the largest lesion (cm²) |
|-----|---------------------|-----------------------|-----------------------------|-------------------|---------------------------------|
| 1   | 2 years; male       | Splenomegaly with Langerhans cell histiocytosis (LCH) | Yes/No                      | 0                 | -                               |
| 2   | 23 years; male      | Fever                 | No                          | 1                 | 6 cm²                           |
| 3   | 43 years; female    | Myalgia and fatigue   | No                          | >10               | 2 cm²                           |
| 4   | 3 years; female     | Splenomegaly and thrombocytopenia | Yes           | 0                 | -                               |
| 5   | 37 years; male      | Known Hodgkin's disease (HD) | No                          | 8                 | 3 cm²                           |
| 6   | 32 years; male      | Known lymphoma in remission | No                      | >10               | 2.5 cm²                         |
| 7   | 10 years; female    | Splenomegaly with abdominal pain | Yes         | 0                 | -                               |
| 8   | 8 years; female     | Splenomegaly with abdominal pain | Yes         | 0                 | -                               |
| 9   | 4 years; female     | Fever and on chemotherapy for leukemia | No                  | >10              | 0.3 cm²                         |
| 10  | 32 years; male      | Acute myeloid leukemia (AML) in remission | No          | >10              | 0.5 cm²                         |
| 11  | 4 years; male       | Fever                 | No                          | 2                 | 3 cm²                           |
| 12  | 50 years; female    | Incidental splenic lesions | No                          | 3                 | 5 cm²                           |
| 13  | 50 years; male      | Known colon cancer    | No                          | 3                 | 3 cm²                           |
| 14  | 48 years; female    | Incidental splenic lesions | No                      | 2                 | 3 cm²                           |
| 15  | 52 years; female    | Known breast cancer   | No                          | 3                 | 4 cm²                           |
| 16  | 57 years; female    | Generalized weakness  | No                          | 6                 | 3 cm²                           |
| 17  | 47 years; female    | Known lung cancer     | No                          | 4                 | 3 cm²                           |
| 18  | 54 years; female    | Known colon cancer    | No                          | 3                 | 4 cm²                           |
| 19  | 21 years; female    | Fever and malaise     | No                          | 5                 | 2 cm²                           |
| 20  | 4 years; female     | Splenomegaly and thrombocytopenia | Yes         | 0                 | -                               |
500–900 × 10^9/L and coagulation profile, which includes, prothrombin time (PT) normal range 10–13 Sec, activated partial thromboplastin time (APTT) normal range 28–42 Sec and international normalized ratio (INR) normal range, 0.9–1.2 were evaluated in all patients (Balduini & Noris, 2014). These results were accepted in case they were within 48 hours prior to the appointment for FNAs and/or tissue core biopsies. Two patients had a platelet count of <50 × 10^9/L for which they received platelet transfusion before and during the procedure. One patient had an INR above the accepted value necessitating transfusion of four units of fresh frozen plasma prior to and during taking the biopsy. When possible, aspirin and clopidogrel were stopped 5 days pre biopsy, and fractionated heparin withheld for 24 hours.

Before the biopsy, patients were asked to provide a telephone number so that a radiology nurse could contact them within 24, 48 and 72 hours of the procedure to assess for potential complications, including continuous bleeding from the biopsy site, shortness of breath, pain at the biopsy site ≥6 on a scale from 1 to 10, erythema, swelling, and fever greater than 38°C. Minor complications included pain-requiring analgesia and asymptomatic bleeding identified incidentally on post procedural imaging. Major bleeding complications were those scored at or above grade 3 according to the National Institutes of Health’s Common Terminology Criteria for Adverse Events, version 4.0 (National Institute of Health [NIH], 2009).

Patients should be fasting for 8 hours prior to administration of the local anesthesia. In the pediatric age group undergoing FNAs and/or tissue core biopsies, the local anesthetic used was intravenous Lidocaine (maximum dose based on the patient’s age and weight, Pharmaceutical solution industry, Jeddah, Saudi Arabia) while in adult patients we used intravenous Fentanyl citrate (25–100 mcg, Janssen pharmaceutical, Beerser, Belgium) and Midazolam (1–2.5 mg, Hikma pharmaceutical, Amman, Jordan). Emergency resuscitation equipment was always being located nearby, and oxygen was administered to the patient via nasal prongs. Post biopsy, the patient’s vital signs and biopsy site should be checked every 15 minutes for the first hour and every 30 minutes for the next 3 hours. Each patient was closely monitored for 4 hours, and if there were no signs or symptoms suggestive of a complication, discharge home is possible after biopsy. The blood pressure, pulse, oxygen saturation and pain status for all patients were continuously monitored by the anesthesiologist or by an assigned interventional nurse based on the mode of anesthesia used.

2.3. CT and US imaging-guided percutaneous FNAs and tissue core biopsy procedures

All imaging data for each patient were reviewed with the attention paid to whether other organs, which were more routinely accessed, for tissue sampling were involved or not. CT and US imaging-guided percutaneous FNAs and tissue core biopsy procedures were done in all patients by one interventional radiologist had 10 years of experience. While the rest of the team, including radiographers, interventional radiology nurse, anesthesiologist and cytotechnologist have varying experience ranging from 10 to 15 years. If CT is the modality of choice, a spiral non-contrast CT (128-slice data acquisition Somaton CT scanner, Siemens, Germany) was performed of the spleen with a radiopaque marker or grid over the area of interest to identify the shortest and safest route for biopsy. Once the route had been identified, the skin entry site was marked using the CT gantry laser light and the radiopaque grid for the Z and X coordinates. Both conventional CT and CT fluoroscopy were feasible for needle and catheter insertion. It was important to confirm safe needle trajectory and needle placement during splenic biopsy under CT. It was preferable to minimize the number of times the splenic capsule was traversed by the access or biopsy needle, and so the needle trajectory was optimized prior to entering the spleen; in particular, pneumothorax and hematoma formation should be sought on all images. The greatest source of radiation exposure to the interventional radiologist was the scatter radiation from the patient. Generally, controlling patient dose also reduces scatter and limits operator dose. In this study, our purpose of radiation protection tools was to improve interventional radiologist safety without impeding the procedure or jeopardizing the patient’s safety. The availability of architectural shielding, equipment mounted shields and personal protective devices were confirmed before starting any CT imaging-guided percutaneous FNAs and tissue core biopsy procedures. Personal protective devices used include aprons, thyroid shields, eyewear and gloves. These personal protective devices were typically 0.25 mm lead-equivalent so that, when worn, the double thickness anteriorly provides 0.5-mm lead-equivalence as reported by Miller et al. (2010).

US modality (HDI 5000, Philips Medical Systems, Netherlands) with 2–5 MHz sector transducer was used in 11 (55%) patients while (Sonoline Antares, Siemens, Germany) with 2–6 MHz sector transducer was used in the rest 9 (45%) patients. The spleen was thoroughly scrutinized by US while a patient in right posterior oblique position before taking the biopsy to select the path of the needle to the enlarged spleen in case of splenomegaly or to the site of the focal lesion if present. Color Doppler was used to ensure there were no major vessels along the planned biopsy tract. The drainage procedures were performed using US on a CT table. This allows quick catheter placement and immediate confirmation of the adequacy of drainage.
at a single visit. If US was not sufficient for image guidance, CT was used for needle or catheter guidance with minimal disruption to the patient. One of the advantages of CT over US is that it lessens the risk of bowel transgression and allows better visualization of deep-seated lesions or collections, thus reducing the risk of unintentional injury to intervening organs or vessels. The use of either CT or US was left to the discretion of the performing radiologist, with consideration given to the location (e.g. Central or peripheral), size, and accessibility (e.g. Presence of overlying bowel or kidney) of the target lesion. In general, large, bulky lesions were targeted by CT and smaller technically challenging lesions were triaged to US. Short biopsy tracks that traversed as little splenic parenchyma as possible were preferred.

After the procedure, the biopsy field was sterilized with aseptic/bactericidal solutions. The FNAs were performed with 22 and 25 gauge spinal needles; 9 cm long (Kawamoto corporation, Osaka, Japan) for culture and sensitivity purposes and cytology, respectively. Once the FNAs spinal needle was placed within the target, the stylet will remove completely, then several in and out thrusts of the needle were made within the target. The needles are self-aspirating and thus used without suction. The needle was then removed and connected to a sterile and empty syringe, then handed to the cytotechnologist to prepare for cytology smears. If the infectious process was suspected then the content of the spinal needle was flushed into a sterile container for culture and sensitivity purposes. All needles were used only once. The peripheral part of the target lesion aimed to avoid sampling the center, which could be necrotic. The number of needleling for FNAs were 4 times for cytology and twice for each culture and sensitivity. Therefore, the total number of needles passing through the splenic parenchyma for FNAs was 44 times (8 for cytology with 25 gauge spinal needles and 36 for cultures and sensitivity purposes with 22 gauge spinal needles).

The tissue core biopsies were performed with tissue cutting, automated biopsy guns. Based on their availability at the time of the procedure, two varieties of biopsy guns were used. One was Bard Monopty (18 gauge, 16 cm long, 22 mm penetration depth and 1.7 cm length of sample notch; disposable core biopsy instrument, Bard peripheral vascular, Inc). The second one was BioPince (18 gauge, 15 cm, with adjustable length of sample notch; full core biopsy instrument, Angiotech full core-medical device technologies Inc). The needle for the tissue core biopsy was passed through the splenic parenchyma and its capsule each time for a new tissue core biopsy, i.e. Coaxial procedure was not employed. The number of passes in tissue core biopsies was 3 in 12 procedures and 2 in 6 procedures. This variation was based on an assessment of the size of the specimen obtained; if it looks sizable enough to be suitable for pathology processing with two passes with the 18-gauge biopsy gun, then a third pass was not done. During and 5 minutes after every procedure, the spleen and its vicinity were carefully assessed for hematoma. The sample size of the tissue obtained using tissue cutting, automated biopsy guns varies due to a number of factors, such as: i) the needle placement within the target, ii) the consistency of the targeted tissue, and iii) the variety of the biopsy gun.

After FNAs and tissue core biopsy procedures, all patients had close observation while in strict bed rest for 6 hours. Monitoring included pain status, blood pressure, pulse, oxygen saturation and swelling over the FNAs and/or the tissue core biopsy sites. They were recorded on a designated interventional radiology sheet every 15 minutes for 2 hours, then every 30 minutes for 4 hours. Eleven patients had been admitted to the hospital for the intended procedures due to lack of radiology day units (RDUs) in the two hospitals and nine patients were already in the hospital for the work up of their diseases. All patients were seen at the end of the day by the interventional radiologist and their vital signs and clinical status were documented in the chart to assess them for possible post procedure complications particularly bleeding. The interventional radiology nurse on duty, the following day contacted the ward to check on each patient for the same goal. Interventional radiology records and chart review confirmed that no major complications resulting in significant morbidity or mortality related to FNAs and/or tissue core biopsies of the enlarged spleen or the focal splenic lesions. The laboratory and pathology records, which include the results of cytology, aerobic and anaerobic culture and sensitivity, fungal and acid-fast bacilli (AFB) cultures and sensitivities, the histopathology of the tissue core biopsies and other obtained specimens were reviewed and recorded for each patient.

2.4. Statistical analysis

All measurable data were initially summarized as a mean±standard deviation (SD) in a form of comparison tables. Statistical analysis was performed using the standard Statistical Package for the Social Sciences (IBM Corporation, Armonk, NY, USA) version 20 for windows. The statistical diagnostic test was used to detect sensitivity, specificity and accuracy of CT and US imaging-guided percutaneous FNAs and tissue core biopsies in patients with splenomegaly and/or focal splenic focal lesions. A biopsy was considered a true positive if the result was corroborated histocytologically by splenectomy or biopsy of tissue obtained from another site or if the result dictated
Further clinical therapy. A biopsy was considered a true-negative if the benign result was confirmed by splenectomy, if it resulted in a clinical decision not to treat a patient for malignancy, or if ensuing imaging studies showed signs of stability or benignity. False-negative or false-positive biopsies were those whose results were contradicted by alternative tissue sampling or clinical or imaging follow-up or both. These classifications were used to calculate specificity, sensitivity and accuracy.

3. Results

After imaging-guided FNAs and tissue core biopsies, diagnoses were reached in 18 (90%) patients out of the 20 (100%). In the current study, all patients underwent 30 percutaneous FNAs and tissue core biopsy procedures; 12 (40%) of patients underwent FNAs and 18 (60%) underwent tissue core biopsies. In addition, 10 (50%) patients had both FNAs and tissue core biopsy procedures in the same setting. Tissue core biopsies were performed in all patients, possibly having tumors and FNAs -especially for cultures- every time infectious process was in question. No patient had to have the procedure performed twice. FNAs were performed for cytology in two patients, while FNAs for cultures and sensitivity (including aerobic and anaerobic, AFB and fungal) were applied in 12 (60%) patients (Table 2).

With respect to the 18 (90%) patients who were diagnosed after imaging-guided FNAs and tissue core biopsies. Tumoral and non-tumoral diagnoses were made for 10 (55%) and 8 (45%) patients, respectively. All 7 (35%) patients with febrile illnesses to be investigated had focal splenic lesions. One neutropenic patient, while on chemotherapy for leukemia, underwent diagnostic CT and US, followed by FNAs. The cytology revealed abundant neutrophils and cellular debris consistent with micro-abscesses. The cytology of another patient, who was in remission post-therapy for leukemia, but had a fever, was similar. Both patients’ cultures grew candida albicans, and the diagnosis of micro-abscesses due to candida albicans was established (Figure 1).

The diagnosis of lymphoma was made in 3 (15%) patients. Two tissue core biopsies in the first patient with a Hodgkin’s disease (HD) in remission were clinically suspected to have recurrence of the disease. This suspicion was confirmed, as the patient had atypical lymphoid infiltrates with Hodgkin’s lymphoma, specifically the nodular lymphocyte predominant type. Aspirations of culture and sensitivity were not acquired due to the high clinical suspicion of recurrent lymphoma. The second patient was newly diagnosed HD following the tissue core biopsy. The third patient, presented with a presumed diagnosis of visceral leishmaniasis, had negative cultures in his single 6 cm lesion. However, histopathology of the tissue core biopsies in these three patients showed partially infarcted splenic tissues with mixed inflammatory cell infiltrates with predominant macrophages/histiocytic infiltrates, as well as extramedullary hematopoiesis. The flow cytometric evaluation revealed features consistent to T-cell lymphoma (Figure 2).

| No. | Patient age; gender | Diagnosis before FNAs and/or tissue core biopsies | Either FNAs and/or tissue core biopsies | Diagnosis after FNAs and/or tissue core biopsies |
|-----|---------------------|-------------------------------------------------|----------------------------------------|-----------------------------------------------|
| 1   | 2 years; male       | Langerhans cell histiocytosis (LCH)             | Both                                   | Not diagnostic (ND)                           |
| 2   | 23 years; male      | Pyrexia of unknown origin (PUD)                | Both                                   | T-cell lymphoma                              |
| 3   | 43 years; female    | Suspected lymphoma                             | Tissue core biopsy                     | Splenic hemangiomias                         |
| 4   | 3 years; female     | Spleenomegaly with thrombocytopenia            | Both                                   | Visceral leishmanias                         |
| 5   | 37 years; male      | Hodgkin’s disease (HD) in remission with fever and multiple splenic lesions | Both                                   | Recurrence of Hodgkin’s disease (HD)          |
| 6   | 32 years; male      | Lymphoma                                       | Both                                   | Chronic granulomatous inflammation           |
| 7   | 10 years; female    | Spleenomegaly                                  | Both                                   | Visceral leishmanias                         |
| 8   | 8 years; female     | Spleenomegaly                                  | Both                                   | Visceral leishmanias                         |
| 9   | 4 years; female     | Acute myeloid leukemia (AML) and multiple small lesions in spleen. | FNAs                                   | Micro-abscesses due to candida albicans      |
| 10  | 32 years; male      | Acute myeloid leukemia (AML) and remission, with systemic candidiasis | FNAs                                   | Micro-abscesses due to candida albicans      |
| 11  | 4 years; male       | Viral infection with spleenomegaly             | Both                                   | Ruled out malignancy and infections          |
| 12  | 50 years; female    | Focal splenic lesion                           | Tissue core biopsy                     | Not diagnostic (ND)                          |
| 13  | 50 years; male      | Colon adenocarcinoma                           | Tissue core biopsy                     | Colon adenocarcinoma                         |
| 14  | 48 years; female    | Incidental splenic lesions                     | Tissue core biopsy                     | Breast cancer with splenic metastasis        |
| 15  | 52 years; female    | Known breast cancer with focal splenic lesion for investigation | Tissue core biopsy                     | Breast cancer with isolated splenic metastasis |
| 16  | 57 years; female    | Focal splenic lesions                          | Tissue core biopsy                     | Lymphoma                                     |
| 17  | 47 years; female    | Known lung cancer post therapy with splenic lesions | Tissue core biopsy                     | Recurrent lung cancer                        |
| 18  | 54 years; female    | Known colon cancer post therapy with splenic lesions | Both                                   | Recurrent colon cancer                       |
| 19  | 21 years; female    | Focal splenic lesions for diagnosis            | Both                                   | Tuberculosis (TB)                            |
| 20  | 4 years; female     | Spleenomegaly, thrombocytopenia and abdominal pain | Tissue core biopsy                     | Visceral leishmanias                         |
Among the results there was one patient with fever and had histopathology confirmation of tuberculosis (TB) with granulomas and positive AFB stain and cultures. In addition, a febrile pediatric patient had a histopathology with unremarkable white and red pulps with negative lymphoma panel immunohistochemistry (IHC), and a negative immunostaining for cytomegalovirus and Epstein-Barr virus (EBV). The various cultures of the focal lesion were negative. Therefore, the procedures were non-contributory to make a final diagnosis. Furthermore, the histopathology of the splenic tissue samples in another patient with splenomegaly revealed Leishman-Donovan bodies, which contributed to a diagnosis of splenic leishmaniasis (Figure 3). One of the patients in the study sample with splenomegaly, was known to have LCH, had negative cultures, but granulomas with areas of hemorrhage and fibrosis, which were possibly due to blood transfusions, evident on histopathology. There were no significant Langerhans cells in morphology or immunohistochemical stains. However, stains for common histiocytes were strongly positive. These findings were not consistent with a specific diagnosis. Therefore, the patient underwent surgery for splenectomy. A histopathology of the spleen was consistent with secondary hypersplenism with considerable hemosiderin laden macrophage infiltration and Gamma-Gandy body formations. In the rest of the samples, there were three patients with incidentally discovered splenic lesions. One of these patients, whose histopathology diagnosed with splenic hemangiomas, had over than 10 lesions and was thought to have lymphoma (Figure 4). In addition, another patient of them had a histopathology diagnosis of lymphoma after tissue core biopsies, while the third patient was diagnosed with metastatic adenocarcinoma due to primary breast malignancy. This diagnosis was confirmed by a mammography and breast US, and with a subsequent biopsy of the breast lesion. In addition, one patient had

Figure 1. A 32-year-old male leukemic patient with micro-abscesses. (a) Axial CT of the abdomen shows innumerable focal hypodense lesions in throughout the splenic parenchyma. (b) US guided FNAs 25 gauge needle (white arrow) within the 3 mm lesion.

Figure 2. A 23-year-old male patient presented with fever. (a) Reformatted coronal CT image of the abdomen reveals 6 cm, single lesion (arrowhead), the periphery of which was biopsied with (b) US guided tissue core biopsy 18-gauge biopsy gun (white arrow). The diagnosis was T-cell lymphoma.
a known malignant tumor and focal splenic lesions that discovered during imaging follow-up. Lastly, another patient with known treated lymphoma underwent a tissue core biopsy. The histopathology showed chronic granulomatous inflammation with no evidence of lymphoma. No AFB or fungal elements were noted in this patient. The rest - colon cancer in two patients, lung cancer in one patient and breast cancer in one patient- underwent tissue core biopsies, which revealed recurrences of their previously treated malignancies.

With reference to the minor and major complications in study samples due to imaging-guided FNAs and tissue core biopsies. It was found that only 3 (15%) patients had left upper quadrant pain requiring intravenous analgesia for less than 24 hours. These were considered as a minor complication related to the procedures. None of the patients developed major complications, particularly hemorrhage of injury to adjacent organs. Eleven patients, who were admitted specifically for the intended procedure, were discharged from the hospital 24 hours from the procedure time in stable condition. The other 9 (45%) patients were already in hospital during the discovery of the splenomegaly and the focal splenic lesion, therefore the procedures were part of the in-hospital work up for their illnesses.

In all patients, the final diagnosis was confirmed by splenectomy or by pathology proven diagnoses from a tissue acquisition of an alternative site. CT and US imaging-guided percutaneous FNAs and tissue core biopsies of the spleen yielded adequate diagnostic tissue in 18 of these 20 cases. In our 20 biopsies, the sensitivity was 94.74% (95% confidence interval (CI), 73.97% to 99.87%), the specificity was 100.00% (95% CI, 15.81% to 100.00%) and the accuracy was 95.24% (95% CI, 76.18% to 99.88%) for both FNAs and tissue core biopsies. Their positive predictive value (PPV) was 100.00% and the negative predictive value (NPV) was 66.67%. Furthermore,
4. Discussion
In contrast to the widely used imaging guided FNAs and tissue core biopsies in tissue sampling of organs for miscellaneous purposes, such procedures, in the setting of focal splenic lesions or diffusion of homogeneous splenomegaly, were not often performed by interventional radiologists. This lack of use is, in part, due to the low incidence of primary and secondary metastatic lesions affecting the spleen (Kang et al., 2007; Lieberman et al., 2003). The worry of catastrophic hemorrhagic complications, due to the high blood flow within the splenic parenchyma, plays a major role in influencing interventional radiologists’ decisions not to perform splenic tissue sampling (Kang et al., 2007; Lieberman et al., 2003). On top of these reasons, and peculiar to our region, was the diverse inhomogeneity in clinical practices among health specialists. This inhomogeneity means that consultants use procedures they are familiar with rather than be innovative and follow updated and already proven safe approaches. It seems that major complications with splenectomies are more widely accepted compared to major complications encountered in imaging guided splenic tissue sampling. The experience of interventional radiologists is still major hesitation in accepting imaging procedures. This hesitance was prevalent despite literature supporting the safety and accuracy of imaging guided splenic tissue sampling in the appropriate clinical setting (Muraca et al., 2001).

Focal splenic lesions, diffuse enlargement and splenomegaly were caused by a wide spectrum of malignant and benign disorders that may affect the spleen in isolation or as part of a systemic illness. Malignant diseases include lymphoma as HD and non-Hodgkin’s lymphoma (NHL), leukemia and metastasis (particularly in the ovaries, gastrointestinal tract, breasts, lungs and melanoma). Non-malignant conditions include infarcts, hamartoma, hemangiomas, sarcoidosis, TB and abscesses (Cavanna et al., 2007). In the majority of cases, focal lesions were encountered during imaging evaluation of patients presenting fever symptoms in an investigation, or during imaging of a known or suspected malignancy. In a few circumstances, these lesions were discovered incidentally on cross-sectional imaging when evaluating a patient for a seemingly unrelated clinical issue. Some focal lesions were discovered while a patient was receiving immune-suppressive therapy for malignancy. Altered and lowered immunity makes affected patients highly susceptible to opportunistic infectious organisms and intra-splenic abscess formation. Therefore, whether a patient has a known malignancy or was suspected to have one or was in immune compromised condition, it is of supreme importance to make a precise diagnosis, so that treatment to be effective. Often, by the time that there is a focal abnormality in the spleen, the cross-sectional imaging detects additional abnormalities in other organs, the tissue of which is more routinely accessed for tissue sampling with FNAs and tissue core biopsies (Cavanna et al., 2007).

The results of the current study (Table 2) were not different from the results of other studies (Lieberman et al., 2003; Lucey et al., 2002). In the current study, all patients underwent 30 percutaneous FNAs and tissue core biopsy procedures; 12 (40%) of patients underwent FNAs and 18 (60%) underwent tissue core biopsies. In addition, 10 (50%) patients had both FNAs and tissue core biopsy procedures in the same setting (Table 2). The splenic parenchyma was transgressed 92 times, 48 (52.2%) times with 18 gauge tissue core biopsy needles, 8 (8.7%) times with 25 gauge spinal needles and 36 (39.1%) times with 22 gauge spinal needles for FNAs. The reviews of radiology records and chart confirmed that none of the patients developed major complications, particularly hemorrhage of significant injuries to adjacent organs. Only 3 (15%) patients had minor complication in a form of left upper quadrant pain. Their discomfort was controlled with intravenous analgesia for less than 24 hours, which did not necessitate an extension of their in-hospital stay. They underwent US examination of the spleen and the rest of the abdomen the following morning to ensure that there was no splenic or perisplenic hematoma. Much more, the FNAs and tissue core biopsy procedures were able to make a precise diagnosis in 18 (90%) of the 20 patients. The current result parallels previously reported studies about safety and efficacy of splenic parenchymal tissue sampling with 20–23 gauge needles under CT and US guidance (Civardi et al., 2001; Lal, Ariga,Gattuso, Nemcek, & Nayar, 2003; Lieberman et al., 2003; Lucey et al., 2002; Tam et al., 2008). Uncontrolled bleeding post-splenic biopsy was reported in literature and this complication could be managed with emergency surgical splenectomy (Civardi et al., 2001; Sammon, Twomey, Crush, Maher, & O’Connor, 2012; Yardeni, Polley, & Coran, 2004). Trans-arterial embolization (TAE) using permanent or temporary embolic agents for traumatic or iatrogenic intra-abdominal and splenic bleeding post trauma is well established and is widely practiced within the medical community (Raikhlin, Baerlocher, Asch, & Myers, 2008). Mortal sepsis has been reported in children post-splenectomy (Yardeni et al., 2004). In our series, no patient was complaining of significant bleeding. However, every attempt should be made to preserve spleens, especially in children, because of the major role of the spleen plays in battling infectious organisms.
According to McInnes et al. (2011) the percutaneous image-guided biopsy of the spleen showed sensitivity of 86.8% (95% CI, 78.2% to 92.4%) and specificity of 96.8% (95% CI, 90.4% to 99%) for tissue core biopsy alone and sensitivity of 84.1% (95% CI, 77% to 93.3%) and specificity of 92.5% (95% CI, 35.6% to 89.4%) for FNAs. Olson et al. (2016) reported that among 91 of 97 patients for whom the tissue core biopsies yielded a diagnosis of the spleen, accuracy was 94.5% (95% CI, 87.6%–98.2%), sensitivity was 90.7% (95% CI, 79.7% to 96.9%) and specificity was 100% (95% CI, 90.5% to 100%). The values mentioned in the previous two studies could be compared to what we found in our research results, where in our 20 biopsies, sensitivity was 94.74% (95% CI, 73.97% to 99.87%), specificity was 100.00% (95% CI, 15.81% to 100.00%) and accuracy was 95.24% (95% CI, 76.18% to 99.88%) when using FNAs and tissue core biopsies together. Furthermore, a sensitivity was 94.12% (95% CI, 71.31% to 99.85%), specificity was 100.00% (95% CI, 2.50% to 100.00%) and accuracy was 94.44% (95% CI, 72.71% to 99.86%) when applied tissue core biopsies alone compared to a sensitivity of 92.31% (95% CI, 63.97% to 99.81%), specificity of 100.00% (95% CI, 2.50% to 100.00%) and accuracy of 92.86% (95% CI, 66.13% to 99.82%) for FNAs.

The current study was inherently limited by its retrospective nature. The cataloging of complications was limited by the lack of standardized definitions in the literature, because many authors create their own definitions and stratifications. We categorized major complications, according to the definitions set forth by the National Institutes of Health (NIH) (National Institute of Health, 2009). Minor complications, including pain requiring analgesia and asymptomatic minor bleeding, were included because that has been the convention in other literature on the subject; whether these constitute true complications is subject to debate (Lieberman et al., 2003; McInnes et al., 2011; Tam et al., 2008).

5. Conclusion

In conclusion, CT and US imaging-guided percutaneous FNAs and tissue core biopsies are safe and effective procedure that should be used more frequently in clinical practice for diagnosing the causes of splenomegaly and the nature of focal splenic lesions. In addition, efforts should be made in every medical centers or hospitals so that the interventional radiologists performing the biopsy should have more experience and comfort with CT and US imaging-guided percutaneous FNAs and tissue core biopsies of organs such as the spleen because it result in the effective diagnosis of splenomegaly and focal splenic lesions. The data presented in this study support the use of CT and US imaging-guided percutaneous FNAs and tissue core biopsies of the spleen as a safe alternative to splenectomy, with a high overall diagnostic accuracy and an acceptable safety profile without major complications.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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