

论著·案例分析

以胰腺炎为首发表现伴腹腔淋巴结肿大1例

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1 病例介绍

患儿,男,14岁,因腹痛12 d入院。患儿腹痛呈脐周及上腹部阵发性疼痛,程度不剧烈,呕吐胃内容物1次,无发热,无皮肤、巩膜黄染,无腹泻、黑便等。至当地医院就诊,查淀粉酶225 U/L(参考值:0~100 U/L),血脂肪酶1506 U/L(参考值:13~60 U/L);血常规:白细胞 $16.48 \times 10^9/L$,中性粒细胞82.7%,余项正常;C反应蛋白(CRP)117 mg/L;腹部B超提示胰腺增大伴回声改变,胰周低弱回声团,盆腔积液;磁共振胰胆管成像(MRCP)提示胰管扩张,胰头部胰管显示不清,胆囊增大。当地医院考虑“急性胰腺炎”,予禁食、补液、抗感染、奥美拉唑、生长抑素等对症支持治疗,住院期间出现发热伴轻微咳嗽,抗感染治疗后患儿体温恢复正常,但仍有上腹部疼痛。既往史、个人史、家族史无特殊。

入院体查:生命体征平稳,体质指数(BMI) 24.1 kg/m^2 ,神清,精神差,急性病容,皮肤、巩膜无黄染,颈部、腋下、腹股沟浅表淋巴结未触及,两肺听诊呼吸音对称、清晰,未闻及罗音,腹软,脐周及上腹部压痛,无反跳痛,肝脾肋下未及,腹部移动性浊音阴性,双下肢无浮肿,神经系统检查阴性。

辅助检查:血常规白细胞 $21.92 \times 10^9/L$,中性粒细胞比值87.5%,余项正常;C反应蛋白111 mg/L;肝功能正常;血淀粉酶正常,脂肪酶71.1 U/L(参考值:13~60 U/L);乳酸脱氢酶386 U/L(参考值:110~295 U/L)。腹部B超:胰腺外形饱满、边缘模糊,胰管扩张(内径约0.45 cm),胰头周围淋

巴结肿大(较大者直径约 $3.2 \text{ cm} \times 2.3 \text{ cm}$)、边界尚清、其内回声减低、尚均匀,腹腔积液、胸腔积液。肺部CT:两肺散在结节影。真菌D-葡聚糖:13.468 pg/mL(参考值: $<10 \text{ pg/mL}$);结核感染T细胞斑点试验(T-spot)阴性。

2 诊断思维

本例患儿无明显诱因出现急性上腹痛,血淀粉酶及脂肪酶高于正常上限三倍,白细胞增高、中性粒细胞增高,C反应蛋白增高,影像学提示胰腺增大、胰管扩张,可临床诊断急性胰腺炎。细菌、病毒、寄生虫等引起的胆道感染均可导致急性胰腺炎;先天性胰胆管异常如胆总管囊肿、胰腺分裂可引起胰腺炎;胆道结石、胆道蛔虫症所致的胆管梗阻,以及腹部外伤、过敏性紫癜、系统性红斑狼疮、炎症性肠病、川崎病等全身性疾病均可伴发胰腺炎;毒物、药物,内分泌疾病如高钙血症、高脂血症,以及遗传代谢病也可能是儿童急性胰腺炎的病因^[1]。本例患儿无其它全身性疾病的临床表现,无特殊用药史,既往、个人史无特殊,血常规提示白细胞、中性粒细胞升高,CRP显著升高,实验室检查未提示高血钙、高血脂。因此,考虑胆道细菌感染引起的急性胰腺炎可能性大。但抗感染、制酸、抑制胰酶分泌治疗效果欠佳,而且胰腺B超提示胰头周围淋巴结肿大、胰管扩张,MRCP提示胰腺头部显示不清,需注意淋巴瘤等肿瘤压迫所致,进一步复查腹部CT及MRCP,并行腹腔淋巴结活检明确诊断。

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3 进一步检查

MRCP (图1)提示:胰腺外形饱满,边界不清,胰周、脾周、左侧肾周间隙及胆囊窝积液,肝门部及后腹膜融合肿大淋巴结。腹部CT:胰腺肿胀、胰腺内多处低密度灶,伴胰管扩张、胰周渗出,肝门部及后腹膜淋巴结肿大。行腹腔镜探查,发现:肝门部多发结节、水肿明显,与周围结构分界不清,胰腺水肿严重。转为剖腹探查可见:胰腺水肿严重,未见明显占位,肝门部多发结节、伴明显水肿、与周围结构分界不清,取肝门部结节及大网膜肿大淋巴结行病理检查。淋巴结病理:淋巴结结构破坏,间变大细胞成片分布;免疫组化:EMA+, Desmin-, CK 散在+, Vim+, CD20 散在+, CD3 局部+, INI-1+, MPO-, ALK+, CD30+, MyoD1-, Ki-67 约97%+;诊断(肝门、胃大弯网膜)间变大细胞淋巴瘤。骨髓细胞学及流式细胞检查正常,脑脊液检查正常。PET/MRI提示弥漫性胰腺恶性淋巴瘤。

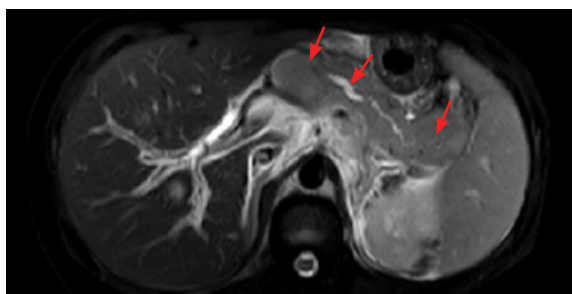


图1 患儿的MRCP表现 MRCP可见胰腺肿胀明显,胰腺内多处低密度灶、以胰头处病变最大,伴胰管明显扩张。如箭头所示。

4 诊断及确诊依据

诊断:原发性胰腺淋巴瘤(primary pancreatic lymphoma, PPL)(间变大细胞淋巴瘤)Ⅲ期,急性胰腺炎。PPL诊断依据:(1)腹痛、呕吐,肝门及腹膜后淋巴结肿大;(2)无肝脾侵犯,无骨髓及中枢受累;(3)腹腔病变不能手术切除;(4)淋巴结活检病理提示间变大细胞淋巴瘤。

5 临床经过

患儿经抗感染、制酸、抑制胰酶分泌治疗病

情仍进展,迅速发生脓毒症、脓毒性休克,并出现多脏器功能衰竭。转入重症监护室,予气管插管、呼吸机支持辅助通气。病理初步诊断为淋巴瘤后,予以VD方案(长春地辛、地塞米松)减轻肿瘤负荷,继续对症支持治疗,患儿肺部感染控制、腹痛好转,血淀粉酶降至正常,逐渐恢复饮食,并脱离呼吸机;考虑患儿因病变范围广且胰腺炎症状好转,予以VDLD(长春地辛、吡柔比星、门冬酰胺酶、地塞米松)方案化疗,第一次门冬酰胺酶应用后患儿再次出现腹痛、血淀粉酶升高至1600 U/L,再次予禁食、抑酸、抑酶治疗后腹痛症状好转、血淀粉酶降至轻度升高。以后予以长春瑞滨(每周一次,8次)+地塞米松化疗,继续空肠营养及静脉营养,血淀粉酶反复波动,并且多次复查影像学仍有腹腔淋巴结肿大及胰腺低密度病灶。应用第8次长春瑞滨后复查胰腺B超仍提示胰头低密度灶及腹腔淋巴结肿大,患儿家长放弃治疗。

6 讨论

非霍奇金淋巴瘤是儿童最常见的肿瘤之一,可以累及结外以及实质性脏器,约三分之一可累及胰腺。PPL约占结外淋巴瘤的1%,发病年龄以50~60岁常见,儿童罕见^[2]。PPL起源于胰腺或仅侵犯胰腺及其区域淋巴结,无肝脾肿大,无浅表及纵膈淋巴结肿大^[3]。PPL病因不明,可能与遗传、免疫缺陷、疱疹病毒、肝炎病毒等病毒感染等有关^[4]。成人PPL或转移性肿瘤侵犯胰腺引发胰腺炎,以及儿童胰腺淋巴瘤引起胰腺炎均极其罕见,仅有少量国外文献报道^[5]。本研究患儿以胰腺炎为表现,影像学提示胰腺肿胀、胰腺内多发低密度病灶、肝门及腹膜后淋巴结肿大,淋巴结病理提示间变大细胞淋巴瘤。

PPL临床表现无特异性,可表现为腹痛、恶心、呕吐及发热、体重下降等,如肿块压迫胆管可有梗阻性黄疸表现。部分患者有血清淀粉酶、脂肪酶、乳酸脱氢酶升高,而肿瘤标志物CA199一般正常,伴胆管梗阻时可轻度升高。部分患儿无明显临床症状仅在影像学检查时偶然发现。胰腺CT或MRI表现为低密度均匀回声包块,以单发病灶多见,位置以胰头最常见。包块因生长迅速,体积一般较大,胰腺淋巴瘤一般直径大于6cm,而胰腺癌

直径一般小于6 cm,呈分叶状,周围胰腺组织强化明显^[2]。个别PPL病变为多灶性分布或弥漫性分布,胰腺呈弥漫性肿大^[5]。本例患儿的影像学未发现单发占位,提示弥漫性胰腺肿大、多处低密度病灶,考虑多灶性病变。PPL确诊主要依靠病理,如超声内镜细针穿刺、腹腔镜肿块或淋巴结活检明确。国外文献报道^[2,6-15]的PPL中,14例儿童PPL的病理类型以Burkitt淋巴瘤最常见(9例),还包括3例弥漫大B细胞淋巴瘤、2例间变细胞淋巴瘤,而成人PPL以弥漫大B细胞淋巴瘤为主,除2例未说明预后、1例仍在化疗中,其余患者化疗后临床症状及影像学缓解。

PPL的治疗与淋巴瘤的病理分型和临床分期有关,文献报道^[2,6-15]大部分儿童PPL通过单纯化疗长期缓解率较高(其病理以Burkitt淋巴瘤和弥漫大B细胞淋巴瘤为主,分期多在I期和II期)。PPL一线化疗用药包括泼尼松龙、长春新碱、阿霉素以及环磷酰胺等^[16]。对于CD20阳性的弥漫大B细胞淋巴瘤,利妥昔单抗可以增加疗效^[17]。放疗并没有证实能增加PPL疗效^[18]。PPL往往因肿块较大或与正常组织分界不清,胰痿发生率高,手术治疗较困难^[19]。本例患者病理提示间变大细胞淋巴瘤,临床进展快,全身情况差,淋巴结活

检初步诊断淋巴瘤后予VD方案减轻瘤负荷,胰腺炎症状控制,予VDLD方案化疗,一次门冬酰胺酶后胰腺炎症状复发,因此对于肿瘤侵犯或者压迫胰胆管导致胰腺炎的PPL患者应慎用门冬酰胺化疗。虽然文献报道大部分儿童PPL通过单纯化疗长期缓解率较高,但对于急性胰腺炎表现、全身情况较差的患者如何结合病理分型、临床分期采取最佳治疗仍需进一步研究。

7 结语

本例患者临床表现为急性胰腺炎,影像学检查发现腹腔淋巴结肿大,经淋巴结活检病理证实为间变大细胞淋巴瘤,PPL为儿童急性胰腺炎的罕见病因。对于疗效不佳、症状反复的急性胰腺炎患者需注意少见病因,尤其是合并腹腔淋巴结肿大伴有乳酸脱氢酶明显增高时,需警惕结外淋巴瘤,尽早进行病理诊断。儿童胰腺淋巴瘤罕见,是否需要手术治疗缺乏经验;而对于有胰腺炎表现者,门冬酰胺酶的使用需谨慎。对于以急性胰腺炎表现的儿童PPL的治疗仍值得进一步探索,尤其是侵袭性较强的间变大细胞淋巴瘤。

[摘要] 患者,男性,14岁,以腹痛为主要表现,血淀粉酶及脂肪酶增高,腹部超声提示胰腺肿大、回声减低,磁共振胰胆管成像(MRCP)提示胰管扩张、胰头显示不清,考虑急性胰腺炎。经禁食、补液、抑酸、生长抑素等治疗症状未缓解,复查腹部CT及MRCP提示胰腺多处低密度灶,肝门部及腹膜后淋巴结肿大,剖腹探查发现胰腺水肿,肝门部多发结节并与周围结构分界不清,活检病理提示间变大细胞淋巴瘤。结合患儿无肝脾、骨髓及中枢神经系统受累,诊断III期原发性胰腺淋巴瘤。予VD减轻肿瘤负荷后,予以一次VDLD化疗及8次长春瑞滨联合地塞米松化疗,影像学仍提示胰腺多发低密度病灶及腹膜后淋巴结肿大。患者家属放弃治疗。对于治疗效果不好的急性胰腺炎需考虑少见原因所致,尤其对于伴腹腔淋巴结肿大者,需警惕结外淋巴瘤,尽早行淋巴结活检以明确诊断。胰腺淋巴瘤预后与临床分期及病理相关。

[中国当代儿科杂志, 2018, 20(10): 844-847]

[关键词] 急性胰腺炎;原发性胰腺淋巴瘤;间变大细胞淋巴瘤;儿童

Pancreatitis as the initial manifestation and abdominal lymph node enlargement in a boy

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Abstract: A boy aged 14 years had abdominal pain as the major manifestation, with elevated serum amylase and lipase. Abdominal ultrasound performed early after onset in another hospital showed enlargement of the pancreas and a reduction in echo. Magnetic resonance cholangiopancreatography (MRCP) showed pancreatic duct dilation and an unclear image of the head of the pancreas. Acute pancreatitis was considered. However, his symptoms were not relieved after fasting, fluid infusion, anti-acid therapy, and somatostatin therapy. Then, abdominal CT scan and MRCP found

multiple low-density lesions of the pancreas and enlargement of the hilar and retroperitoneal lymph nodes. Exploratory laparotomy found pancreatic edema and multiple hilar nodules with unclear boundaries, and pathological biopsy showed anaplastic large-cell lymphoma. Since the liver, the spleen, bone marrow, and the central nervous system were not involved, he was diagnosed with stage III primary pancreatic lymphoma. After vindesine and dexamethasone were used to reduce tumor load, the patient underwent vindesine-pirarubicin-asparaginase-dexamethasone chemotherapy once and vinorelbine-dexamethasone chemotherapy 8 times. Imaging examination still showed multiple low-density lesions of the pancreas and retroperitoneal lymph node enlargement. His parents discontinued treatment. It is concluded that the rare causes of acute pancreatitis with poor response to conventional treatment should be considered, especially for patients with abdominal lymph node enlargement. Extranodal lymphoma should be considered, and lymph node biopsy should be performed as early as possible to confirm diagnosis. The prognosis of pancreatic lymphoma is associated with clinical stage and pathology.

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Key words: Acute pancreatitis; Primary pancreatic lymphoma; Anaplastic large-cell lymphoma; Child

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