

• 专题研究:肿瘤 •

单中心胰腺腺泡细胞癌23例临床诊治分析

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[摘要] 目的:探讨胰腺腺泡细胞癌(acinar cell carcinoma, ACC)的临床、影像、病理特点、诊治及预后。方法:回顾性分析2015年4月—2024年12月南京医科大学第一附属医院收治并经病理确诊ACC的临床资料,总结其临床表现、影像与病理特点、诊治经过及预后。结果:共23例ACC入组,男15例,中位年龄63岁。入院症状以腹痛为主(13例),肿瘤位于胰头15例,胰体尾7例,全胰腺1例。肿瘤平均直径(54 ± 34)mm,实性8例(44.4%),实性伴坏死5例(27.8%),囊实性5例(27.8%)。行手术切除22例,病理+单纯ACC 21例,ACC混合导管腺癌1例,ACC混合神经内分泌肿瘤1例,淋巴结转移10例,神经脉管侵犯20例,R0切除19例。15例行术后辅助化疗。有效随访21例,术后中位生存期26个月,无复发中位生存期15个月,术后1年、3年生存率分别为90.5%、44.4%。术后首次转移复发部位以肝脏和后腹膜淋巴结最常见,其次为骨、肺、肠系膜淋巴结及术区局部复发。结论:ACC是一种罕见的恶性肿瘤,临床症状以腹痛为主,肿瘤多呈实性且侵袭性较强。手术切除联合术后辅助化疗是主要诊治模式,术后需重点关注肝脏及后腹膜淋巴结以早期识别复发转移。

[关键词] 胰腺腺泡细胞癌;手术治疗;化疗;生存时间

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Clinical diagnosis and treatment of pancreatic acinar cell carcinoma: a single - center analysis of 23 cases

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[Abstract] **Objective:** To investigate the clinical, imaging, and pathological characteristics, diagnosis, treatment, and prognosis of pancreatic acinar cell carcinoma (ACC). **Methods:** A retrospective analysis was conducted on clinical data of patients with pathologically confirmed ACC admitted to the First Affiliated Hospital of Nanjing Medical University from April 2015 to December 2024. The clinical manifestations, imaging and pathological features, diagnosis, treatment, and prognosis were summarized. **Results:** A total of 23 ACC cases were enrolled, with 15 males and a median age of 63 years. The most common presenting symptom was abdominal pain (13 cases). Tumors were located in the pancreatic head (15 cases), pancreatic body/tail (7 cases), and diffusely involved the entire pancreas (1 case). The mean tumor diameter was (54 ± 34)mm. Tumors presented as solid (8 cases, 44.4%), solid with necrosis (5 cases, 27.8%), and cystic-solid (5 cases, 27.8%). Surgical resection was performed in 22 cases. Pathologically, 21 cases were pure ACC, one case was mixed with ductal adenocarcinoma, and one case was mixed with neuroendocrine tumor. Lymph node metastasis was observed in 10 cases, and neurovascular invasion was present in 20 cases. R0 resection was achieved in 19 cases. Postoperative adjuvant chemotherapy was administered to 15 cases. Among 21 patients with effective follow-up, the median overall survival was 26 months, and the median recurrence-free survival was 15 months. The 1-year and 3-year survival rates were 90.5% and 44.4%, respectively. The most common sites of initial recurrence were the liver and retroperitoneal lymph nodes, followed by bone, lung, mesenteric lymph nodes, and local recurrence. **Conclusion:** ACC is a rare malignant tumor characterized mainly by abdominal pain, often presenting as a solid mass with aggressive features. Surgical resection combined with adjuvant chemotherapy is the main treatment approach. Postoperative surveillance should focus on the liver and retroperitoneal lymph nodes for early detection of

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recurrence and metastasis.

[Key words] acinar cell carcinoma; surgical treatment; chemotherapy; survival time

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胰腺腺泡细胞癌(acinar cell carcinoma, ACC)是一种少见的胰腺外分泌恶性肿瘤,1908年由Berner首次报道,其发病率占胰腺肿瘤的1%~2%^[1-2]。ACC起源于胰腺腺泡细胞并具有外分泌功能,可分泌胰蛋白酶、脂肪酶等消化酶。文献报道,与胰腺导管腺癌相比,ACC预后相对较好,手术切除能延长患者生存期,术后辅助化疗的获益仍存在争议^[3-4]。ACC缺乏特异性的临床表现和实验室检查指标,术前诊断困难。因此,为提高对ACC的认识,进一步指导临床诊治,本研究回顾性分析了南京医科大学第一附属医院胰腺中心23例经病理确诊的ACC病例,总结其临床、影像、病理特点、诊疗经过和预后情况。

1 对象和方法

1.1 对象

回顾性分析2015年4月—2024年12月南京医科大学第一附属医院胰腺中心收治的23例病理报告确诊为ACC患者的临床资料。本研究经医院伦理委员会批准,所有患者术前签署知情同意书。

1.2 方法

临床资料从医院电子病历系统获得,包括入院主诉、实验室检查结果、手术方式及化疗方案等。影像资料由放射科提供,观察指标包括肿瘤的部位、大小、肿瘤成分及生长方式。病理资料记录肿瘤组织学形态及免疫组织化学检测结果。采用Kaplan-Meier法绘制生存曲线,计算中位生存时间、生存率及无复发生存期。

1.3 随访

定期门诊复查和电话随访获取预后信息。随访频率为术后1年内每3个月1次,此后每6个月1次,末次随访时间为2025年5月。

2 结果

2.1 临床资料及诊治情况

本组23例ACC,男15例,女8例;年龄32~81岁,中位年龄63岁。入院主诉为腹痛13例,梗阻性黄疸3例。糖类抗原199(carbohydrate antigen 199,

CA199)升高11例(>30 U/mL)。22例患者行手术治疗,R0切除19例,R1切除3例,1例因第16组淋巴结转移未行手术,行超声内镜下细针穿刺活检确诊并接受综合治疗。具体情况见表1。

2.2 CT检查影像学特征

18例于本院行腹部CT,结合术后病理结果,肿瘤位于胰头15例,胰体尾7例,全胰腺1例。胆管扩张8例(>8 mm),胰管扩张5例(>3 mm),胆胰管均扩张5例。肿瘤成分多为实性13例,生长方式为膨胀性生长7例,浸润性生长11例。CT影像特征见图1。

2.3 病理、免疫组织化学特点

病理检查示21例为单纯ACC,1例为ACC伴导管腺癌成分,1例为ACC伴神经内分泌肿瘤成分。肿瘤直径7~155 mm,平均(54±34)mm。10例发生淋巴结转移,20例有神经或脉管侵犯,远处转移4例(肝脏、肠系膜、第16组淋巴结)。免疫组织化学结果显示:胰蛋白酶阳性15例(65.2%)、糜蛋白酶阳性11例(47.8%)、脂肪酶阳性3例(13.0%)。Ki-67>50%为8例(34.8%),其余病例Ki-67为5%~45%,具体见表2。

2.4 治疗、随访预后

15例患者行术后辅助化疗,方案包括Gemox(吉西他滨+奥沙利铂)、Sox(替吉奥+奥沙利铂)、AG(白蛋白紫杉醇+吉西他滨)、FOLFIRINOX(亚叶酸钙+氟尿嘧啶+盐酸伊立替康+奥沙利铂)、TP(紫杉醇+顺铂)、Gemcap(吉西他滨+卡培他滨)。6例患者拒绝化疗,2例不详。22例手术患者中,21例得到随访(1例失访),随访时间4~55个月,中位随访时间40个月。术后中位生存期为26个月,中位无复发生存期为15个月;术后1年、3年生存率分别为90.5%、44.4%。术后辅助化疗对生存期无明显影响($P=0.40$)。复发转移部位以肝脏(7例)和后腹膜淋巴结(5例)最常见,其次为骨(1例)、肺(1例)、肠系膜淋巴结(1例)及术区局部复发(1例)。详见表2、图2。

3 讨论

ACC是一种罕见的起源于腺泡细胞的恶性肿瘤,其发生机制尚不清楚,研究表明基因突变和染

表1 患者临床资料

Table 1 Clinical characteristics of patients

Variable	Case[n(%)]	Variable	Case[n(%)]
Sex(n=23)		CT imaging features(n=18)	
Male	15(65.2)	Tumor composition	
Female	8(34.8)	Solid	8(44.4)
Presenting symptom(n=23)		Solid with necrosis	5(27.8)
Abdominal pain	13(56.5)	Cystic-solid	5(27.8)
Jaundice	3(13.0)	Biliary duct dilation(>8 mm)	8(44.4)
Other	7(30.4)	Pancreatic duct dilation(>3 mm)	5(27.8)
Laboratory tests		Both biliary and pancreatic duct dilation	5(27.8)
CA199(>30 U/mL)	11(47.8)	Imaging growth pattern	
CEA(>5 ng/mL)	4(17.4)	Expansile growth	7(38.9)
AFP(>7 ng/mL)	3(13.0)	Infiltrative growth	11(61.1)
Total bilirubin(>23 μmol/L)	5(21.7)	Surgical procedure(n=23)	
AST(>35 U/L)	7(30.4)	PPPD/PD	10(43.5)
ALT(>40 U/L)	4(17.4)	PPPD/PD+SMV resection	2(9.0)
Tumor location(n=23)		PD/DP+partial colectomy	2(9.0)
Pancreatic head	15(65.2)	DP	4(17.5)
Pancreatic body/tail	7(30.4)	DP/PD+liver metastasectomy	2(9.0)
Entire pancreas	1(4.3)	DP+mesentericmetastasectomy	1(4.3)
		TP	1(4.3)
		EUS+FNA	1(4.3)

PPPD/PD: pylorus-preserving/standard pancreatoduodenectomy; PPPD/PD + SMV: PPPD/PD with superior mesenteric vein resection; DP: distal pancreatectomy; PD: pancreatoduodenectomy; TP: total pancreatectomy; EUS+FNA: endoscopic ultrasound + fine-needle aspiration.

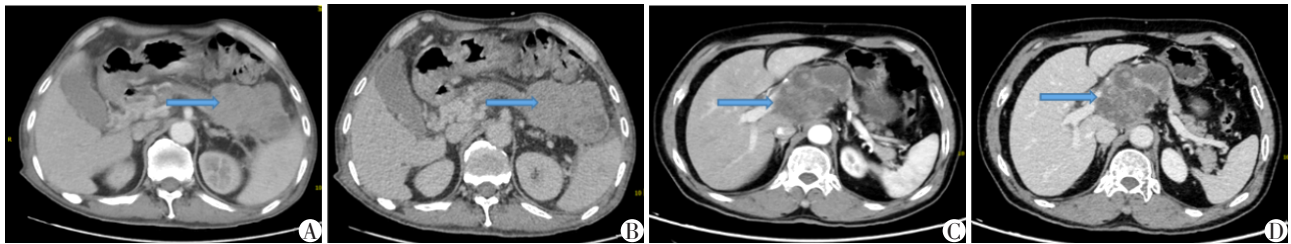


图1 ACC患者CT影像特征
Figure 1 CT imaging features of ACC patients

色体不稳定性可能在 ACC 的发生发展过程中起一定作用^[4]。ACC 多见于中老年男性, Zhou 等^[5]回顾性分析 45 例 ACC 患者, 中位年龄 58 岁, 男女比例为 3.1:1。本组研究患者中位年龄 63 岁, 男女比例为 1.9:1。ACC 无典型的临床症状, 主要表现为腹痛腹胀、体重减轻等, 与导管腺癌相比, 较少发生梗阻性黄疸。Holen 等^[6]报道, ACC 可伴有高脂肪酶综合征的临床表现, 患者常出现发热、皮下脂肪坏死、嗜酸性粒细胞增多等症状。本组 13 例有腹痛症状, 未

出现高脂肪酶综合征。

ACC 影像表现缺乏特异性, 常需与胰腺导管腺癌、实性假乳头状瘤、神经内分泌肿瘤相鉴别^[7]。胰腺导管腺癌通常为乏血供、体积较小的浸润性肿块, 早期即可引起胆管和胰管扩张, 且多伴 CA199 升高。实性假乳头状瘤好发于年轻女性, 肿瘤呈类圆形且有包膜, 影像增强呈渐进性强化, 可见钙化, 一般不引起胆胰管扩张。胰腺神经内分泌肿瘤血供丰富, 动脉期和静脉期均明显强化, 部分伴有相

表2 病理、治疗及预后
Table 2 Pathology, treatment, and prognosis

Variable	Case[n(%)]	Variable	Case[n(%)]
Pathological type(n=23)		Stage(n=23)	
Acinar cell carcinoma	21(91.4)	I A	1(4.4)
ACC mixed with ductal adenocarcinoma	1(4.3)	I B	5(21.7)
ACC mixed with neuroendocrine neoplasm	1(4.3)	II A	5(21.7)
Tumor diameter(n=23)		II B	4(17.4)
T1	2(8.7)	III	4(17.4)
T2	9(39.2)	IV	4(17.4)
T3	11(47.8)	Adjuvant chemotherapy(n=15)	
T4	1(4.3)	Gemox	4(26.7)
Lymph nodes(n=22)		Sox	4(26.7)
N0	12(54.5)	AG	2(13.3)
N1	7(31.9)	FOLFIRINOX	3(20)
N2	3(13.6)	TP	1(6.7)
Distant metastasis(n=23)		Gemcap	1(6.7)
M0	19(82.6)	No adjuvant chemotherapy(n=22)	6(27.3)
M1	4(17.4)	Site of recurrence(n=21)	
Perineural invasion	10(43.5)	No recurrence	5(23.8)
Lymphovascular invasion	10(43.5)	Retroperitoneal lymph nodes	5(23.8)
Vascular invasion	2(8.7)	Liver	7(33.2)
Immunohistochemistry(n=23)		Lung	1(4.8)
Trypsin(+)	15(65.2)	Bone	1(4.8)
Chymotrypsin(+)	11(47.8)	Mesenteric lymph nodes	1(4.8)
Lipase(+)	3(13.0)	Local(surgical site)	1(4.8)
Ki-67>50%	8(34.8)	Survival rate(n=21)	
Resection margin(n=22)		1-year survival rate	19(90.5)
R0	19(86.4)	3-year survival rate	9(44.4)
R1	3(13.6)		
R2	0		

RFS: recurrence-free survival; Gemox: gemcitabine+oxaliplatin; Sox: S-1+oxaliplatin; AG: Nab-paclitaxel+gemcitabine; FOLFIRINOX: leucovorin+fluorouracil+irinotecan+oxaliplatin; TP: paclitaxel+cisplatin; Gemcap: gemcitabine+capecitabine. Staging per AJCC 8th edition.

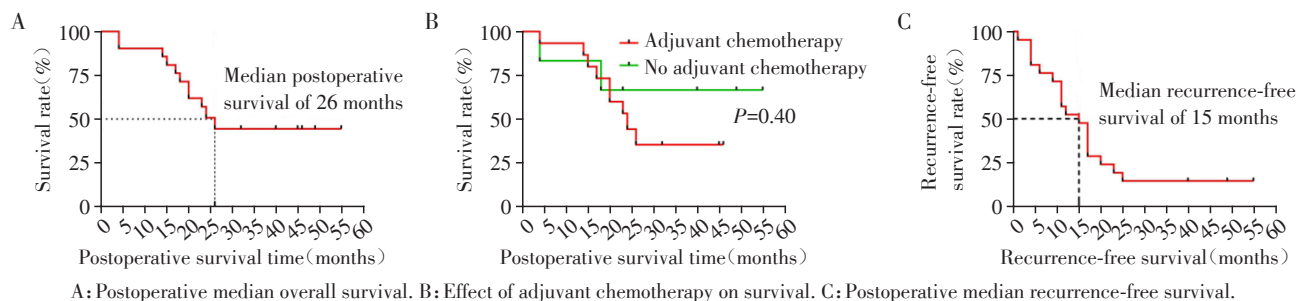


图2 ACC预后

Figure 2 Prognosis of ACC

应内分泌症状。Barat等^[8]报道ACC体积通常较大,平均直径52 mm,约10%出现胆管扩张,明显低于胰腺导管腺癌,约30%出现胰管扩张。本组患者肿瘤平

均直径为54 mm,其中胆管扩张8例,胰管扩张5例,与文献报道相符。

ACC的确诊依靠病理学和免疫组织化学检测^[9]。

其在细胞形态学上与实性假乳头状瘤、神经内分泌肿瘤相似,常需要通过免疫组织化学特异性标记来明确诊断。ACC肿瘤可产生胰蛋白酶、糜蛋白酶、脂肪酶、弹性蛋白酶和淀粉酶等消化酶,这些酶的抗体已经用于辅助诊断。Mustafa等^[3]报道约65%的ACC病例消化酶相关的免疫标记呈阳性。本研究中胰蛋白酶阳性率65.2%,糜蛋白酶47.8%,脂肪酶13.0%,与文献基本一致。

根治性手术是ACC的首选治疗方式,可改善预后。Petrova等^[10]通过对德国癌症中心数据库进行回顾性分析,2000—2019年共有52 518例胰腺恶性肿瘤患者,其中233例(0.44%)为ACC。与胰腺导管腺癌相比,ACC患者更年轻(中位年龄:66岁 vs. 70岁, $P < 0.001$),ACC的估计总中位生存期更长(22个月 vs. 12个月, $P < 0.001$),在调整性别、年龄和远处转移后,手术切除是ACC最强的阳性预后因素。Huang等^[11]报道ACC患者的1年、3年、5年生存率分别为90.4%、55.9%、21.4%,中位生存时间达39个月,这些数据显著优于胰腺导管腺癌(1年、3年、5年生存率分别仅为65.2%、24.7%和9.7%,中位生存时间17个月),两组差异均有统计学意义($P < 0.05$)。其中接受根治性切除的ACC患者,其1年、3年、5年生存率分别提升至96.7%、71.7%和31.8%,中位生存时间延长至48个月。本研究中术后中位生存时间为26个月,术后1年、3年生存率分别为90.5%、44.4%。

联合肝转移灶切除在ACC治疗中的价值少有报道。Hartwig等^[12]报道的ACC同期行肝脏、网膜转移灶切除与可切除患者的生存期相当。Huang等^[11]也报告3例ACC接受了原发灶和孤立肝转移灶的联合切除术,其总生存期分别达到16、19和21个月。相比之下,11例同时接受肝转移灶和原发灶姑息性切除的胰腺导管腺癌患者中位生存期仅9个月。在本研究中,3例患者术中探查发现孤立转移病灶,行联合切除,其中肝转移患者2例,1例在术后24个月因肿瘤进展死亡,另1例随访至45个月仍存活。肠系膜转移1例,患者在术后26个月因肿瘤进展死亡。上述结果提示,对晚期ACC选择性实施包括转移灶在内的扩大手术切除有可能延长总体生存期。

ACC术后辅助化疗的作用尚存在争议, Schmidt等^[13]通过美国国家癌症数据库(National Cancer Database, NCDB)分析了865例ACC患者,认为术后接受或未接受辅助化疗的患者具有相似的总体生存期。Patel等^[14]报道ACC患者淋巴结阳性、切缘阳性与死亡风险增加相关,与单纯手术相比,术后辅

助化疗可延长患者生存期。Zhou等^[5]报道ACC患者术后接受辅助化疗较未接受者生存期明显延长(37.7个月 vs. 18.9个月, $P=0.01$),且辅助化疗是独立的预后保护因素。既往文献中的ACC术后化疗方案多为以吉西他滨或氟尿嘧啶为基础的联合方案,但各方案的有效性因样本量有限而难以确定。针对晚期ACC,有研究表明以铂类为基础的一线治疗方案(FOLFOX或FOLFIRINOX)相比以卡培他滨或吉西他滨为基础的方案,能带来更长的总生存期^[15]。Sridharan等^[6]研究认为,含铂类和伊立替康的化疗方案(如FOLFIRINOX方案)可能是不可切除或复发性ACC的潜在有效治疗方案。本研究15例患者接受术后辅助化疗,方案以AG、Folifirinox、GS、Gemox、Sox为主,但统计分析未见术后化疗显著延长患者生存期($P=0.40$)。本研究样本量较小可能导致统计效能不足,此结果为初步结论,需更大样本研究验证。

基因组学研究显示ACC与胰腺导管腺癌的分子特征存在明显差异。ACC中KRAS、TP53、CDKN2A等驱动基因突变少见,而BRCA1/2、ATM等同源重组修复相关基因的突变率明显高于胰腺导管腺癌^[18]。这提示ACC可能对含铂类化疗和PARP抑制剂等更为敏感,针对特定基因突变的靶向治疗在ACC中具有潜在疗效。因此,对ACC患者进行基因检测对于制定个体化治疗策略具有重要意义^[17]。

综上所述,ACC发病率低,临床症状和影像缺乏特异性,术前影像诊断率低,根治性手术是ACC患者的首选治疗方案,可显著改善患者预后。术后辅助化疗及方案的选择尚需高质量临床研究进一步探索。胰腺腺泡细胞癌与胰腺导管腺癌具有不同的基因组特征。因此,基因检测对胰腺腺泡细胞癌患者选择最佳治疗策略至关重要。

利益冲突声明:

所有作者声明无利益冲突。

Conflict of Interests:

All authors declare no conflict of interests.

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胡乐负责研究设计、数据收集与统计分析、论文撰写;戴存才、蒋奎荣、郭峰负责研究指导、论文审阅与修订。

Author's Contributions:

HU Le was responsible for the research design, data collection, and statistical analysis, and manuscript writing; DAI Cuncai, JIANG Kuirong, and GUO Feng were responsible for research supervision, manuscript review and revision.

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