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儿童氨氯地平中毒1例及文献复习

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摘　要

目的：通过分析1例氨氯地平中毒患儿症状、体征、辅助检查及治疗，使广大临床医师了解疾病特点。方法：对青岛大学附属医院儿童重症医学科1例氨氯地平中毒患儿进行分析。结果：本文报道了一例氨氯地平中毒引起肺水肿患儿。该患儿系青春期女童，因“发现吞服胶囊刀片、过量降压药7小时”入院。入院第2天出现肺水肿，给予去甲肾上腺素、钙剂、呼吸机辅助通气、血浆置换及补液等治疗，并予灌肠治疗促进刀片排出。入院第15天，患儿症状消失，复查腹部正位片未见金属影，胸部CT较前明显好转，予出院。结论：氨氯地平是一种二氢吡啶类长效钙通道阻滞剂。过量氨氯地平可引起低血压、心律失常、高血糖、代谢性酸中毒、非心源性肺水肿等，甚至心脏骤停，病死率高。本文就氨氯地平中毒的临床表现、相关病理机制及治疗进行了探讨。

关键词

氨氯地平中毒，肺水肿，儿童

A Case of Amlodipine Poisoning in Children and Literature Review

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Abstract

Objective: The aim of this paper is to enable clinical physicians to gain a more complete understanding of the characteristics of amlodipine poisoning by analyzing the symptoms, signs, auxiliary examinations, and treatment of a child with the illness. Methods: Analyzing an amlodipine

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poisoning case involving a child hospitalized in the PICU of The Affiliated Hospital of Qingdao University. Results: This paper describes a youngster who developed pulmonary edema from amlodipine poisoning. The patient is a teenage girl admitted to the hospital after "overdose of antihypertensive medications and swallowing capsule blades for roughly 7 hours". The second day of the hospital stay saw the development of pulmonary edema. Norepinephrine, calcium, ventilator-assisted breathing, plasma exchange and an enema to encourage blade discharge were used to treat the girl. The patient's symptoms disappeared on the 15th day after being admitted, a reexamination of the abdominal X-ray revealed no metal shadow, and the chest CT showed significant improvements over the previous results. The girl was then discharged from the hospital. Conclusions: Amlodipine is a dihydropyridine Calcium channel blocker. A significant mortality is associated with the adverse effects of amlodipine overdose, which include hypotension, arrhythmia, hyperglycemia, metabolic acidosis, non-cardiogenic pulmonary edema, and even cardiac arrest. This paper discusses the clinical manifestations, related pathological mechanisms, and treatment of amlodipine poisoning.

Keywords

Amlodipine Poisoning, Pulmonary Edema, Children

1. 引言

氨氯地平是一种钙通道阻滞剂，目前临床常用于治疗高血压、心绞痛等疾病。儿童过量氨氯地平中毒相对罕见，如果不积极识别和治疗，可能导致心动过缓、低血压、非心源性肺水肿和死亡。本文介绍了一例氨氯地平中毒儿童，该患儿存在肺水肿、低血压，给予呼吸支持、血浆置换等治疗后痊愈出院。

2. 病例介绍

患者，女，14 岁，因“发现吞服胶囊刀片、过量降压药 7 小时”入院。7 小时前患者因“情绪障碍”吞服胶囊数个，胶囊内共置 8 个菱形刀片(约 10 × 20 mm)，同时口服降压药(具体药物及剂量不详)，无腹痛，无头痛、头晕，无心悸、胸闷、憋气。就诊于当地医院，行胸腹 X 线平片示肠道内多个高密度影，为进一步诊治，急诊以“消化道异物、过量药物中毒”收入儿童重症监护室。患儿既往体健，个人史、家族史无特殊。入院查体：T：37℃，P：110 次/分，R：19 次/分，BP：105/52 mmHg，体重 60 kg。神志清，精神可。呼吸平稳，双肺呼吸音清，双肺未闻及干湿性啰音。HR110 次/分，心律齐，各瓣膜听诊区未闻及杂音。腹软，无压痛及反跳痛，肠鸣音存在。四肢肌力 5 级，双下肢无浮肿，病理征阴性。双侧手臂可见多处划痕。辅助检查：腹部正位片：腹部多发高密度影，结合病史考虑异物(图 1)。血常规、CRP、血气分析、血凝常规、尿常规、粪便常规、心肌酶、铁蛋白、肝肾功、电解质、血氨大致正常。患儿入院后予心电监护，入院后 1 小时血压降至 80/40 mmHg，予去甲肾上腺素(0.04 ug/kg·min)持续泵入，同时予补液、利尿等治疗。追问病史，患儿诉口服苯磺酸氨氯地平，共 40 片(200 mg)，立即采集外周血行氨氯地平药物浓度检测。

入院 12 小时，患儿自述胸闷，并逐渐加重，出现发热，体温 38.1℃，行胸部 CT 平扫示双肺可见斑片状、大片状密度增高影，边缘模糊，内见支气管影；双侧胸腔内见少量液体密度影；考虑肺水肿、双侧胸腔积液、双肺炎症(图 2、图 3)。心脏超声检查大致正常。考虑患儿系过量氨氯地平引起双肺水肿及

少量胸腔积液合并肺部感染，予面罩吸氧(5 L/min)，予甲强龙(1 mg/kg·d)减轻水肿，葡萄糖酸钙补钙，药用炭片吸附药物，哌拉西林钠他唑巴坦抗感染。患儿病情持续加重，伴呼吸困难，氧合不能维持，行血气分析全项：氧分压 53.0 mmHg，氧饱和度 94.8%，二氧化碳分压 26.0 mmHg，全血碱剩余−6.4 mmol/L，实际碳酸氢盐 16.5 mmol/L，乳酸 4.90 mmol/L，游离钙 1.04 mmol/L，葡萄糖 10.40 mmol/L，钠 132.0 mmol/L，钾 2.70 mmol/L。考虑呼吸衰竭，予气管插管，接呼吸机辅助通气。心电监护示短阵室速。患儿药物浓度检测示氨氯地平浓度 129 ng/ml，高于治疗量 15 倍，予股静脉置管，血浆置换(1 次/日，连续 3 日)，复查血药浓度，氨氯地平浓度 72 ng/ml，高于治疗量 9 倍。继续行血浆置换(1 次/日，连续 3 日)，复查血药浓度 21 ng/ml，停用血浆置换。经治疗，患儿呼吸平稳，体温正常，入院第 7 天复查床旁胸片明显好转，拔出气管插管停用呼吸机。

患儿存在多个消化道金属异物，予温盐水、中药、开塞露灌肠，动态监测患儿大便及腹片确定刀片数量及位置。

入院第 15 天，复查血常规、肝肾功、心肌酶、电解质大致正常，胸部 CT 肺部较前明显减轻(图 4)，复查腹片刀片全部排出体外。予出院并建议院外精神心理治疗。

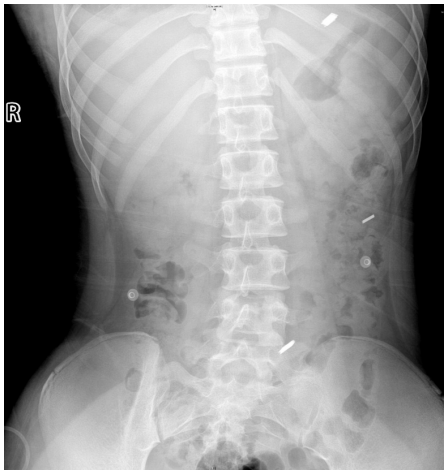

Figure 1. Abdominal X-ray
图 1. 腹部 X 线片

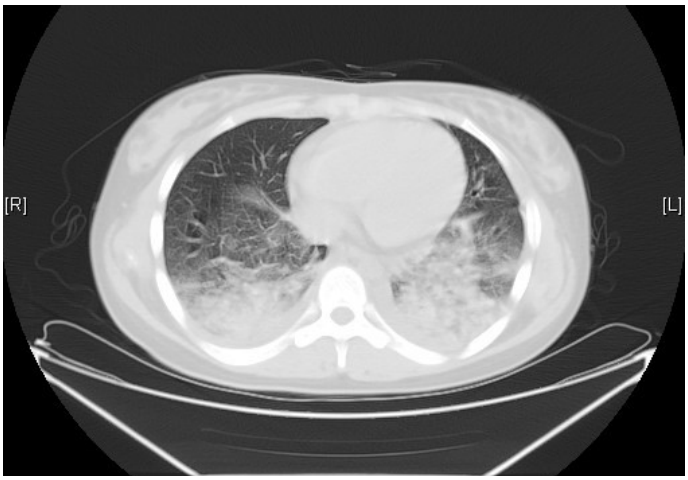

Figure 2. Computed Tomography of the Chest in acute stage
图 2. 急性期肺 CT

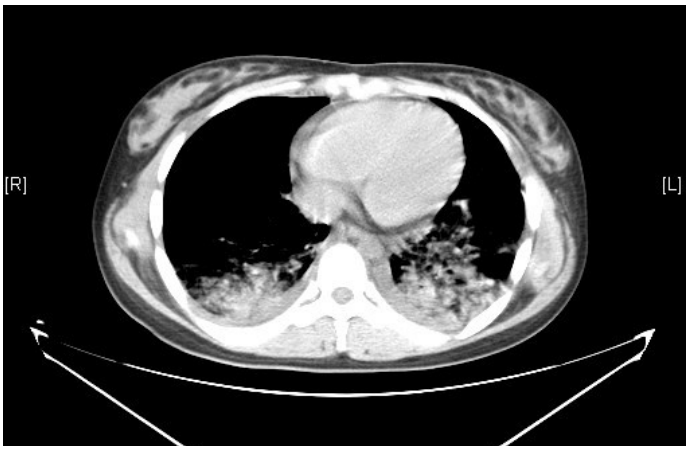

Figure 3. Computed Tomography of the Chest in acute stage
图 3. 急性期肺 CT

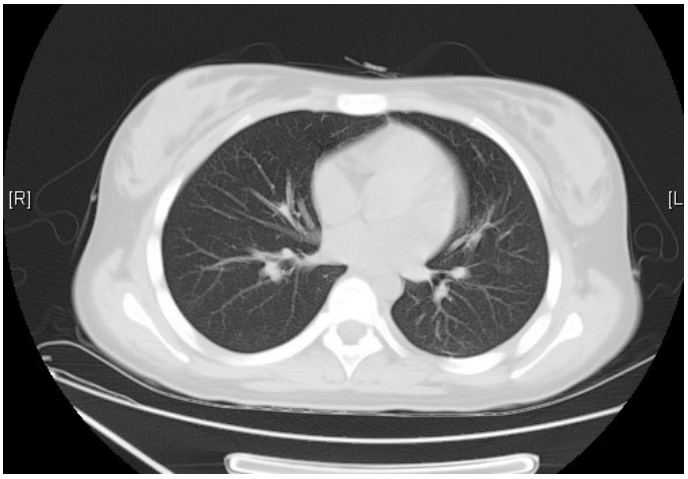

Figure 4. Computed Tomography of the Chest in restoration stage
图 4. 恢复期肺 CT

3. 讨论

氨氯地平是一种二氢吡啶类长效钙通道阻滞剂，口服吸收缓慢，达峰时间 6~12 h，生物利用度为64%~90%，清除半衰期 30~60 h [1]。氨氯地平可选择性地抑制心肌及血管平滑肌细胞钙离子跨膜转运，从而松弛心脏及血管的平滑肌，对血管平滑肌的作用强于对心肌细胞的作用，目前临床常用于高血压、心绞痛等疾病的治疗。

氨氯地平常规剂量下的不良反应主要有头痛、水肿、疲劳、恶心、腹痛、面红等。多篇文献报道，过量氨氯地平可引起低血压、心律失常、高血糖、代谢性酸中毒、非心源性肺水肿等，甚至会导致心脏骤停[2]-[7]。其机制系氨氯地平过量时失去对钙离子通道的选择性[8]，钙离子通道位于心肌细胞、平滑肌细胞和胰腺的胰岛细胞中，过量氨氯地平抑制全身钙离子通道的跨膜转运[3]。心肌内的钙离子通道被抑制导致心肌收缩力下降，窦房结和房室结的钙离子通道被抑制可导致心率下降[9]。血管平滑肌的钙离子通道被抑制表现为血压降低、冠脉扩张和后负荷减少[3]。胰腺中的钙离子通道被抑制表现为抑制胰岛素分泌和促进胰岛素抵抗，引起高血糖和代谢性酸中毒，同时降低心脏和血管平滑肌细胞的葡萄糖摄取，使心脏功能进一步下降[3]。非心源性肺水肿是氨氯地平过量的一种常见的并发症，几乎半数患者会出现

[6] [10]，其机制尚不完全清楚，可能是由于肺毛细血管舒张导致的肺血流量增加，从而导致肺毛细血管内跨毛细血管静水压力及渗漏增加，液体复苏会加剧此水肿，并可能导致呼吸衰竭[5] [11]。

氨氯地平中毒导致低血压的治疗包括升压药、钙剂和血液动力学支持。氨氯地平中毒可应用肾上腺素、去甲肾上腺素、多巴胺、多巴酚丁胺和异丙肾上腺素等血管活性药物治疗[3]。该患儿入院后出现低血压，给予去甲肾上腺素持续泵入治疗。对于氨氯地平中毒引起的低血压及休克，其机制为钙通道阻滞引起血管舒张，治疗上可连续输注甚至推注钙剂，以克服钙通道的拮抗作用，但临床大多数治疗效果较差，需同时予以其他血管活性药物治疗，但钙剂治疗目前仍是一线治疗方法[11] [12]。

脂肪乳、胰高血糖素和亚甲蓝也可应用于氨氯地平中毒。静脉输注脂肪乳可以结合过量的氨氯地平并促进其清除，而联合输注胰岛素－葡萄糖(高胰岛素血症－高血糖血症)可以对抗胰岛素抵抗，从而增加葡萄糖摄取并促进外周血管阻力和心脏收缩力的改善[9] [13]。亚甲蓝通过降低细胞内环磷酸腺苷、清除一氧化氮和抑制一氧化氮合成来抑制血管舒张[14]，研究表明，亚甲蓝能改善严重氨氯地平中毒患者的心脏射血分数及心输出量[15]，但其治疗效果并不优于脂肪乳及去甲肾上腺素[16] [17]，亚甲蓝可作为严重氨氯地平中毒的辅助用药。

由于缺乏氨氯地平中毒的特效药，洗胃、导泻及活性炭仍是防止药物吸收的首选，且应尽早进行[18]。氨氯地平分子98%与蛋白质结合，血液透析不能去除，因此需行血浆置换(TPE)以清除体内药物，国内外均有报道使用血浆置换治疗取得较好临床疗效[19] [20] [21]，该患儿给予血浆置换后亦有显著治疗效果。已有报道，体外膜肺氧合(ECMO)技术应用于严重氨氯地平中毒，多中心研究表明，早期对于患有难治性休克的严重氨氯地平中毒儿童及成人使用ECMO，能改善患者预后[14] [22] [23] [24]。

本例氨氯地平中毒患儿因存在精神障碍，同时吞服多个刀片，且诊疗初期隐瞒了大量服用氨氯地平病史，未能及时洗胃及导泻，在治疗过程中出现低血压、急性肺水肿并胸腔积液，积极给予血管活性药物、呼吸支持、血浆置换、钙剂等治疗，最终挽救了患儿生命。血药浓度的监测为治疗提供了重要的保障。

4. 小结

目前关于氨氯地平中毒仍无相关指南指导临床治疗，国内外相关文献大都以对症治疗为主。结合该患儿诊疗过程，有以下经验及教训：

1) 对于过量药物中毒，应在第一时间进行洗胃、导泻及活性炭药物吸附治疗。

2) 对于氨氯地平中毒合并低血压甚至休克患者，需积极应用升压药物，如去甲肾上腺素、肾上腺素等。

3) 在液体复苏的同时需密切关注出入量，注意液体平衡。

4) 如患者出现胸闷、呼吸困难，需警惕急性肺水肿的可能性，应积极给予呼吸支持，并予限制补液。

5) 应尽早进行血浆置换。

利益冲突

所有作者声明无利益冲突。

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