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肝脏假性淋巴瘤的临床病理学研究及分析 *

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摘要 目的:探讨肝脏假性淋巴瘤的临床病理特征、免疫表型及鉴别诊断。**方法:**在光学显微镜下对肝脏假性淋巴瘤进行组织学形态观察,并借助免疫组化进一步对其形态进行分析。由于原发于肝脏的假性淋巴瘤极为罕见,故本文将报道一例发生于肝脏的假性淋巴瘤,结合文献探讨其临床病理特点,以提高诊断及鉴别诊断水平。**结果:**大体上为切面可见灰白结节,结节切面灰白色,质地中等,与周围分界清,周围肝组织灰红质软。显微镜下组织学表现为肝周边淋巴结淋巴组织增生,细胞大小较一致,核圆形,细胞无异型,未见明显核分裂,其中见嗜酸性白细胞浸润及少数异型细胞。免疫组化显示肿瘤细胞表达 CD3、CD20 及 CD30。**结论:**肝脏假性淋巴瘤为罕见的、良性淋巴组织增生性病变,形态学特征、免疫组化染色在肝假性淋巴瘤诊断中具有重要价值。在临床病理实践中,必须首先与常见的发生于该部位恶性肿瘤如霍奇金淋巴瘤肿瘤等鉴别。

关键词:假性淋巴瘤;肝脏;病理诊断;鉴别诊断

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Research and Analysis of Clinical Pathology of Liver Pseudo Lymphoma*

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ABSTRACT Objective: To explore the clinical pathological characteristics of liver pseudo lymphoma, immune phenotype and differential diagnosis. **Methods:** Under optical microscope to histological morphology of liver pseudo lymphoma, and with the aid of immunohistochemical further analysis of its shape. Due to primary pseudo lymphoma is rare in the liver, so this article will report a pseudo lymphoma occurring in the liver, as well as to explore the clinical and pathological characteristics to improve the levels of differential diagnosis. **Results:** In general for the section visible gray nodules, nodal plane hoar, quality of a material medium, with the surrounding boundaries clear, red soft liver tissue around the ashes.Microscope histological characterized by hepatic peripheral lymphoid tissue lymph node hyperplasia, cell size is consistent, circular, nuclear cells without atypia, did not see obvious nuclear fission,see the eosinophilic leukocyte infiltration and a few different cells. Immunohistochemistry showed that tumor cells expressed CD3, CD20 and CD30. **Conclusion:** Pseudo liver lymphoma is a rare, benign lymphoid tissue proliferative lesions, morphology, immunohistochemical staining is of important value in the diagnosis of liver pseudo lymphoma. In clinical practice, must first occurred in the region of common malignant tumor with identification such as Hodgkin's lymphoma tumor.

Key words: Pseudolymphoma; Liver; Pathological diagnosis; Differential diagnosis

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前言

假性淋巴瘤又称反应性淋巴组织样增生或结节样淋巴组织样增生。除肝脏外,可见于不同的脏器,如胃肠道、肺、皮肤、甲状腺和胰腺等。Snover 等[1]在 1981 年首次报道了一例原发于肝脏的假性淋巴瘤,极为罕见。肝假性淋巴瘤是肝脏良性肿瘤病变中最为少见的,迄今国外文献报道 46 例[2],国内少见报道。有学者认为本病是不同于炎性假瘤的一种独立性病变,其病因和临床病理特点并未完全明了[3,4]。患者多为中老年,常为偶然发现,一般无特殊临床表现[5]。术前诊断相当困难,影像学难与肝脏其他恶性肿瘤相区别。因其临床相对罕见,人们对其临床表现、病理特征等方面仍不甚了解,且需要与肝局灶性结节状增生、低级别淋巴瘤及典型霍奇金淋巴瘤等相鉴别[7]。故本文将报道一例发生于肝脏的假性淋巴瘤,为提高诊断及鉴别诊断水平,将结合文献探讨肝脏假性淋巴瘤临床病理特点。

1 资料与方法

1.1 临床资料

患者女性,58 岁,因发现肝占位 1 日入院。查体:皮肤巩膜黄染,无腹痛、腹胀,无恶心、呕吐、发热。实验室检查: Hb 150 g/L;腹部超声:肝右叶低回声结节;腹部 MRI 平扫 + 增强:肝右叶有一直径约 1 cm 大小的肿瘤,呈 T2、T1,动脉期增强,静脉期廓清。术中行肝右叶肿瘤切除术,探查肝脏无明显肝硬化表现,肿瘤位于肝右前叶,大小约 1× 1× 1 cm,其余肝脏未触

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及明显转移结节。腹腔内无腹水，胆囊无增大，大网膜、肠系膜根部、盆腔，无明显转移结节。

1.2 方法

手术切除组织采用10%中性缓冲福尔马林液进行固定，肉眼检查，将标本切开取材，利用石蜡包埋制片，进行常规HE染色及免疫组织化学染色。免疫组织化学染色采用Envision两步法，所用一抗有CD3、CD15、CD20、CD30、Ki-67，均由北京中杉公司提供。最后结合相关文献探讨、阐述肝脏假性淋巴瘤这一罕见疾病的临床病理学特点。

2 结果

2.1 肉眼检查

肝组织1块，大小5× 3× 1.8 cm，切面可见灰白结节，大小0.8× 0.8× 0.8 cm，结节切面灰白色，质地中等，与周围组织分界清，无明显出血、坏死，周围肝组织灰红质软，无肝硬化表现。临床诊断首先考虑原发性肝癌。

2.2 镜下观察

肝周边淋巴结淋巴组织增生，细胞大小较一致，核圆形，细胞无异型，未见明显核分裂，可见淋巴滤泡形成，其中见嗜酸性白细胞浸润及少数异型细胞。病灶内夹杂正常肝组织，多灶性分布，病灶周围无包膜，其余肝组织无假小叶结构，汇管区无炎细胞浸润。

2.3 免疫表型

肿瘤细胞表达CD3、CD20及CD30，对CD15不表达，Ki67指数约35%。

2.4 病理诊断

结合免疫组化染色结果，诊断为肝脏假性淋巴瘤。

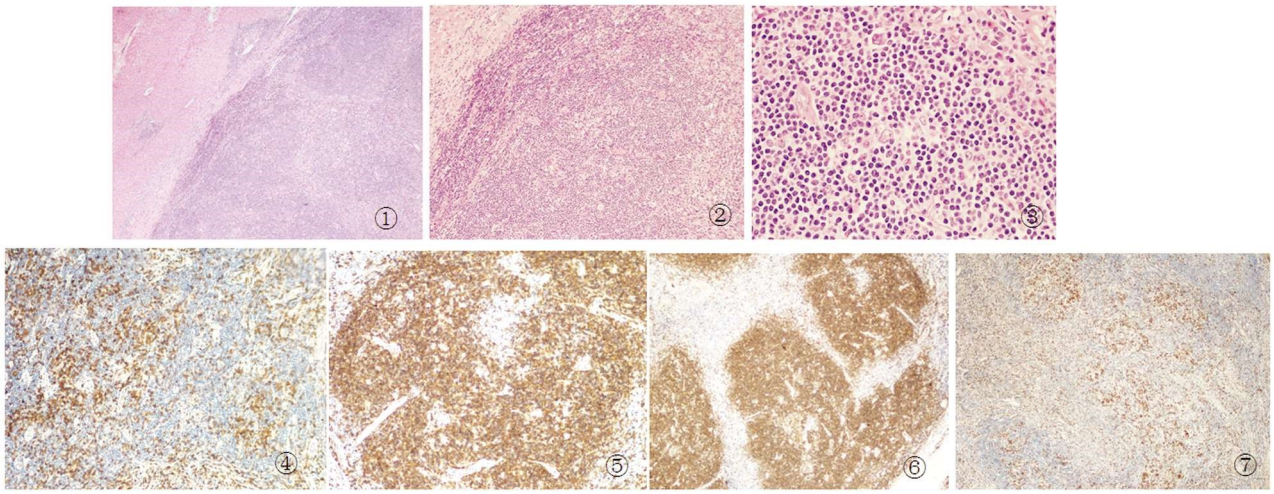

图1 低倍镜下，肝周边淋巴结淋巴组织增生，病灶周围无包膜，呈多灶性分布，余肝无假小叶结构，汇管区无炎细胞浸润

Fig.1 At low magnification, liver surrounding lymph nodes lymphoid tissue hyperplasia, around the lesions without envelope, the multiple focal distribution, residual liver structure without false flocculus, collect abbacy no inflammatory cells infiltration

图2 低倍镜下，为成熟的小淋巴细胞和浆细胞组成的结节性增生，细胞大小较一致，细胞无明显异型性，可见淋巴滤泡形成

Fig.2 At low magnification, for mature small nodular hyperplasia of lymphocytes and plasma cells, cell size is consistent, the cell has no obvious atypia, lymphoid follicle is forming

图3 高倍镜下，细胞大小较一致，核圆形，细胞无异型，未见明显核分裂，其中见嗜酸性白细胞浸润及少数异型细胞

Fig.3 At high magnification, the cell size is consistent, circular, nuclear cells without atypia, did not see obvious nuclear fission, which see eosinophilic leukocyte infiltration and a few different cells

图4 肿瘤细胞胞膜高表达CD3，Envision二步法

Fig.4 Tumor cell membrane high expression of CD3, Envision two footwork

图5 肿瘤细胞胞膜高表达CD20，Envision二步法

Fig.5 Tumor cell membrane high expression of CD20, Envision two footwork

图6 肿瘤细胞胞质和胞膜高表达CD30，Envision二步法

Fig.6 Tumor cell membrane high expression of CD30, Envision two footwork

图7 Ki-67阳性主要位于淋巴滤泡，指数约35%，Envision二步法

Fig.7 Ki - 67 positive mainly in the lymph follicles, index of about 35%, Envision two footwork

3 讨论

假性淋巴瘤又称反应性淋巴组织样增生，首先在肺部发现，由Saltzstein于1963年报道[8]。除肝脏外，可发生于不同的脏器，包括胃肠道、肺、甲状腺、皮肤、和胰腺等。Snover等[1]在1981年首次报道了一例原发于肝脏的假性淋巴瘤，极为罕见。肝脏假性淋巴瘤是一种非常罕见的良性淋巴组织增生性病变，多为个案报道，至今未见肝假性淋巴瘤恶变的报道。患者多为中老年，且绝大多数为女性。影像学无明显特征，在手术切除前很难作出正确诊断，因此组织病理诊断对于肝脏假性淋巴瘤尤为重要。

3.1 病因

肝脏假性淋巴瘤发病机制目前仍然未知,可能包括传染病及自身免疫反应。据文献报道,有原发性胆汁性肝硬化[9]和(或)非酒精性脂肪性肝炎[10]等慢性肝病背景的患者会发生肝脏假性淋巴瘤。通过对该肿瘤临床过程的思考表明病毒感染可能与肝脏假性淋巴瘤的发生有关,有报道称肝炎病毒的持续感染刺激可能导致肝脏假性淋巴瘤的发生[12],但本例患者否认肝炎病史。另外假性淋巴瘤可能来自淋巴组织相关门户,可以扩大并涉及附近的门管区。有干燥综合征、原发性局部或全身的肝外器官的自身免疫性疾病患者更易患病,故而有人认为该病的发生与机体免疫调节障碍有关。另外,胃、直肠癌等恶性肿瘤,有可能诱发肝脏假性淋巴瘤,病因可能是由于其频繁的腹部放射学检查导致[11]。肝结节和肝脏肿瘤也可能与其发病有关。

3.2 临床及影像学表现

假性淋巴瘤可发生于全身任何部位,在不同年龄、性别患者中均可发生,高峰年龄为 40-75 岁,女性好发。肝脏假性淋巴瘤的临床症状无腹痛、腹胀,无恶心、呕吐、发热,只有皮肤黄染,无特异性,这种非特异性的表现通常会延误诊断。本例患者以周身皮肤黄染为首发症状,腹部超声:肝右叶低回声结节;腹部 MRI 平扫 + 增强:肝右叶有一直径约 1 cm 大小的肿瘤,呈 T2、T1,动脉期增强,静脉期廓清,考虑原发性肝癌。

3.3 病理学特点

病理诊断对于肝脏假性淋巴瘤尤为重要。本例肉眼观为单发肿物,肿物与周围组织分界清,切面灰白色,质地中等,无明显出血、坏死,周围肝组织灰红质软,无肝硬化表现。有文献称肿瘤细胞主要由增生的淋巴滤泡、淋巴细胞及其他炎性细胞组成[13]。本例患者显微镜下肝周边淋巴结淋巴组织增生,细胞大小较一致,核圆形,细胞无异型,未见明显核分裂,可见淋巴滤泡形成,其中见嗜酸性白细胞浸润及少数异型细胞。病灶内夹杂正常肝组织,多灶性分布,病灶周围无包膜,其余肝组织无假小叶结构,汇管区无炎细胞浸润。与文献报道相似。

3.4 免疫表型

免疫组化对肝脏假性淋巴瘤诊断有重要意义,可以表达不同的细胞标志。本例肿瘤细胞高表达 CD3、CD20 及 CD30,对 CD15 不表达, Ki67 指数约 35%。CD3 分子表达于所有成熟 T 细胞表面,B 细胞不表达。CD20 是 B 淋巴细胞较特异的标记物。CD30 表达于活化的淋巴细胞(免疫母细胞)、R-S 细胞和大多数间变性大细胞淋巴瘤。CD15 表达于成熟粒细胞、活化的淋巴细胞等。有文献报道肝脏假性淋巴瘤免疫组化 B 细胞和 T 细胞数量大致相等,原位杂交显示免疫球蛋白轻链为多克隆性浆细胞病变,免疫球蛋白重链基因的 PCR 分析显示无克隆重组,呈多克隆性[3]。

3.5 鉴别诊断

当肝脏出现的增生性肿块以淋巴细胞成分为主时,应与肝局灶性结节状增生、低级别淋巴瘤及典型霍奇金淋巴瘤等相鉴别。肝局灶性结节状增生镜下见放射状纤维组织将肝组织分割成大小不等的结节,纤维组织内见增生的小胆管、扩张的小血管以及大量淋巴细胞、浆细胞浸润。在增生小胆管间有炎性细胞浸润,以淋巴细胞为主,个别以中性粒细胞以及嗜酸性细胞为主。上皮标志物 CK8、CK19 阳性。淋巴上皮损伤和细胞异型性是鉴别肝脏假性淋巴瘤及低级别淋巴瘤的重要诊断。典型霍奇金淋巴瘤细胞异型明显,核分裂像多见,瘤细胞界不清,有特征性淋巴上皮病变,有数量不等的 R-S 细胞及其变异细胞散布在淋巴细胞浸润的背景中。典型的 H/R-S 细胞为 CD30、CD15 阳性。

3.6 治疗及预后

肝脏假性淋巴瘤术前诊断非常困难,临床上极为少见,其是一种良性病变行为。影像学肝脏假性淋巴瘤与肝脏其他恶性肿瘤较难区别,故肝脏假性淋巴瘤的治疗一般都采用手术切除的方法。但也有文献报道肝脏假性淋巴瘤采用保守治疗的病例,一位 63 岁的女性患者在经穿刺活检确诊为肝脏假性淋巴瘤后未进行外科手术,期间成功根除油门螺旋杆菌,18 个月后随访研究表明肿瘤直接从 16 mm 降至 8 mm,没有证据表明其向恶性转化[14]。有文献报道一例有干燥综合征背景的患者,患肝脏假性淋巴瘤后未进行外科手术,随访 2 年后恶化。目前外科手术治疗是肝脏假性淋巴瘤的主要治疗手段。因此治疗模式可能是影响预后的重要因素。本例患者手术切除后效果理想,术后随访 5 年,未发现复发。

综上所述,肝脏假性淋巴瘤极其罕见,迄今国外文献报道 46 例[2],国内少见报道。文献表明,肝脏假性淋巴瘤是一种良性肿瘤病变,而手术切除仍然是目前已知的有效治疗方式。由于术前诊断困难,与肝脏恶性肿瘤难以区分,因此对于肝脏假性淋巴瘤的最终诊断依然要靠术后组织病理学检查,对疑难病例则需通过多种抗体免疫组织化学染色、原位杂交等进行鉴别,尤其与低级别 B 细胞来源淋巴瘤相鉴别,以免漏诊和误诊。

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