ISSN 2666-0873

LETTERS TO THE EDITOR

Cisplatin-Associated Aortic Thrombosis

A Review of Cases Reported to the FDA Adverse Event Reporting System

We read with interest the paper by Cameron et al. (1) characterizing vascular effects of cisplatin-based chemotherapy. Using the U.S. Food and Drug Administration Adverse Event Reporting System (FAERS), we assessed the risk of aortic thrombosis (AT) associated with cisplatin. AT occurring in the absence of baseline atherosclerotic or aneurysmal disease is rare and associated with significant morbidity and mortality related to thrombus propagation including sudden aortic occlusion (2,3). We identified 37 postmarket cases of AT with cisplatin from FAERS and the literature as of May 9, 2019. Cases that reported atrial fibrillation, valvular heart disease, left ventricular thrombi, or wall motion abnormalities were excluded. We applied the WHO causality assessment to our cases and determined causality as probable in 12, and as possible in the remaining cases (4). The median time to onset of AT was 38 days from the first dose of cisplatin with 94% of cases occurring within 90 days of cisplatin initiation among the cases reporting this information (n = 33). Seventeen cases reported the use of cisplatin for treatment of lung cancer. The median case age was 55 years and most cases occurred in females (n = 22). Thirteen cases described a coincidental finding of AT on restaging imaging. The primary confounding factors included smoking history (n = 22) and other cardiovascular risk factors. However, in 15 of these cases, baseline imaging preceding cisplatin initiation reported an absence of aortic abnormalities, likely supporting a drug-related cause given the rarity of AT and the thrombogenic potential of cisplatin.

All cases reported a serious outcome, including death attributed to AT in 4 cases. Of 10 that were treated with urgent revascularization procedures, there were no AT-related deaths. Acute limb ischemia was the most common clinical manifestation of AT, including 1 case that was not treated with a revascularization procedure and subsequently required limb amputation. Four cases also described intestinal ischemia, including 1 fatal case that reported ischemic bowel at the time of death. Seven cases were restarted or continued cisplatin with anticoagulation; there was no reported AT recurrence or complications related to anticoagulation among these cases.

Cameron et al. (1) describe several mechanisms for cisplatin-associated vascular effects, including endothelial dysfunction. The cisplatin product label includes arterial thromboembolism described in adverse reactions (5). Although cisplatin-associated AT may be rare, awareness of the potential for cisplatin-associated thrombotic events should facilitate prompt diagnosis and definitive treatment to decrease the associated morbidity and mortality risk.

*Michelle C. Nadeau Nguyen, PharmD
Daniel Woronow, MD
Bailee Binks, PharmD
Afrouz Nayernama, PharmD
S. Christopher Jones, PharmD, MPH, MS
*U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, Maryland 20993, USA
E-mail: michelle.nadeau-nguyen@fda.hhs.gov

https://dx.doi.org/10.1016/j.jaccao.2020.11.017

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.
The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

REFERENCES

1. Cameron AC, McMahon K, Hall M, et al. Comprehensive characterization of the vascular effects of cisplatin-based chemotherapy in patients with testicular cancer. J Am Coll Cardiol CardioOnc 2020;2:443–55.

2. O'Donnell M, Shatzel JJ, Olson SR, et al. Arterial thrombosis in unusual sites: a practical review. Eur J Hematol 2018;101:728–36.

3. Kaschwich M, Behrendt CA, Tsilimparis N, Kölbel T, Wipper SH, Debus ES. Management of acute aortic thrombosis. J Cardiovasc Surg 2017;58:313–20.

4. WHO-UMC system for causality assessment. Available at, http://www.who.int/medicines/areas/quality_safety/safety_efficacy/WHOcausality_assessment.pdf. Accessed November 2018.

5. U.S. Food and Drug Administration. Cisplatin. Full prescribing information. U.S. Department of Health and Human Services. Available at, https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/018057s089lbl.pdf. Accessed November 2020.