European Journal of Radiology 73 (2010) 588–593

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Regenerative nodules in patients with chronic Budd-Chiari syndrome: A longitudinal study using multiphase contrast-enhanced multidetector CT

Nicola Flor[a,*], Massimo Zuin[b], Francesca Brovelli[c], Marco Maggioni[d], Augusta Tentori[e], Francesco Sardanelli[f], Gian Paolo Cornalba[a]

[a] Unità Operativa di Radiologia Diagnostica Interventistica, University of Milan School of Medicine, Ospedale San Paolo, Milan, Italy
[b] Unità Operativa di Epatologia e Gastroenterologia Medica, University of Milan School of Medicine, Ospedale San Paolo, Via A. di Rudinì 8, 20142 Milan, Italy
[c] Department of Radiology, Centro Diagnostico Italiano, Milan, Italy
[d] Servizio di Anatomia Patologica, Ospedale San Paolo, Milan, Italy
[e] Servizio di Radiologia, Ospedale di Voghera, Italy
[f] Radiology, IRCCS Policlinico San Donato, University of Milan School of Medicine, Milan, Italy

ARTICLE INFO

Article history:
Received 22 September 2008
Received in revised form 18 December 2008
Accepted 8 January 2009

Keywords:
Budd-Chiari syndrome
Regenerative nodules
Liver
Computer tomography (CT)

ABSTRACT

Objective: Our aim was to evaluate the serial evolution of regenerative nodules in patients with Budd-Chiari syndrome (BCS) treated with portal-systemic shunts, using multiphasic multidetector computed tomography (MDCT).
Materials and methods: Five patients each underwent three MDCT exams over an extended period ranging from 36 to 42 months. Two radiologists in consensus retrospectively reviewed each exam for each patient. Individual nodules were grouped according to size (size I: nodules with diameter ≤15 mm; size II: >15 mm but <30 mm; size III: ≥30 mm), pattern of enhancement (A: homogeneously hypervascular or B: with central scar), and segmental location. Four nodules classified as size II, which increased in size over time, were needle-biopsied.
Results: We detected 61 nodules at the first exam, 66 nodules at the second exam (7 nodules disappeared and 12 new nodules), and 85 nodules at the third exam (8 disappeared and 27 new) for a total of 212 findings. Nodules were mostly found in the right hepatic lobe. Fourteen of the 15 nodules that disappeared over time were size I and enhancement pattern A. At unenhanced MDCT, 204 (96%) of the 212 findings were isodense. Overall, 100 nodules, including the 61 initially detected, were considered newly diagnosed; of these 84 (84%) were size I and pattern A. Of 57 nodules considered size I and pattern A at the first or second exam, 24 (42%) changed to pattern B at the third exam and either size II ($n = 18$) or III ($n = 6$). The four biopsied nodules were each confirmed as benign regenerative nodule. No patient developed HCC at 5-year follow-up period.
Conclusion: Hepatic nodules in BCS patients not only increase in number over time but may also increase in size and develop a central scar.

1. Introduction

Budd-Chiari syndrome (BCS) is a heterogeneous group of disorders characterized by hepatic venous outflow obstruction at different levels from the small hepatic veins to the junction of the inferior vena cava and the right atrium, regardless of the cause of the obstruction [1]. In BCS patients, benign hepatic regenerative nodules appear during the chronic phase of the disease [2–7]. In the past decades, these hepatic nodules were named "adenomatous hyperplastic nodules" [8], "nodular regenerative hyperplasia" [2,7], or simply "regenerative nodules" [3–6]. About 10 years ago, they were finally defined as "multiacinar regenerative nodules" [9].

These nodules are generally multiple, hypervascularized, disseminated throughout the liver but with a preferential periportal distribution [3–5,10]. Their pathogenesis is unclear but they can be thought of as a response to a focal loss of portal perfusion and hyperarterialization in areas with preserved hepatic venous outflow [3,6,11,12].

Only a few studies have described the imaging characteristics of these lesions [12–15]. Typically, the nodules are bright on unenhanced T1-weighted MR images and enhance strongly following intravenous administration of gadolinium-based contrast agents. On T2-weighted images they are predominantly isointense or hypointense relative to the normal liver [14].

* Corresponding author. Tel.: +39 02 81844307; fax: +39 02 50323393.
E-mail addresses: flornic@hotmail.com, nicola.flor@ao-sanpaolo.it (N. Flor).

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doi:10.1016/j.ejrad.2009.01.012

On conventional CT scans, large regenerative nodules have been described as markedly and homogeneously hyperattenuating on arterial phase images and remaining slightly hyperattenuating on portal-venous phase images [12]. As yet however, there are no reports describing the appearance and serial evaluation of regenerative nodules on contrast-enhanced multiphase multidetector computed tomography (MDCT).

The purpose of this observational retrospective study was to describe the number, size, location, imaging features, and serial evolution of regenerative hepatic nodules in chronic BCS patients on contrast-enhanced multiphase MDCT.

2. Materials and methods

2.1. Study population

The Institutional Review Board of our Hospital approved the study. The study population comprised five BCS patients (3 women, 2 men; aged from 24 to 54 years, median 38 years) who underwent multiple MDCT examinations at our institution from February 2000 to April 2004. Each patient had hematologic abnormalities: three patients had a myeloproliferative disorder, one an antiphospholipid syndrome and one an anti-cardiolipin syndrome. The site of venous obstruction was a small hepatic vein in all patients. None of the patients had a history of hepatitis or cirrhosis; serum alpha-fetoprotein values were normal in all subjects.

A final diagnosis of BCS was obtained by means of liver biopsy in all patients. The median interval between the initial diagnosis of BCS and the first MDCT exam in this study was 20 months (range: 7–36 months). Four patients were treated with a surgical portosystemic shunt (one with mesocaval shunt with hepatic vein stenting and three with a portocaval shunt and inferior vena cava stenting) while the remaining patient was treated with a transjugular intrahepatic portosystemic shunt (TIPS). The median time interval between the surgical procedure and the first MDCT examination in this study was 17 months (range: 8–36 months).

Three MDCT examinations were considered for each patient in the present study (i.e., 15 examinations in total). The intervals between the first and second examination were 21, 29, 24, 16 and 19 months (median: 21.8), those between the second and the third examinations were 18, 9, 12, 25 and 23 months (median: 17.4), and those between the first and the third examinations were 39, 38, 36, 41 and 42 months (median: 39.2).

Informed consent for the MDCT examinations and for the intravenous administration of iodinated contrast agent was obtained from all patients.

2.2. MDCT protocol

All the examinations were performed using a four-row spiral MDCT scanner (LightSpeed Qx/I, General Electric Medical Systems, Milwaukee, Wisconsin), before and after a single-bolus intravenous injection into the antecubital right vein of 110–135 ml of non-ionic contrast agent containing 350 mg/mL iodine (Iomeron, Bracco SpA, Milan, Italy) at a rate of 4 ml/s, administered by power injector (9000 CT ADV, Liebel-Flesheim, Mallinkrodt, USA). A multiphasic protocol was used with image acquisition before contrast administration (unenhanced phase) and during the arterial, portal-venous and delayed phases after contrast administration. A bolus tracking technique was used to time the arterial phase; the portal-venous and delayed phases were obtained with delay times after injection of 75 and 300 s, respectively. The exposure parameters were: 120 kVp, 200 effective mAs; detector configuration 4 mm × 2.5 mm; rotation time 0.8 s; pitch 6; effective slice thickness 2.5 mm; reconstruction thickness 1.25 mm with 0.8-mm reconstruction increment.

2.3. Image analysis

CT images were evaluated retrospectively by two radiologists in consensus with 10 years (first author) and 3 years (third author) of experience in CT imaging of the liver. The number, size, distribution, and pattern of CT contrast enhancement was recorded for each individual nodule, with care taken to accurately match lesions from one CT exam to the next for each patient.

Each hepatic nodule was classified according to its size. Size I nodules were those with a maximal diameter of ≤15 mm while size II and III nodules were those with maximal diameters of >15 mm but <30 mm, and ≥30 mm, respectively. Thereafter, nodules were classified according to the pattern of CT contrast enhancement on arterial, portal-venous and delayed phases; pattern A nodules were those that were homogeneously hypervascular while pattern B nodules were those with a central scar (Table 1). On unenhanced scans, almost all nodules (96%) were isodense (i.e., undetectable) in comparison with the surrounding liver parenchyma. As a consequence, the unenhanced images were not used for characterizing the nodules.

2.4. Histopathologic examination

At about 2 years after the diagnosis of BCS, at the time of the second MDCT examination, an intralesional ultrasound-guided needle-biopsy (18 Gauge) was performed in four of the five patients. Four nodules which were size II and increased in size over time were biopsied. Three of them showed a type-B pattern and the remaining one a type-A pattern. Samples were routinely paraffin-embedded and stained for hematoxylin-eosin, Masson thrichrome and PAS after diastase digestion. Histological slides were reviewed by a liver pathologist (fourth author) with 10 years of experience in liver pathology.

3. Results

A total of 61 nodules were detected in the five patients at the first MDCT examination. At the second examination a total of 66 nodules were detected. Seven (11%; all with size/pattern I/A) of the nodules seen at the first MDCT examination had disappeared while 12 new nodules were seen. At the third MDCT examination 85 nodules were detected. At this time 8 (12%; seven with size/pattern I/A, one with size/pattern I/B) of the nodules seen at the second MDCT examination had disappeared while 27 new nodules were seen.

Overall a total of 212 findings were obtained across the 15 MDCT examinations. At unenhanced MDCT 204 (96%) of these 212 nodules

Table 1
Pattern of contrast enhancement of the BCS nodules on arterial, portal-venous and delayed phase.

	Arterial phase	Portal-venous phase	Delayed phase
Pattern A	Hyperdense	Isodense or hyperdense, with peripheral hypodense rim	Isodense
Pattern B	Hyperdense with central hypodensity with peripheral hypodense rim	Hyperdensity with central hypodensity with peripheral hypodense rim	Isodense or hypodense with central hyperdensity