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·论 著·

肝脏血管平滑肌脂肪瘤的诊断和治疗

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[摘要] **目的** 分析并总结肝脏血管平滑肌脂肪瘤(AML)的临床表现和诊断,探讨其治疗策略。**方法** 对1992-2006年第二军医大学东方肝胆外科医院手术病理证实的79例肝AML临床资料进行回顾性分析研究,总结其诊治经验。**结果** 患者女58例,男21例。发病年龄17~69岁,平均(43±8.14)岁,均无合并肾血管平滑肌脂肪瘤或结节性硬化症。有临床症状者25例。肿瘤大小1.0~25 cm,平均(6.1±4.08) cm,均为单发肿瘤。肝右叶53例,左叶22例,尾状叶4例。术前正确诊断者41例(52%)。自发性破裂出血1例。79例均手术切除,无手术死亡或严重并发症。术后随访3~13年,1例术后6年复发,1年后死亡。**结论** 肝血管平滑肌脂肪瘤无特异性临床症状,综合影像学检查有助于术前正确诊断,但鉴别诊断困难,特别是对直径小于5 cm的肿瘤术前难以确诊。最终诊断依赖于病理组织学检查和HMB-45免疫组化染色。手术切除是治疗肝血管平滑肌脂肪瘤的安全、有效方法。应警惕潜在恶性和自发性破裂出血可能,一旦诊断明确宜尽早手术,术后应密切随访。

[关键词] 肝肿瘤;血管平滑肌脂肪瘤;诊断;肝切除术
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Diagnosis and treatment of hepatic angiomyolipoma

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[**Abstract**] **Objective** To analyze the clinical features and diagnosis of hepatic angiomyolipoma patients, and to investigate its treatment strategy. **Methods** The clinical data of 79 patients with pathologically-confirmed hepatic angiomyolipoma, who were treated in the Eastern Hepatobiliary Surgery Hospital during 1992-2006, were retrospectively reviewed. **Results** The patients included 58 women and 21 men with a median age of (43±8.14) years old (ranging 17 to 69 years). None of the patients was found complicated with renal angiomyolipoma or tuberous sclerosis complex. Twenty-five patients were symptomatic on presentation. All the patients had a single hepatic lesion, with the tumor size ranging 1.0-25 cm and a median of (6.1±4.08) cm. Fifty-three tumors were located in the right lobe, 22 in the left lobe, and 4 in the caudate lobe. Preoperative diagnoses were correctly made in 41 (52%) patients. Spontaneous rupture of tumor occurred in 1 patient. All the patients underwent surgical treatment without operative mortality and serious morbidity. The patients were regularly followed-up for 3-13 years. Tumor recurrence occurred in one patient 6 years after the surgery, and the patient died 1 year later. **Conclusion** Hepatic angiomyolipoma has no specific clinical signs and symptoms. Comprehensive imaging studies can help to make correct diagnosis, but the differential diagnosis is difficult, especially for small tumors with diameter less than 5 cm. The final diagnosis depends on pathologic examination and HMB-45 special staining. Surgical resection is safe and effective for the disease. Attention should be paid to the potential of malignant transformation and risk of rupture as a life-threatening complication. Early operation is needed once a diagnosis is made, and the patients should be followed up after operation.

[**Key words**] liver neoplasms; angiomyolipoma; diagnosis; hepatectomy
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血管平滑肌脂肪瘤(angiomyolipoma, AML)是一种间叶性肿瘤,由血管、平滑肌和脂肪3种成分组成,好发于肾脏,少见于肝脏。国外Ishak[1]于1976年报道了首例尸检肝脏病例,Kawarada等[2]于1983

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年报道了首例临床肝脏病例，国内丛文铭等[3]于 1992 年报道了国内首例肝脏病例。随着影像技术的发展和广泛应用，肝脏 AML 的发现率逐渐提高，但仍有较高的误诊率。肝脏 AML 的治疗目前仍存争议。部分观点认为肝脏 AML 是良性肿瘤，主张保守治疗；但也有研究[4-8]发现其具有自发性破裂出血、术后远期复发及恶变的可能，主张积极治疗。因此，本研究回顾了 79 例手术切除的肝脏 AML 患者的临床资料，总结临床诊治经验，以提高该病的诊治水平。

1　资料和方法

1.1　一般资料　1992 年 1 月至 2006 年 12 月第二军医大学东方肝胆外科医院共手术切除 79 例肝脏 AML。所有患者均经术后病理证实。术前检查包括：血常规、血生化、肝炎免疫、肿瘤标志物（AFP、CEA、CA19-9）；腹部 B 超、CT、MRI 检查。

1.2　手术指征　(1)肿瘤引起临床症状（如右上腹胀痛或饱胀感）经内科治疗或休息不能缓解；(2)肿瘤生长，术前观察至少 1 个月；(3)肿瘤呈外生性生长，有破裂出血的可能；(4)鉴别诊断困难，不能完全排除恶性肿瘤。考虑到有肿瘤细胞腹腔种植、肿瘤出血和破裂的危险，对可切除的肝脏肿瘤，一般不采用术前穿刺活检。

1.3　标本处理　手术标本经常规 4%中性甲醛固定，石蜡切片，H-E 染色及特殊染色（Masson 三色法）。免疫组织化学采用 EnVision 二步法。术后患者常规门诊随访。

1.4　统计学处理　采用 SPSS 11.5 统计软件完成统计学分析。检验水平（α）为 0.05。

2　结　果

2.1　临床特点　79 例肝脏 AML 患者，男 21 例，女 58 例，男女之比为 1∶2.7；年龄 17～69 岁，平均（43±8.14）岁。54 例（68%）为体检或因其他疾病手术时偶然发现，其余 25 例（32%）有临床症状。最常见的临床表现是右上腹不适，多为胀痛或饱胀感，共 20 例；其他 5 例表现为发热、体质量减轻和全身不适等。绝大多数患者肝功能正常。7 例（8.9%）肝炎免疫阳性，其中 HBsAg 阳性 5 例，丙肝抗体阳性 2 例。所有患者的肿瘤标志物均在正常范围。全组患者均无合并肾血管平滑肌脂肪瘤或结节性硬化症。肿瘤直径 1.0～25 cm，平均（6.1±4.08）cm，均为单发。肿瘤位于肝右叶 53 例，左叶 22 例，尾状叶 4 例。有症状者与无症状者肿瘤直径有统计学差异（表 1、表 2）。

来本院就诊前，2 例已行肿瘤穿刺活检，均提示恶性；3 例已行剖腹探查术，其中 2 例为试图切除肝脏“巨大海绵状血管瘤”，另 1 例为肝脏“海绵状血管瘤”自发性破裂出血而行缝合止血；5 例已行 1 次或多次肝动脉栓塞化疗术（TACE），2 例患者已行无水乙醇注射术（PEIT）；另 3 例为恶性肿瘤术后随访患者（原发性肝癌、直肠癌和胃癌各 1 例）。

表 1　79 例肝脏 AML 患者的临床资料

Tab 1　Clinical data of 79 patients with hepatic angiomyolipoma

Items	Results
Age	43 (17-69) year
Gender (female∶male)	58∶21 (ratio: 2.7)
Symptoms (asymptomatic∶symptomatic)	54∶25
Abdominal discomfort	20
Weight loss	1
General malaise	3
Fever	1
Tumor location	
Right lobe	53 (67%)
Left lobe	22 (28%)
Caudate lobe	4 (5%)
Tumor size	6.1 (1-25 cm)
≤5 cm	45 (57%)
5-10 cm	22 (28%)
≥10 cm	12 (15%)
Associated liver disease	7 (8.9%)
HBV infection	5
HCV infection	2
Associated tuberous sclerosis	0

表 2　有、无症状患者临床资料对比

Tab 2　Clinical data of symptomatic and asymptomatic patients

Clinical parameter	Symptomatic (n=25)	Asymptomatic (n=54)	P value
Male∶female	6∶19	15∶39	> 0.05
Age (year)	42.88±7.29	43.39±10.8	> 0.05
Tumor size d/cm	6.60±4.22	5.54±4.19	< 0.05

2.2　影像学诊断　联合 B 超、CT 或 MRI，术前诊断正确者 41 例（52%）。在 34 例直径大于 5 cm 的肿瘤中，22 例有血管平滑肌脂肪瘤的典型影像学表现，但在 45 例直径小于 5 cm 的肿瘤中，只有 19 例具有典型表现，两组差异有统计学意义（P<0.05）。术前误诊者共 38 例（48%），20 例怀疑为恶性病变，其中原发性肝癌占 18 例，另 2 例为肝脏转移性癌。其余 18 例误诊为肝脏良性肿瘤如海绵状血管瘤（7 例）、肝腺瘤（5 例）、错构瘤（3 例）、局灶性结节增生（2 例）及脂肪瘤（1 例，表 3）。

2.3　手术及术后随访　79 例均行手术治疗，手术方式见表 4。无手术死亡及严重并发症。术后患者定

期门诊随访,随访 3～13 年,平均(4.8±3.75)年。92%的有症状者术后症状消失。1 例于术后 6 年复发,次年死亡。

表 3 79 例肝脏 AML 的术前诊断

Tab 3 Preoperative diagnosis of 79 patients with hepatic angiomyolipoma

Preoperative diagnosis	No. of patients
Correct diagnosis of AML	41 (52%)
Tumor size≤5 cm	19
Tumor size>5 cm	22
Misdiagnosis	38 (48%)
Malignancy	20
HCC	18
Gastric metastasis	1
Colorectal metastasis	1
Benign lesion	18
Hemangioma	7
Hepatic adenoma	5
FNH	3
Hamartoma	2
Lipoma	1

2.4 *病理及免疫组织化学特征* 按 Tsui 等[9]的分类标准分为 4 型:(1)经典型,肿瘤由血管、平滑肌和脂肪 3 种成分按大致相同比例组成(图 1A);(2)脂肪瘤型,脂肪组织超过 70%;(3)肌细胞型,脂肪组织少于 10%;(4)血管瘤型。肌细胞型又进一步按其细胞形态细分为:①上皮样细胞型,②中间细胞型,③梭形细胞型(图 1C),④嗜酸细胞型,⑤多形细胞型(图 1D)。

表 4 79 例肝脏 AML 的手术方式

Tab 4 Surgical resection of 79 patients with hepatic angiomyolipoma

Treatment	No. of patients
Major resection	9
Right hepatectomy	4
Left hepatectomy	2
Segment Ⅰ+Ⅱ+Ⅲ	3
Bisegmentectomy	27
Segment Ⅱ+Ⅲ resection	11
Segment Ⅵ+Ⅶ resection	10
Segment Ⅴ+Ⅵ resection	6
Segmentectomy	16
Segment Ⅴ	5
Segment Ⅵ	9
Segment Ⅷ	1
Segment Ⅰ	1
Wedge resection	15
Tumoral enucleation	12

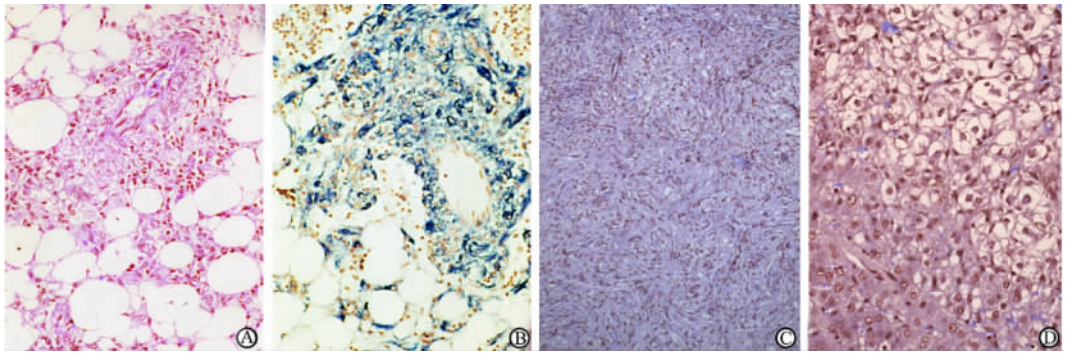

图 1 肝脏 AML 的组织病理学表现及免疫组化染色

Fig 1 Pathologic study and immunochemical staining of patients with hepatic angiomyolipoma

A: Classic mixed type, tumor is composed of myoid cells, mature adipocytes and abnormal vessels(H-E staining). B: Strong granular HMB-45 immunoreactivity in myoid cells(EnVision). C: Tumor is exclusively composed of proliferated spindle-shaped smooth muscle cells, which forming an interlacing fascicular pattern(H-E staining). D: Pleomorphic tumor cells with "spider web" cytoplasm(H-E staining). Original magnification: ×200

本组结果为经典型 23 例,肌细胞型 46 例,血管瘤型 4 例,脂肪瘤型 6 例。另外,14 例肿瘤可见髓外造血,5 例可见浸润性边界,2 例可见肿瘤内坏死出血(表 5)。除 7 例合并病毒性肝炎或肝硬化外,其余的肿瘤旁肝组织均正常。全组肿瘤 HMB-45 染色阳性,呈颗粒状,上皮样细胞大多染色均匀(图 1B,表 6)。

3 讨 论

3.1 *AML 发病情况* AML 好发于肾脏,少见于肝脏,国外报道的肝脏 AML 共约 200 例[10],本组为至今最大的一组病例。随着影像技术,特别是超声检查的广泛应用,越来越多无临床症状者被发现。本组中超过半数的患者无临床症状,多因体检而发现肝脏占位性病变。即使出现症状,这些症状也是非特异性的,最常见的是肿瘤压迫而引起的右上腹不适,如钝痛或饱胀感。本研究结果表明肝脏 AML 好发于女性,常为单发,多位于肝右叶。肝脏 AML 与病毒性肝炎或肝硬化无关。

表 5　79 例 AML 的病理分型及特征

Tab 5　Pathologic typing of 79 patients with hepatic angiomyolipoma

Pathologic classification	No. of patients
Classic mixed type	23 (29%)
Myomatous type	46 (58%)
Epithelioid cell	17
Intermediate cell	20
Spindle cell	4
Eosinophilic epithelioid cell	4
Pleomorphic cell	1
Lipomatous type	6 (7%)
Angiomatous type	4 (5%)
Sclerosis	3
Pelioid	1
Other pathology feathers	
Extramedullar hematopoiesis	14
Intratumoral necrosis and hemorrhage	2
Neighboring liver invasion	5
Background liver disease	7

表 6　79 例肝脏 AML 的免疫组织化学特征

Tab 6　Immunohistochemical studies of 79 patients with hepatic angiomyolipoma

Antibody	Positivity(n)			Total [n/N(%)]
	+	++	+++	
HMB-45	0	27	41	79/79 (100)
α-SMA	10	30	15	55/61 (90)
CD117	10	14	8	32/41 (78)
CD34	20	13	21	54/72 (75)
CD68	4	10	1	15/21 (71)
PCNA	15	3	4	22/47 (46.8)
HepPar-1	0	0	0	0/70 (0)
CK18	0	0	0	0/65 (0)
CK19	0	0	0	0/65 (0)

All antibodies were supplied by Dako patts, Glostrup, Denmark

3.2　关于恶变　以前曾认为肝脏 AML 是良性间质性肿瘤，但自 2000 年 Dalle[5] 报道首例肝脏恶性 AML 以来，已有 9 例类似报道[6,11-18]，主要表现为术后远期复发、侵犯血管及肿瘤快速生长压迫下腔静脉而造成的 Budd-Chiari 综合征等。一旦复发，预后极差。本组有 1 例 31 岁女性患者，体检发现中肝有一直径 8 cm 的肿瘤，于 1999 年 1 月 21 日手术切除，术后病理证实为 AML，术后 6 年复发，次年死亡。这些结果表明不能完全认为肝脏 AML 都是良性病变，至少它有恶变的可能，应引起高度重视。

3.3　关于破裂出血　肿瘤破裂出血是手术切除的指征之一，但肝脏 AML 自发性破裂出血的发生率仍不清楚，目前文献报道的仅 2 例[4,19]。本组有 1 例自发性破裂出血病例。患者为 56 岁女性，1985 年因急性阑尾炎进行术前检查时发现肝脏Ⅵ段有一直径 6 cm 的肿瘤，术中探查诊断为海绵状血管瘤。之后每年复查肝脏 B 超，肿瘤未见明显增大。2004 年 9 月 8 日因突发性腹痛、腹腔内急性出血合并休克在当地医院行急诊剖腹探查，证实肿瘤破裂出血，行缝合止血，术中活检示肝脏海绵状血管瘤。2005 年 3 月 3 日在本院行肿瘤切除术，术后病理证实肝脏 AML。在迄今报道的肝脏 AML 中，大多数肿瘤都有持续生长的趋势[20-24]，自然消退的病例极罕见[25]。即使肿瘤大小无明显改变，其内在脂肪、血管和平滑肌的构成比例亦可发生变化[23]，可合并瘤内坏死出血。这些发现提示，肝脏 AML 不是一种稳定的病变，不宜只行观察而置之不理。

3.4　术前影像学诊断　肝脏 AML 术前影像学诊断较困难。其典型性表现[26-31]有：(1)超声检查多表现为杂乱高回声区(图 2D)；(2)CT 平扫显示不均匀的低密度区(一般低于－20 HU)(图 2A、3A)，增强后肿瘤明显强化(图 2B、3B)，延迟期可超过 4 min，呈血管瘤样表现，并可显示肿瘤内血管(图 2C)；(3)在 MRI 的 T_1 和 T_2 加权上均为高信号；(4)肝动脉造影显示肿瘤血供丰富及肿瘤染色。但这些表现都是非特异性的[32-35]，显示的只是肿瘤内脂肪组织和血管成分，还需与肝内其他含脂肪组织的病变相鉴别，包括恶性病变，如原发性肝癌、脂肪肉瘤、多血供的转移癌等，以及良性病变，如局灶性结节增生、肝腺瘤、脂肪瘤、脂肪肝的局部脂肪浸润等。另外，使影像学诊断显得困难的另一原因是肝脏 AML 内 3 种成分含量不定，差别大时肿瘤可呈单一的组织形态，如单一型类上皮细胞性 AML(monotypic epithelioid angiomyolipoma)[13,36]，从而导致了各种不典型的影像学表现(图 2A、2B、2C)。我们发现肿瘤越小，其不典型表现越多，鉴别诊断越困难，本组中多数误诊发生在直径小于 5 cm 的肿瘤中。

3.5　鉴别诊断　我国是原发性肝癌高发区。在肝脏 AML 的鉴别诊断中，最重要的就是排除原发性肝癌。众所周知，原发性肝癌常合并脂肪变性，小肝癌(直径小于 3.5 cm)中的脂肪变性常呈弥漫性，大肝癌(直径大于 3.5 cm)中的脂肪变性常呈局灶性[37]。对大肝癌来说，瘤内脂肪对诊断影响不大，但小肝癌合并弥漫性脂肪变性常引起混淆，仅凭上述影像学检查仍无法鉴别。本组中有 1 例 54 岁的男性患者，右肝癌切除术后 11 年，随访发现其左肝有一小肿瘤，结合其病史，综合影像学检查均提示肝癌复发，之后手术切除。即使是术后病理检查，初见之下也诊断为高分化原发性肝癌，但仔细观察未见病理核分裂像，加上 HMB-45 染色阳性，最终才诊断为肝脏 AML。因此，有时仅根据影像学表现很难区别肝脏 AML 和小肝癌合并脂肪变性。更有甚者，在合并病毒性肝炎的肝脏中可同时发生 AML

和肝癌[38-39],这更增加了二者的鉴别难度。

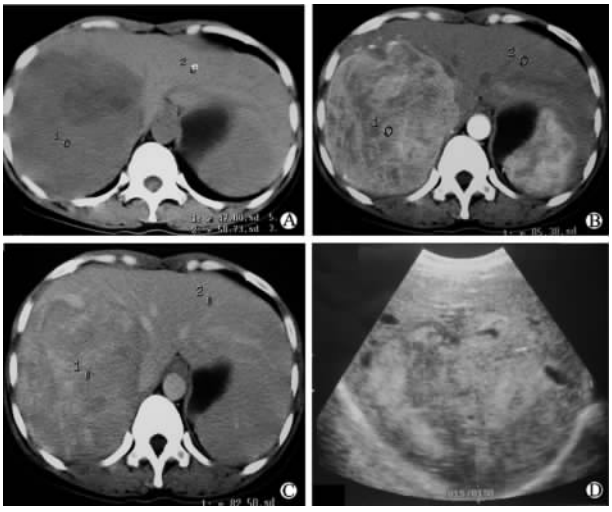

图 2 一例 33 岁女性患者肝脏 AML 的影像学表现

Fig 2 Imaging studies of hepatic AML in a 33-year-old woman

A: Plain CT shows a huge hypo-attenuating lesion completely takes up the right liver. B: Contrast-enhanced imaging shows the mass is intensively enhanced, blurred with hypodense areas. C: In late phase, the density of the lesion becomes slightly lower than the liver parenchyma, but a blush of central enhancement is obvious. The inferior vena cava is markedly compressed by the tumor, the right hepatic vein is involved in the tumor, and the middle hepatic vein is displaced by the tumor. No discrete fatty component is evident by CT anywhere in the mass. D: Abdominal US shows a heteroechogenic mass

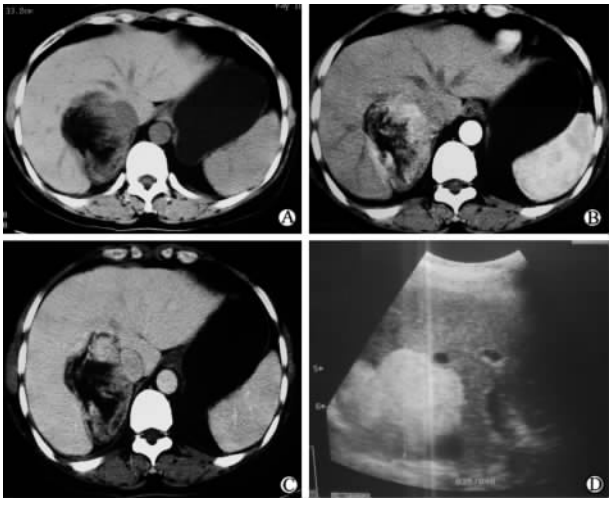

图 3 一例 47 岁女性患者肝脏 AML 的影像学表现

Fig 3 Imaging studies of hepatic AML in a 47-year-old woman

She had been under observation for 5 years with a diagnosis of liver hemagioma, and had received TAE treatment once, which did not control the lesion. A: Plain CT shows an irregularly-shaped lesion in the posterior of the right liver, with predominant fatty content. B: Contrast-enhanced imaging shows characteristic finding, the enhanced periphery is corresponding to the vascular portions of the tumor. C: In the portal venous phase, the mass is juxtaposed on the inferior vena cava. D: Abdominal US shows a hyperechogenic mass interposed between the right hepatic vein and the inferior vena cava

3.6 *关于肿瘤穿刺活检* 虽然肿瘤穿刺活检可减少误诊,但对可能是恶性的病变、外生性生长或多血供的肝脏肿瘤,大多数临床医生都不主张这项检查,因为引起并发症的可能性大。另外,由于穿刺不一定能同时获得 AML 的 3 种组织,而且 AML 中的 3 种组织含量不定,有许多变异型,有时反而会导致误诊[40-42]。针道肿瘤细胞种植也是人们担心的一个问题[43]。因此,我们对可切除的肝脏肿瘤不做常规的穿刺活检,除非在微创治疗前。

3.7 *肝脏 AML 的治疗* 肝脏 AML 的治疗目前仍存争议。很明显,肿瘤有可能恶变以及破裂出血需手术切除。另外,有时肝脏 AML 与小肝癌鉴别诊断困难,而我国又是肝癌高发地区,因此保守治疗风险较大。当影像学结果不确定时,我们选择手术切除肝脏肿瘤。手术切除是治疗肝脏 AML 的一个安全有效方法。我们认为切除肝脏 AML 的适应证:(1)肿瘤引起临床症状,影响正常生活或工作,应切除肿瘤;(2)肿瘤直径大于 5 cm;(3)肿瘤呈外生性生长,有破裂出血倾向;(4)临床观察发现肿瘤有生长增大趋势;(5)影像学检查和(或)穿刺活检不能确诊时。若采用保守治疗,在严密随访观察的同时,还必须满足以下条件:(1)肿瘤小于 5 cm,且患者无任何临床症状;(2)经穿刺活检及 HMB-45 染色证实肝脏 AML;(3)患者顺从配合,能坚持定期复查;(4)不是肝炎病毒携带者。

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