Discussion & Summary

Chapter 11

Matthanja Bieze
PART I  CHAPTER 1  of this thesis provides an appraisal of the
colourful history of medical imaging and an introduction to the
hypervascular hepatic tumors discussed in this thesis: hepatocellular
adenoma; focal nodular hyperplasia, hepatocellular carcinoma, and he-
patitis hemangioma. The general application of imaging modalities has
long been established. However, fine-tuning of these techniques to spe-
cific diseases and abnormalities is still an ongoing process.

PART II discusses imaging and clinical management of hepatocellular
adenoma (HCA) and focal nodular hyperplasia (FNH). Benign liver lesions
do not always display typical characteristics for diagnosis and with that mind-
set; CHAPTER 2 discusses dynamic MR imaging with Primovist® for HCA and
FNH. Accurate diagnosis is essential, because FNH and HCA have opposing thera-
peutic consequences. The risk of complications, such as bleeding or even malignant
transformation, are known to occur in HCAs larger than 5 cm, unlike in FNH. This
MRI technique proved highly accurate and makes invasive liver biopsy redundant.

The study was designed to differentiate two benign hepatic lesions, two benign hepatic lesions,
the function of hepatocytes is preserved enabling the uptake of contrast agent [3].
This implies that diagnosis is difficult solely on the basis of the hepatobiliary phase of the
MRI in patients with a liver tumor. If a patient presents with a positive history of malignancy or
with a lesion with washout on the portal phase, the working diagnosis should be malignancy
until proven otherwise. Therefore, if any suspicion of malignancy exists, a more aggressive diag-
nostic work-up is required with early invasive intervention whenever possible.

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nostic work-up is required with early invasive intervention whenever possible.

The study was designed to differentiate between HCA and FNH, the “F-FCH PET/CT as described in
CHAPTER 3.” “F-FCH PET/CT can be used as an additional tool when MR
imaging with Primovist® remains inconclusive. Even with accuracy higher than MR imaging with
Primovist® for differentiation of HCA and FNH, this modality will probably be impractical in many
centers as a special cyclotron is necessary to synthesize “F-FCH in close proximity to the hospital.
Furthermore, as discussed in CHAPTEr 7, the “F-FCH PET/CT is useful in detection of hepatocel-
lular carcinoma (HCC). Therefore, when HCC is not in the differential diagnosis the “F-FCH PET/
CT can be used to differentiate HCA from FNH. When dynamic MR imaging can be accurately incor-
porated in the process of imaging, two very accurate imaging modalities can be combined with less im-
port for the patient [4]. In CHAPTER 4, the fine line between indicated surgical interventions against
non-invasive care is discussed. Benign lesions will only need intervention when medically indicated by
their associated risk factors and decreased quality of life expressed by the patient.

An important indication for intervention has been revealed in the past few years by enabling subclassi-
fication of HCA [5]. In the present day it is believed that beta-catenin mutated HCA are prone to ma-
lignant transformation [6]. Unfortunately, the subclassification is best assessed on resection specimen
with immunohistochemical analyses while liver biopsy could very well miss the mutated part of HCA
or result in sampling errors. Therefore, future studies will have to define non-invasive characteristics
of HCA subtypes. MRI is shown most promising [7] for classification and if HCA subtypes can be ac-
curately assessed, clinical implications should be assessed in large patient group to provide a treatment
algorithm.

Malignant transformation of HCA occurs in an estimated 4.3% of the patients with HCA
larger than 5 cm [8] and is overshadowed by the risk of lesional bleeding. Bleeding is more frequent and
demands emergency care with transarterial embolization in case of active bleeding or severe intra-ab-
dominale Grade III bleeding as discussed in CHAPTEr 5. The specific risk factors for lesional bleeding in
HCA were identified in CHAPTEr 6, being: patients with obesity, HCA size >35 mm, HCA pro-
truding from the liver (exophytic growth), HCA located in the left liver lobe, and HCA with radiologi-
cal presence of central or peripheral arteries. HCA located deeper in the liver might have a lower risk of
severe bleeding as none of the intrahepatic lesions showed extraparenchymal bleeding (n = 82) and only 13%
showed Grade I or II bleeding. Based on these findings, preventive treatment can be better focused on
the patients who are at risk. However, the best method of preventive treatment remains under debate.
A preventive surgical intervention, even laparoscopically, in a patient with a benign liver tumor could
be regarded as somewhat excessive. On the other hand, radio frequency ablation has been shown to be a safe
alternative in small lesions and studies have shown that HCA under 3 cm can be completely and
safely ablated [9, 10]. Another less invasive treatment option could be transarterial embolization (TAE).

CHAPTEr 5 already discusses the use of TAE in emergency care of bleeding HCA. Its potential in
the preventive setting is clear when the arterial blood supply of the HCA lesion can be targeted and
undermined. Revasculatization may occur with time and unfortunately, no studies have yet assessed
this method for its safety and effectiveness. Especially in lesions with a higher risk of malignant trans-
formation (HCA with a beta-catenin mutation) the effects of TAE need to be investigated.

PART III discusses hepatocellular carcinomas (HCC) and unlike HCA and FNH this lesion has the
potential to be life threatening. It is essential to detect HCC as early as possible to be able to re-
move and obtain curation. Multiple HCC lesions over 3 cm intraparenchymal or extraparenchymal spread of
the disease means that curative treatment will no longer be possible [11]. Therefore, accurate staging of
the disease is crucial for appropriate treatment implementations. In that respect, CHAPTEr 7 shows the
additional value of “F-FCH PET/CT imaging in staging and detection of extraparenchymal disease with
direct treatment implication in a third of the patients of the study. Even though this imaging modal-
ity has been proven highly accurate and of additional value to diagnosis and treatment plans; logistics
and associated costs make its general use controversial. “F-FCH has to be specially synthesized and
has a half-life time of 10 minutes. Therefore, the cyclotron cannot be located far from the medical center
where the patients undergo the imaging. However, if it is a high-volume medical center regarding
HCC patients or involved in a HCC screening program, the “F-FCH PET/CT will be of clear
additional value. The additional value of the “F-FCH PET/CT for HCC lies in accurate whole body
assessment in regards to the extent of disease, which has direct implications for staging and treatment
decisions. Further studies need to determine its place in diagnostic work-up and show which patients
will profit most from the “F-FCH PET/CT.

Another possibility to assess local extent of the disease is by staging laparoscopy (SL). A lapa-
roscopy can be performed in the work-up prior to hepatic resection to assess local extent of disease
and the overall condition of the liver (cirrhosis and fibrosis) by biopsy of non-tumorous tissue with
consecutive histopathological evaluation. CHAPTEr 8 shows that staging laparoscopy is outdated as
imaging modalities are of such quality that ‘an initial peek’ with more invasive laparoscopy holds no additional value. In this retrospective evaluation of patients undergoing staging laparoscopy prior to hepatic resection the yield was only 7%. Therefore, only in cases in which local or distant metastases are suspected SL can still be considered. In light of Chapter 7, the 18F-FCH PET/CT might however be a more elegant non-invasive tool to assess extent of disease. An overview and discussion of the patients with HCC seen at the Academic Medical Center of Amsterdam, a non-liver-transplant center is presented in Chapter 9. Overall survival in patients treated with curative intent and with palliative or symptomatic treatment is similar to data from literature. Transarterial chemoembolization is highlighted as this treatment is the most commonly used local treatment in the palliative setting for HCC and in some patients complete response to treatment occurs with subsequent high survival. Further study into TACE and optimal (re)treatment will have to be conducted in a center with a high patient load to determine the best possible outcome for the individual patient with HCC requiring palliative TACE.

The differential diagnosis of hypervascular liver tumors is multifold. PART IV discusses 4 different case studies of hepatic tumors. Many hepatic tumors can have an atypical presentation and these cases are fine examples. The 1st CASE presents a young female patient (18 years old) suspected of having HCC. An 18F-FCH PET/CT was performed to assess extent of disease as described in Chapter 7, and 18F-FCH PET imaging showed four hepatic tumors without extrahepatic disease. However, histopathology after resection of the lesion showed hepatoblastoma. With this patient we showed that the 18F-FCH PET/CT can detect a hepatic hepatoblastoma. The 2nd CASE study discusses the co-existence of HCA and hepatic granulomas. We proposed that the hepatic granulomas in these cases are a response to persistent inflammation caused by (inflammatory) HCA, a local reaction to a neoplasm, chronic use of oral contraceptives, or a combination of these factors. The 3rd CASE discussed diagnosis is the most common benign hepatic tumor: hemangiomas. Invasive treatment is only indicated when abdominal complaints impair quality of life. These symptoms usually only occur in giant hemangioma larger than 5cm. Intervention is also required when, although rare, a complication of disseminated intravascular coagulation (Kasabach-Merritt syndrome) occurs. Surgical enucleation has proven effective in relief of symptoms. The 4th CASE study shows images of a patient with FNH with severe abdominal complaints in whom resection was decided. At laparotomy a liver with multiple greyish lesions was found similar to metastatic disease. This was not expected as FNH is a benign lesion and no other signs of malignant disease were present. Frozen sections showed bile duct hamartomas, and resection of the FNH was continued as planned.

References

IMAGING OF HEPATIC HYPERVASCULAR TUMORS & CLINICAL IMPLICATIONS

SUMMARY

Matthanja Bieze
Promotor: T.M. van Gulik, Chirurg
Co-promoters: R.J. Bennink, Nucl. Med, J.Verheij, Pathology

UvA; Academic Medical Center
PART I of this thesis is the introduction of the hypervascular hepatic tumors discussed in this thesis.

PART II discusses imaging of benign hypervascular hepatic tumors and clinical implications. Consecutive patients with suspected hepatocellular adenoma (HCA) or focal nodular hyperplasia (FNH) were enrolled in a prospective study designed to test whether improvements in diagnosis and management can be made. CHAPTER 2 evaluates the additional value of the hepatobiliary phase of Gd-EOB-DTPA (Primovist®) magnetic resonance (MR) imaging compared to standard MR imaging. The accuracy of standard MR imaging for HCA was 50% (12/24) and for FNH 68% (19/28). After reviewing the hepatobiliary phase the accuracy for HCA improved to 96% (23/24) and accuracy for FNH to 96% (27/28). Lesional features with predictive value for diagnosis in HCA included bleeding, fat, and glycogen. The presence of a central scar was highly predictive for FNH. This study shows high accuracy of the Gd-EOB-DTPA enhanced MRI when standard contrast enhanced series are combined with the hepatobiliary phase for differentiation of HCA and FNH in lesions larger than 2 cm. In the same patient cohort the additional value of positron emission tomography (PET) computed tomography (CT) with 18F-fluoromethylcholine (18F-FCH) as a novel diagnostic approach in the differentiation of HCA and FNH is discussed. CHAPTER 3. Evaluation of PET imaging was done with a ratio: the maximum standard uptake value (SUV) of the lesion, divided by the mean SUV of the surrounding liver. The mean SUV ratio for FNH was 1.67±0.31 (mean ±SD, n=28), resulting in a positive likelihood ratio of 32.3 for PET-positive FNH. The mean SUV ratio for HCA was 0.82±0.17 (n=32), with a likelihood ratio of ≈100 for PET-negative HCA. Receiver operating characteristic curve analysis revealed an optimal SUV ratio cut-off value of 1.13, which reached 100% sensitivity and 97% specificity in differentiating FNH from HCA. This prospective study shows that PET/CT with 18F-FCH can accurately differentiate FNH from HCA and may become a valuable diagnostic tool when conventional imaging techniques fail to do so. CHAPTER 4 discusses the controversy of management of hepatocellular adenoma (HCA) and focal nodular hyperplasia (FNH), especially with respect to patient selection for surgery. This was the final study of the full cohort of 110 patients in which 51 patients with HCA and 59 with FNH were included. If patients with HCA and FNH require surgery, limited resection or enucleation of the lesion can be carried out with low morbidity and without mortality, using either an open or laparoscopic approach. Patients with preoperative symptoms show a high rate of postoperative symptom relief. The debate about invasive (preventive) treatment of HCA is further discussed in CHAPTER 5 & 6. Even though HCA is a benign hepatic lesion it does carry the risk of spontaneous bleeding. Bleeding was scored and graded on CT and/or MR imaging: intralesional (Grade I), intraparenchymal (Grade II), or extraparenchymal (Grade III). Treatment of bleeding consisted of observation in hemodynamically stable patients and selective transarterial embolization (TAE) in patients whom required blood transfusion. We propose a grading system of bleeding HCA in which Grade I and II with bleeding-areas larger than 6cm, and preferably all Grade III bleedings are treated with TAE. Additional care, being follow-up or preventive treatment, is advised in patients with exophytic adenomas in FNH. In CHAPTER 6 we aimed to assess risk factors for bleeding in patients with HCA. Standard of reference for diagnosis was histopathology, or dynamic CT and/or MR imaging. Bleeding was scored and evaluated on CT and/or MR imaging. As mentioned in CHAPTER 5 bleeding was seen in 29 (64%) patients and in 42 (22%) lesions. Patients with a body mass index (BMI) >25 showed
an increased risk for severe bleeding Grade II and III. In lesions >35 mm, exophytic lesions, lesions in segments 2-3, and lesions with peripheral or central arteries the risk of bleeding is increased.

PART III of the thesis discusses hepatocellular carcinoma (HCC); a hypervascular, malign hepatic tumor. In the past two decades an increasing incidence of HCC was noticed in Western Europe, including in The Netherlands. At the Academic Medical Center a special dedicated team (GIOTA: gastro-intestinal oncology center Amsterdam) has taken responsibility for the management of the patients presenting with liver lesions suspected for malignant disease, including HCC. Whereas diagnosis of HCC primarily involves imaging, the aim of Chapter 7 was to assess the advantage of 18F-FCH PET/CT for detection of HCC and evaluation of the extent of disease. Similar to Chapter 3 the SUV ratio was used to evaluate PET images. Intrahepatic lesions on 18F-FCH PET/CT imaging were positive with an SUV ratio >1.5 and an accuracy of 88%. Eighteen extrahepatic lesions showed 18F-FCH uptake on PET/CT while uptake was absent in 3 affirmed non-HCC lesions by additional investigation, resulting in an accuracy of 100%. In 17 of 19 patients additional lesions were found on PET/CT imaging, with implications for treatment in 15 patients. The 18F-FCH PET/CT has implications for staging, management, and treatment evaluation, due to accurate assessment of extrahepatic disease. While imaging modalities have become more and more of importance as shown above Chapter 8 evaluated if staging laparoscopy (SL) for patients with HCC is still useful. Patients with HCC who underwent SL between January 1999 and December 2011 at the AMC were included. The 56 patients in this study underwent SL for assessment of the extent of disease and the quality of liver parenchyma. The additional value or yield of SL was 7% with an accuracy of 27%. A biopsy of the non-tumoral liver was performed in 45 patients who underwent SL, leading to changes in management in 4 patients (17%). This study addressed the most common benign hepatic lesions: the liver hemangioma. Fortunately liver hemangiomas are readily detected by abdominal ultrasonography, contrast enhanced CT or MR imaging on which giant liver hemangiomas are defined by a diameter larger than 5 cm. In asymptomatic patients with a giant liver hemangioma observation is justified. However, surgical resection is indicated in patients with (mechanical) abdominal complaints, or when diagnosis remains inconclusive. In these cases, enucleation is the preferred surgical method, according to existing literature and our own experience. Finally a rare coexistence of two benign hepatic lesions was presented in the 4th Case Study. FNH and hepatic bile duct hamartomas. MR imaging with the hepatobiliary contrast agent Gd-EOB-DTPA, Primovist® was used showing a 6 cm lesion in segment 2-3 of the liver typical of focal nodular hyperplasia. Because of severe complaints attributed to the lesion, the patient was scheduled for resection. During the laparotomy multiple small white lesions were found throughout the liver with enlarged locoregional lymph nodes. Macroscopically, the findings could be consistent with widespread metastases and the surgeon felt compelled to determine the nature of these lesions before continuing the resection. The final diagnosis revealed multiple bile duct hamartomas and an FNH lesion as was expected.

PART IV Chapter 10 discusses 4 different images of hepatic tumors. The 1st Case shows the hepatoblastoma, a rare carcinoma mostly seen in children. We report the case of an 18-year-old girl who presented with abdominal pain, nausea, bloating, and fatigue. MRI showed three hepatic lesions with high signal intensity on arterial phase T1-weighted images and slight washout on the late phase, being suggestive of hepatocellular carcinoma. Laboratory examinations revealed plasma alpha-fetoprotein of 11245 ng/L. Baseline 18F-FCH PET/CT was performed followed by a post-treatment 18F-FCH PET/CT after neo-adjuvant chemotherapy to assess the extent of disease and treatment response. Standard CT imaging was used as standard of reference as this is standard of care. 18F-FCH PET/CT proved to be a promising additional imaging tool for hepatoblastomas and useful for staging and assessment of treatment response of this patient. The 2nd Case study, presents five cases in whom two rare lesions were simultaneously found within the liver, i.e. HCA and hepatic granulomas. The coexistence of both entities in these patients confused diagnosis. HCA and especially the inflammatory subtype may cause formation of granulomas in (peri-)tumorous tissue as a local response to persistent inflammation and/or the presence of a tumor. Both HCA and hepatic granulomas have also been associated with oral contraceptive use and was thought to be (partially) causative in these patients. We suggested that HCAs associated with hepatic granulomas derive from a local response to (inflammatory) HCA or neoplasm, chronic use of oral contraceptives, or a combination of these factors. The 3rd Case study addressed the most common benign hepatic lesions: the liver hemangioma.
The Gd-EOB-DTPA enhanced MRI shows high accuracy when standard contrast enhanced series are combined with the hepatobiliary phase for differentiation of HCA and FNH in lesions larger than 2 cm.

PET/CT imaging with $^{18}$F-FCH can accurately differentiate HCA from FNH and may become a valuable diagnostic tool when conventional imaging techniques fail to do so.

If patients with HCA and FNH require surgery, limited resection or enucleation of the lesion can be carried out with low morbidity and without mortality, using either an open or laparoscopic approach. Patients with preoperative symptoms show a high rate of postoperative symptom relief.

Bleeding HCA can be graded on which treatment can be based: Grade I and II with bleeding-areas larger than 6cm, and all Grade III bleedings are preferably treated with TAE. Additional care, being follow-up or preventive treatment, is advised in patients with exophytic adenomas.

Bleeding was seen in 64% patients and in 22% lesions. Patients with a body mass index $>$25 showed an increased risk for severe bleeding Grade II and III. Lesions $>$35mm, exophytic lesions, lesions in segments 2-3, and lesions with associated peripheral or central arteries have a higher risk for bleeding.

The $^{18}$F-FCH PET/CT has additional value for patients with HCC. The $^{18}$F-FCH PET/CT has implications for staging, management, and treatment evaluation due to accurate assessment of extrahepatic disease.

With the current accurate imaging methods and the implementation of additional percutaneous biopsy of non-tumorous parenchyma as a standard procedure in the pre-operative workup of patients with HCC, the benefit of staging laparoscopy is lost.

Overview of the cohort of hepatocellular carcinoma patients was similar to data of Western centers. Factors associated with survival of patients with HCC are AST, low albumine, presence of ascites, macrovascular involvement, and size of the largest HCC lesion.

$^{18}$F-FCH PET/CT proved to be a promising additional imaging tool for hepatoblastomas and useful for staging and assessment of treatment response of this patient.

We suggested that HCAs associated with hepatic granulomas derive from a local response to (inflammatory) HCA or neoplasm, chronic use of oral contraceptives, or a combination of these factors.

In asymptomatic patients with a giant liver hemangioma observation is justified. However, surgical resection is indicated in patients with (mechanical) abdominal complaints, or when diagnosis remains inconclusive. In these cases, enucleation is the preferred surgical method, according to existing literature and our own experience.

Looks can be deceiving: macroscopically, the findings could be consistent with widespread metastases, frozen section analysis revealed multiple bile duct hamartomas and a lesion as was expected.
IMAGING OF HEPATIC HYPERVASCULAR TUMORS & CLINICAL IMPLICATIONS

SAMENVATTING

Matthanja Bieze
Promotor: T.M. van Gulik, Chirurg
J. Verheij, Pathology

UVA; Academic Medical Center
DEEL I van dit proefschrift leidt de levertumoren in die in dit proefschrift worden besproken.

HOOFDSTUK 1. Het leveradenoom, focale nodulaire dysplasie (FNH) en lever hemangiomen zijn goedaardige tumoren die vaak bij toeval in de lever worden gevonden. Van FNH worden geen complicaties gezien en van hemangiomen zijn complicaties heel zeldzaam, daarom worden deze tumoren alleen behandeld als de klachten opwegen tegen de risico’s voor een eventuele ingrijpende behandeling. Het leveradenoom kent wel complicaties zoals bloeding en in zeldzame gevallen kan het kanker worden. Voor patiënten met leveradenomen zijn deze risico’s de reden waarom een operatie geadviseerd wordt. Als laatste wordt het hepatocellulair carcinoom (HCC), leverkanker besproken. Deze vorm van kank-er wordt steeds vaker in Nederland gezien en als een patiënt zich presenteert met verdening op leverkanker dan wordt een multidisciplinair team van specialisten ingezet om de diagnose en uitbreiding van de ziekte te evalueren om de behandeling zo snel mogelijk te kunnen starten.

DEEL II bespreekt de beeldvorming van goedaardige hypervasculair levertumoren en de klinische implicaties hiervan. Alle patiënten die verdacht werden van een leveradenoom of focale nodulaire dysplasie (FNH) werden gevraagd deel te nemen aan beeldvormende onderzoeken met het doel diagnose implicaties hiervan. Alle patiënten die verdacht werden van leveradenomen of focale nodulaire dysplasie van de ziekte te evalueren om de behandeling zo snel mogelijk te kunnen starten.

DEEL III van dit proefschrift bespreekt leverkanker (hepatocellulair carcinoom; HCC). In de afgelopen twee decennia wordt het hepatocellulair carcinoom (HCC) bij patiënten met leveradenomen en FNH geïncludeerd in de diagnose van leveradenomen. De diagnose HCC wordt meestal met een CT scan gedaan. In het leveradenoom en FNH heerst er een relatief grotere kans op bloeding in de nieuw ontwikkelde tumoren of onzekerheid in de diagnose. Bij leveradenomen is de kans op bloeding in de nieuw ontwikkelde tumoren of onzekerheid in de diagnose lager dan bij leveradenomen. Bij leveradenomen is de kans op bloeding in de nieuw ontwikkelde tumoren of onzekerheid in de diagnose lager dan bij leveradenomen.
en voor evaluatie van de uitgebreidheid van de ziekte. Net als in DEEL IV was de SUVratio om de PET beelden te evalueren. Intrahepatische HCC lesies waren positief op de 18F-FCH PET/CT met een nauwkeurigheid van 88% en een SUVratio van 1,95 ± 0,66 (bij een afkap waarde van 1,12). Achtzien bewezen manifestaties van HCC buiten de lever lieten opname van 18F-FCH zien, terwijl 3 lesies die bewezen GEEN HCC waren, ook geen 18F-FCH opname vertoonden, hetgeen neerkomt op een nauwkeurigheid van 100%. In 17 van 29 patiënten werden extra afwijkingen gevonden op de 18F-FCH PET/CT die van invloed waren op de behandeling in 15 patiënten. Deze studie laat zien dat 18F-FCH PET/CT van toegevoegde waarde is bij de behandeling van HCC, met name door de nauwkeurige detectie van extrahepatische ziekte. Beeldvormende technieken zijn tegenwoordig diagnostisch voor HCC en eventuele metastasen. In HOOFDSTUK 8 wordt de rol van diagnostische laparoscopie (DL) in patiënten met HCC onderzocht. In deze studie werden alle patiënten met HCC die een DL ondergingen tussen januari 1999 en december 2011 geïncludeerd. Vijfendertig patiënten ondergingen DL om de uitgebreidheid van het HCC en de kwaliteit van het leverparenchym in kaart te brengen. Een biopsi van de niet-aangedane lever werd verricht in 45 patiënten die een DL ondergingen, hetgeen leidde tot een verandering in behandeling in 4 patiënten met cirrose (17%). In slechts 67% van de patiënten was DL een toegevoegde waarde met een nauwkeurigheid van 27%. Met de huidige radiologische klachten gerelateerd aan de tumor, of wanneer de diagnose onzeker is, is chirurgisch ingrijpen geïndiceerd. Enucleatie is op basis van de huidige literatuur en onze eigen ervaring, de chirurgische behandeling van keuze. In de laatste, 4e CASUS wordt een zeldzaam samengaan van twee goed-afgebakken leverafwijkingen beschreven, namelijk FNH en galganghamartomen. Deze combinatie kan worden verward met uitzandingen van een kwaadaardige tumor. Een MRI met hepatobiliar contrast toonde een 6cm grote tumor in segmenten 2-3 van de lever met typische kenmerken van een FNH. Door ernstige klachten te gescutteerd bij de tumor, werd de patiënt gepland voor resectie. Tijdens de operatie werden meerdere kleine, witte afwijkingen verspreid door de lever gevonden en vergrootte lymfeklieren. Gezien het vermoeden van een uitgebreid gemetastaseerde tumor werden bioplen genomen. Deze lieten echter multiple galganghamartomen en conform de preoperatieve diagnose, een FNH zien. Het samengaan van FNH en galganghamartomen berust op toeval.
**CONCLUSIES**

2 De Gd-EOB-DTPA MRI laat een hoge nauwkeurigheid zien wanneer standaard dynamische series gecombineerd worden met de hepatobiliaire fase voor de differentiatie van HCA en FNH in afwijkingen groter dan 2 cm.

3 PET/CT met 18F-FCH kan een HCA accuraat onderscheiden van FNH en kan een waardevolle aanvullende techniek zijn als De Gd-EOB-DTPA MRI geen uitsluiting geeft.

4 Wanneer in patiënten met HCA of FNH een chirurgische behandeling geïndiceerd is, kan een beperkte resectie of enucleatie uitgevoerd worden met lage morbiditeit en zonder mortaliteit. Hierbij kan gebruik worden gemaakt van een open of laparoscopische benadering. Patiënten met pre-operatieve klachten lieten een hoog percentage aan symptoomverlichting zien na chirurgische interventie.

5 Een gradersysteem voor bloedingen in HCA wordt voorgesteld waarin Graad I & II bloedingen met een bloedingsgebied groter dan 6 cm en alle Graad III bloedingen behandeld worden met transarteriële embolisatie. Extra zorg door middel van controle of preventief ingrijpen wordt geadviseerd in patiënten met exofytische lesion.

6 Bloedingen in HCA wordt gezien in 64% van patiënten en in 22% van alle HCA lesions. Patiënten met een ‘body mass index’ (BMI) van 25 of meer hebben een verhoogde kans op een ernstige Graad II & III bloeding. HCA groter dan 35 mm, exofytische HCA, HCA in segment 2-3 van de lever en HCA met centrale of perifere voedende arteriën, hebben een hoger risico voor bloeding.

7 De 18F-FCH PET/CT heeft toegevoegde waarde in patiënten met HCC met implicaties voor stagering, behandeling en evaluatie van behandeling, door de accurate detectie van extrahepatische ziekte.

8 Met de huidige accurate beeldvorming en de implementatie van percutane biopsie van het niet-aangedane leverparenchym in de pre-operatieve work-up van patiënten met HCC, is het voordeel van een diagnostische laparoscoopie weggeval.

9 Een overzicht van een cohort patiënten met HCC behandeld in het AMC kwam overeen met data van Westerse centra. Factoren die geassocieerd zijn met overleving van patiënten met HCC zijn ASAT, albumine, ascites, macrovasculaire betrokkenheid en de grootte van de tumor.

10 18F-FCH PET/CT bleek een veelbelovende aanvullende beeldvormende techniek voor het hepatoblastoom en bleek nuttig voor stagering van de ziekte en evaluatie van de behandeling.

2 Levergranulomen die simultaan met HCA voorkomen ontstaan waarschijnlijk door een lokale respons op een (inflammatoire) adenoom of neoplasma, chronische gebruik van de pil, of een combinatie van deze factoren.

3 In asymptomatische patiënten met een reuzenhe mangiom van de lever is observatie gerechtvaardigd. Wanneer een patiënt mechanisme klachten heeft, of wanneer de diagnose onzeker is, is chirurgische interventie geïndiceerd. In deze patiënten is enucleatie de aangewezen methode.

4 Eerste indruk kan bedriegen: macroscopisch kan een bevinding de indruk geven van uitgebreide metastasering, maar aanvullende virescoups kunnen de diagnose bevestigen wanneer nodig. In deze patiënt bleken multiple galgang hamartomen samen te gaan met een FNH.