CLINICAL STUDY

Safety of Percutaneous Biopsy for Hepatic Angiosarcoma: Results of a Multicenter Korean Survey

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ABSTRACT

Purpose: To evaluate the incidence of severe bleeding and mortality associated with percutaneous biopsy for hepatic angiosarcoma in a multicenter retrospective cohort.

Materials and Methods: A retrospective review of 33 patients with biopsy-proven hepatic angiosarcoma (29 male; median age, 57 y; age range, 24–96 y) was performed at seven tertiary academic hospitals between January 1998 and March 2015. The mean maximum tumor size was 5.5 cm (range, 1.7–20 cm). An 18-gauge automated cutting biopsy needle was used with a freehand technique in all patients who underwent ultrasonography-guided percutaneous core needle biopsy on an inpatient basis. The incidences of severe bleeding and procedure-related mortality were evaluated per Society of Interventional Radiology (SIR) guidelines.

Results: There was a mean of 2.8 needle passes per patient during the procedure (range, 1–6). The overall incidence of severe bleeding events (SIR grade C/D) was 9.1% (3 of 33). Two patients were managed with blood transfusion, and one patient underwent embolization for bleeding control. No other major complications were encountered. There were no cases of mortality associated with the biopsy.

Conclusions: Severe bleeding was not a frequent complication after percutaneous biopsy for hepatic angiosarcoma. The majority of bleeding complications could be controlled with conservative management.

ABBREVIATIONS

PT = prothrombin time, INR = International Normalized Ratio, FNAB = fine-needle aspiration biopsy, CNB = core needle biopsy

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Primary hepatic angiosarcoma is a rare, high-grade malignant tumor composed of spindle or pleomorphic cells that line blood spaces and grow in an infiltrative manner along the hepatic sinusoids and vascular channels (1). Although it represents fewer than 2% of all primary liver neoplasms, it is the most common primary malignant mesenchymal tumor in the liver (2).

Imaging findings of hepatic angiosarcoma include multiple focal masses or diffuse infiltrative lesions (2,3). However, in general, it shows nonspecific imaging findings even on dynamic magnetic resonance (MR) imaging (4). Therefore, in clinical practice, it is difficult to differentiate vascular tumors such as atypical hemangiomas and epithelioid hemangioendotheliomas from hepatic angiosarcomas because of the considerable overlap in imaging findings (1,5). However, differential diagnosis is important because a patient with epithelioid hemangioendothelioma is a potential candidate for liver transplantation because of its low- to intermediate-grade malignancy,

whereas a patient with hepatic angiosarcoma is contraindicated to undergo liver transplantation (1,6). Therefore, a pathologic diagnosis is necessary in optimizing treatment plans.

To date, the role of percutaneous biopsy for hepatic angiosarcoma is controversial, and it is currently not recommended because of the risk of severe bleeding (2,7). However, this recommendation was derived from several case reports (8–11), not from a large cohort study. Therefore, the purpose of the present study was to assess the safety of percutaneous biopsy for hepatic angiosarcoma and to analyze the risk factors for severe bleeding after biopsy in a multicenter retrospective cohort.

MATERIALS AND METHODS

Patients

This study involved seven Korean tertiary academic centers. The institutional review board of each center approved the study, and the need for patient informed consent was waived. Between January 1998 and March 2015, a total of 41 consecutive patients across the seven centers were histopathologically confirmed as having hepatic angiosarcoma. The histologic diagnosis was based on specific microscopic findings and results of immunohistochemistry analysis, including positivity of an endothelial marker such as CD31, CD34, or factor VIII–related antigen. Among them, patients who met the following inclusion criteria were included in the study: (*i*) percutaneous biopsy-proven hepatic angiosarcoma, (*ii*) presence of preprocedural imaging studies including computed tomography (CT) or MR imaging, (*iii*) presence of ultrasonography (US) images during the procedure, (*iv*) presence of laboratory data regarding hemostasis including prothrombin time (PT) and platelet count, (*v*) absence of impaired hemostasis before biopsy (International Normalized Ratio [INR] < 1.5 and platelet count $\geq 50\times10^9$/L per Society of Interventional Radiology [SIR] guidelines [12]), (*vi*) no aspirin and clopidogrel received for at least 5 days before the procedure, and (*vii*) presence of medical records, including vital signs and any kind of treatment until discharge after the biopsy. Eight patients were excluded for the following reasons: absence of laboratory data, biopsy procedure, or follow-up records ($n = 6$) and diagnosis by open biopsy or liver transplantation ($n = 2$). Therefore, 33 patients were finally included in the study.

Biopsy and Follow-up Protocol

The protocols of percutaneous biopsy for focal hepatic lesions in each institution were similar and are generally as follows (12,13). (*i*) Percutaneous liver biopsy was performed under US guidance on an inpatient basis. (*ii*) Sedative medications during biopsy were not routinely used. (*iii*) Direct puncture of the subcapsular lesion was generally avoided if there was an accessible pathway to the index tumor to minimize tract bleeding or tumor seeding. (*iv*) If the patient had multiple lesions showing similar imaging characteristics on preprocedural imaging studies, lesions with the best accessibility based on tumor size and location were chosen as the target lesions. (*v*) Two or three needle passes were routinely performed during biopsy, and the procedure was completed after confirming that needle penetrated through the target lesion on a US image. Repeated sampling was performed if needed. (*vi*) Immediately after biopsy, Doppler US was routinely performed to evaluate any bleeding along the needle pathway showing a "patent tract sign" (14). Finally, (*vii*) if bleeding was suspected after biopsy based on unstable vital signs or follow-up CT angiography, transfusion or emergency embolization was performed.

Outcome Assessment

Baseline tumor characteristics were retrospectively collected by using the electronic medical record system and picture archiving and communication system from each hospital. To assess the technical factors of the biopsy, the following factors were evaluated: the level of operator experience with liver biopsy, the type of biopsy needle used, whether direct puncture of a subcapsular tumor during the biopsy had occurred, the total number of biopsy needle passes, and the presence of a patent tract sign on US immediately after biopsy. In addition, patients' medical records were also reviewed to assess any exposure to arsenic, vinyl chloride monomer, and thorium dioxide.

Regarding laboratory findings for hemostasis, PT/INR and platelet count before biopsy were assessed. Among clinical parameters, the presence of unstable vital signs after biopsy and the presence of subsequent transfusion or embolization for bleeding control were recorded. Severe bleeding was defined as a major complication requiring additional treatment or hospitalization and/or resulting in permanent adverse sequelae or death as a result of procedure-related bleeding and was classified according to SIR guidelines (15).

Patient Demographics and Tumor Characteristics

The baseline characteristics of 33 patients with hepatic angiosarcoma are summarized in **Table 1**. There was a male predominance, with a male-to-female ratio of 7.3:1. No patient had been exposed to the investigated chemical agents. All patients underwent a contrast material–enhanced CT scan for preprocedural imaging studies, and nine patients underwent additional liver MR imaging for further characterization of the hepatic lesions. Before biopsy, angiosarcoma was suspected in 17 patients (51.5%) based on imaging findings. The mean maximum tumor size was 5.5 cm (range, 1.8–20 cm).