SHORT REPORT

Radiologically guided percutaneous core needle biopsy of the spleen: a reliable and safe diagnostic procedure for neoplastic and reactive conditions

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Rationale: Percutaneous core needle biopsy (CNB) of the spleen is rarely performed, due to concerns about its complications and low diagnostic yield. However, this procedure represents a potentially useful diagnostic tool, especially in patients with splenomegaly and no definitive diagnosis after a clinical and radiological work-up.

Methods and results: We report the data on a cohort of 45 radiologically guided percutaneous core needle biopsies of the spleen from 44 patients performed at two centres. Platelet count and prothrombin time were within normal limits in all patients at the time of the procedure. The biopsy was ultrasound-guided in all cases except one, which was guided by computed tomography. An 18G needle was used in 82% of the cases, followed by 16G (10.2%) and 20G (7.8%) needles. The biopsy provided sufficient material for histological examination (including immunohistochemical studies) in 41 cases (91.1%). Haematological malignancies were most commonly diagnosed (52.3%); diffuse large B cell lymphoma (DLBCL) was the most frequent, followed by splenic marginal zone lymphoma (SMZL). For the most recent cases of DLBCL, the CNB provided sufficient material for fluorescence in-situ hybridisation to assess the status of MYC, BCL2 and BCL6. This allowed the identification of a case of high-grade B cell lymphoma with MYC and BCL2 rearrangement. Major complications were not reported; minor complications occurred in three cases (6.7%).

Conclusions: Our data demonstrate that radiologically guided percutaneous CNB should be considered as a valid diagnostic tool, as it provides quick and reliable histological diagnoses avoiding the complications and risks of splenectomy.

Keywords: complication, diagnosis, diagnostic yield, percutaneous core needle biopsy, radiologically guided, safety, spleen

Introduction

In the majority of patients with splenomegaly and/or focal lesions of the spleen, a reliable diagnosis can be obtained integrating clinical, laboratory and
radiological data alongside the microscopic examination of blood film, bone marrow samples and flow cytometry studies. However, in a subset of cases diagnostic uncertainty persists, and a radiologically guided CNB of the spleen may represent a quick, inexpensive and informative diagnostic tool, also with the advantage of avoiding unnecessary splenectomy and its potential complications. Historically, however, there has been some reluctance in performing this procedure due to concern about complications and low diagnostic yield.

We have performed a retrospective review of percutaneous CNB of the spleen from two centres in the United Kingdom, with the aim of reporting safety and diagnostic accuracy of this procedure. During a time interval of approximately 10 years, we have identified a total of 45 biopsies from 44 patients. The main clinical and radiological characteristics of the cohort under investigation are reported in Table 1. Mean age at the time of the procedure was 66 years. Mean platelet count was $200 \times 10^9/l$; mean prothrombin time (PT) was 11.9 s. Forty-four biopsies were ultrasound (US)-guided, one was computerised tomography (CT)-guided. An 18G needle was used in the majority of the cases (82%), followed by 16G (10.2%) and 20G (7.8%) needles. The mean number of cores obtained per case was three (range = one to five cores). The biopsy provided sufficient material for histological examination in 41 cases (91.1%), while it was inadequate in four cases (8.9%), three of which were obtained with an 18G needle and one with a 20G needle. Major complications were not reported. Minor complications occurred in three cases: one patient complained of mild left shoulder discomfort, which resolved shortly after the procedure; two patients developed a perisplenic haematoma, as identified on post-procedure imaging. The first was a 74-year-old woman with a platelet count of $27 \times 10^9/l$ who underwent the splenic biopsy using a 16G needle following prophylactic platelet transfusion. Pre-biopsy haemoglobin (Hb) was 74g/l, which dropped to 54g/l, necessitating red cell transfusion after the procedure. Patient made a full recovery and was discharged the following day. The splenic biopsy showed extramedullary haematopoiiesis (EMH). In general, a platelet count of $30 \times 10^9/l$ was the threshold to consider a prophylactic platelet transfusion. With the exception of this case, none of the other patients received platelet transfusions preceding the biopsy.

Table 1. General characteristics and radiological aspects in a cohort of 45 consecutive percutaneous splenic core needle biopsies

| Clinical characteristics          |            |
|----------------------------------|------------|
| Sex                              |            |
| Female                           | 18         |
| Male                             | 27         |
| Age, years (mean, range):        | 66; 23–94  |
| Platelet count $\times 10^9/l$   | 200; 27–643|
| PT (mean, range):                | 11.9; 10.5–15|
| Spleen involvement (% of cases): |            |
| Focal lesion/s:                  | 87.2%      |
| Diffuse splenomegaly:            | 12.8%      |
| Complications (number of cases): |            |
| Minor                            | 3          |
| Major                            | 0          |
| Biopsy procedure                 |            |
| Guide (number of cases):         |            |
| US guide                         | 44         |
| CT guide                         | 1          |
| Needle (% of cases):             |            |
| 18G:                             | 82%        |
| 16G:                             | 10.2%      |
| 20G:                             | 7.8%       |
| Number of cores (mean, range):   | 3; 1–5     |

CT, Computerised tomography; US, Ultrasound; PT, Prothrombin time.
large granular lymphocytic leukaemia, T cell/histiocyte-rich large B cell lymphoma (THRLBCL), high-grade B cell lymphoma with MYC and BCL2 rearrangement [also known as ‘double-hit (DH) lymphoma’] and a histiocytic sarcoma were reported. Among the patients with lymphoproliferative disorders, three had known disease (one case of SMZL, one case of DLBCL and the patient with histiocytic sarcoma); in all other cases the spleen biopsy was performed at time of first diagnosis. All patients with high-grade B cell lymphoma (including DLBCL, THRLBCL and DH lymphoma) were stage IV, and the spleen was considered the most amenable site for biopsy.

Among the non-haematological neoplasms, one case of splenic haemangioma and one littoral cell angioma were diagnosed. The group of non-neoplastic conditions comprised a miscellanea of cases with necrotising granulomatous inflammation, EMH (one case) and 12 cases showing non-specific reactive findings. In the two cases featuring non necrotising granulomatous inflammation, sarcoidosis was subsequently diagnosed on further clinical and radiological work-up. In the case showing necrotising granulomatous inflammation, microbiology investigations did not prove a mycobacterial aetiology. Twelve cases showed non-specific changes. Among these, four patients had a history of malignancy and focal lesion/s of the spleen and the biopsy was performed to rule out splenic metastases. Three cases were clinically suspicious for a lymphoproliferative disease, which was eventually excluded on haematological investigation and bone marrow examination. In a patient with known tuberculosis and splenomegaly, the biopsy was performed to investigate possible splenic involvement. In the remaining patients, splenomegaly/splenic lesion/s were subsequently attributed to medical conditions including hepatic cirrhosis and inflammatory bowel diseases.

Of the three inadequate biopsies, one was a follow-up investigation of the patient with initial diagnosis of DH lymphoma on a spleen CNB. The remaining two biopsies were performed to investigate possible splenic metastases from solid tumours. In one case the biopsy showed findings ‘suspicious for involvement by lymphoproliferative disease’. The patient underwent clinical investigations with persistent inconclusive results.

In all 41 adequate biopsies, immunohistochemistry was successfully performed as needed. Moreover, in the most recent cases of DLBCL, the CNB provided sufficient tissue to perform fluorescence in-situ hybridisation (FISH) studies to assess the status of MYC, as per our institutional protocol. A splenectomy was subsequently performed in five patients with lymphoproliferative diseases: three DLBCL, one SMZL and one HCL. In all five cases, the splenectomy was required for therapeutic reasons and confirmed the diagnosis provided on the spleen CNB.

The first studies on biopsy procedures of the spleen used US-guided fine needle aspiration biopsy (FNAB) with 20–22G needles. These studies have reported variable diagnostic yield for the procedure, ranging from 62.8% to 100% and a low rate of complication. The major disadvantage of FNAB is the lack of information on tissue architecture; this represents a limitation especially for lymphoproliferative neoplasms, which in many cases require histological assessment of tissue architecture for a reliable conclusive diagnosis. Such limitation is overcome by percutaneous CNB, which represents a valid alternative. In the setting of lymphoid malignancies, CNB has a very high diagnostic accuracy, approaching 100% in some studies. In a large cohort of percutaneous needle biopsies of the spleen including FNAB and CNB,

| Table 2. Final histological diagnosis |
|--------------------------------------|
| Diagnostic samples (41; 91.1%)       |
| Haematological malignancies (23 cases) |
| Diffuse large B cell lymphoma: 15     |
| Splenic marginal zone lymphoma: 3     |
| T cell histiocyte-rich large B cell lymphoma: 1 |
| High-grade B cell lymphoma with MYC and BCL2 lymphoma: 1 |
| Hairy cell leukaemia: 1               |
| T cell large granular lymphocytic leukaemia: 1 |
| Histiocytic sarcoma: 1                |
| Non-haematological malignancies (2 cases) |
| Littoral cell angioma: 1              |
| Haemangioma: 1                       |
| Other conditions (16 cases)           |
| Extramedullary haematopoiesis: 1      |
| Necrotising granulomatous inflammation: 1 |
| Non-necrotising granulomatous inflammation: 2 |
| Reactive: 12                         |
| Atypical infiltrate/non-diagnostic samples (4; 8.9%) |
Civardi et al. have documented an overall similar diagnostic yield of the two approaches; however, CNB had a higher diagnostic accuracy for lymphomas (90.9% versus 68.5% of FNAB).\(^7\) Gomez-Rubio et al. have replicated these results, reporting similar overall diagnostic accuracy for FNAB and CNB (86.5% and 92%, respectively).\(^8\) Of note is the safety of FNAB (with 20–22G needles) and CNB (with 18–22G needles), which harbour a similar risk of both minor and major complications (fewer than 1% and 4%, respectively) on pooled data.\(^7,9\) Only one study reported a relevant risk of major complications (of 12.1%) for CNB; however, in this study a 14G needle was used which may explain the result.\(^10\) Currently, the use of a 14G needle for percutaneous spleen CNB is no longer justified. Conversely, Liang et al. have documented better tissue cores and a higher diagnostic rate for splenic percutaneous CNB with an 18G needle compared to 21G.\(^11\) As such, we believe an 18G needle should be the choice to maximise the diagnostic rate, limiting the risk of complications.

**Figure 1.** Histologic findings of representative cases. Case 1: Extramedullary haematopoeisis. At low power the white and red pulp are identifiable (A: H&E). On higher magnification, numerous megakaryocytes are seen within the red pulp (B: H&E). Immunostaining for CD8 highlights preserved splenic vascular architecture (C: CD8). Megakaryocytes (D: CD61), erythroid precursors (E: CD71) and myeloid elements (F: Myeloperoxidase) are scattered throughout the red pulp. Case 2: Necrotizing granulomatous inflammation. The white pulp is attenuated; the red pulp is effaced by poorly formed granulomas and large areas of necrosis (G, H&E). Case 3: Diffuse large B cell lymphoma. The splenic parenchyma is effaced by a pleomorphic population of lymphoid blasts, many with anaplastic morphology (H: H&E). The neoplastic cells diffusely express CD20 which also stains the necrotic areas (I: CD20). Case 4: Histiocytic sarcoma. Low magnification (x2) shows loss of the normal splenic architecture with foci of tumour necrosis (J: H&E). At higher power there is diffuse infiltration by a pleomorphic proliferation of large histiocytic cells with irregularly folded nuclei, open chromatin, occasionally prominent nucleoli and abundant eosinophilic cytoplasm (K: HE). The neoplastic cells show diffuse expression of CD163 (L: CD16) alongside CD68 (not shown). CD, cluster of differentiation; H&E, hematoxylin and eosin.
US-guided percutaneous CNB represents a diagnostic procedure of choice not only in lymphoproliferative diseases, but also in a large setting of reactive conditions of the spleen, including vascular neoplasms, splenic metastases, granulomatous and non-granulomatous inflammation and reactive conditions such as extramedullary haematopoiesis.\textsuperscript{9,11–15} In the most recent studies, overall accuracy ranges from 90.4% to 100%, with a low risk of minor complications (1.9–7.2%) and a negligible risk of major complications (0–1%).\textsuperscript{9,11,12,15} In these studies an 18–20G needle was used, and the procedure was US-guided in most cases; fewer were CT-guided. Percutaneous CNB of the spleen has also been proven to be a safe and reliable diagnostic tool in the paediatric population.\textsuperscript{16}

We have investigated the diagnostic applications and safety of US-guided percutaneous CNB in a large cohort of patients with neoplastic and reactive conditions of the spleen. In this study we have reported a high diagnostic yield of the procedure (91.1%), with a low incidence of minor complications (6.7%) and no major complications. Whenever required, we could successfully perform immunohistochemical studies for the optimal characterisation of the disease (mean number of stains per case = 9.7; range = 6–21). Of note for the most recent cases of DLBCL, the CNB also provided enough tissue for molecular investigations such as FISH: this allowed us to identify a case of DH lymphoma which would have been missed otherwise (in this case FISH for MYC, BCL2 and BCL6 was performed). The final diagnosis provided on CNB was satisfactory for clinical purposes in all cases but one (2.2%), in which a suspicion of malignancy was raised. We could compare the diagnosis on CNB with a subsequently splenectomy in only five cases. Reassuringly, in all five cases, the original diagnosis made on CNB was confirmed on the splenectomy.

Even though our cohort spans a time interval of almost 10 years, an increasing number of biopsies has been performed during the last few years. This may reflect a growing awareness of the safety and reliability of splenic CNB, as we have confirmed with our data. Moreover, we believe the hesitancy in performing splenic CNB is not justified, considering that this procedure has a similar, if not lower, rate of complications compared to CNB of other solid organs, including difficult-to-assess sites such as lung and pancreas.\textsuperscript{17,18} As such, whenever uncertainties persist after pre-existing investigations, we believe radiologically guided percutaneous CNB performed by an experienced operator in carefully selected patients should be considered a valid diagnostic alternative, as it provides quick and reliable results avoiding unnecessary complications and the risk of subsequent immunosuppression that a splenectomy would imply.

References

1. Silverman JF, Geisinger KR, Raab SS \textit{et al}. Fine needle aspiration biopsy of the spleen in the evaluation of neoplastic disorders. \textit{Acta Cytol.} 1993; 37: 158–162.
2. Zeppa P, Vetrani A, Luciano I, \textit{et al}. Fine needle aspiration biopsy of the spleen. A useful procedure in the diagnosis of splenomegaly. \textit{Acta Cytol.} 1994; 38: 299–309.
3. Caraway NP, Fanning CV. Use of fine-needle aspiration biopsy in the evaluation of splenical lesions in a cancer center. \textit{Diagn. Cytopathol.} 1997; 16: 312–316.
4. Venkataramu NK, Gupta S, Sood BP \textit{et al}. Ultrasound guided fine needle aspiration biopsy of splenic lesions. \textit{Br. J. Radiol.} 1999; 72: 953–956.
5. Suzuki T, Shibuya H, Yoshimatsu S, Suzuki S. Ultrasonically guided staging splenic tissue core biopsy in patients with non-Hodgkin’s lymphoma. \textit{Cancer} 1987; 60: 879–882.
6. Cavanna L, Civardi G, Fornari F \textit{et al}. Ultrasonically guided percutaneous splenic tissue core biopsy in patients with malignant lymphomas. \textit{Cancer} 1992; 69: 2932–2936.
7. Cividri G, Vallisa D, Berté R \textit{et al}. Ultrasound-guided fine needle biopsy of the spleen: high clinical efficacy and low risk in a multicenter Italian study. \textit{Am. J. Hematol.} 2001; 67: 93–99.
8. Gómez-Rubio M, López-Cano A, Rendón P \textit{et al}. Safety and diagnostic accuracy of percutaneous ultrasound-guided biopsy of the spleen: a multicenter study. \textit{J. Clin. Ultrasound} 2009; 37: 445–450.
9. Patel N, Dawe G, Tung K. Ultrasound-guided percutaneous splenic biopsy using an 18-G core biopsy needle: our experience with 52 cases. \textit{Br. J. Radiol.} 2015; 88: 20150400.
10. Liang P, Gao Y, Wang Y, Yu X, Yu D, Dong B. US-guided percutaneous needle biopsy of the spleen using 18-gauge versus 21-gauge needles. \textit{J. Clin. Ultrasound} 2007; 35: 477–482.
11. Lindgren PG, Hagberg H, Eriksson B \textit{et al}. Excision biopsy of the spleen by ultrasonic guidance. \textit{Br. J. Radiol.} 1985; 58: 853–857.
12. Olson MC, Atwell TD, Harmson WS \textit{et al}. Safety and accuracy of percutaneous image-guided core biopsy of the spleen. \textit{Am. J. Roentgenol.} 2016; 206: 653–659.
13. López JJ, Del Cura JL, De Larrinoa AF, Gorriño O, Zabala R, Bilbao FJ. Role of ultrasound-guided core biopsy in the evaluation of spleen pathology. \textit{APMIS} 2006; 114: 492–499.
14. Hanlon K, Wilson MR, Kay D \textit{et al}. Safety and diagnostic yield of splenic core biopsy: a methodical approach using combined haematology/radiology assessment in a tertiary referral centre. \textit{Br. J. Haematol.} 2019; 186: 371–373.
15. Sammon J, Twomey M, Crush L \textit{et al}. Image-guided percutaneous splenic biopsy and drainage. \textit{Semin. Intervent. Radiol.} 2012; 29: 301–310.
16. Muraca S, Chait PG, Connolly BL \textit{et al}. US-guided core biopsy of the spleen in children. \textit{Radiology} 2001; 218: 200–206.
17. Heerink WJ, de Bock GH, de Jonge GJ \textit{et al}. Complication rates of CT-guided transthoracic lung biopsy: meta-analysis. \textit{Eur. Radiol.} 2017; 27: 138–148.
18. Atwell TD, Smith RL, Hesley GK \textit{et al}. Incidence of bleeding after 15,181 percutaneous biopsies and the role of aspirin. \textit{Am. J. Roentgenol.} 2010; 194: 784–789.