

generally develop depending on the degree of the pulmonary flow impairment (7). Our patient was asymptomatic because the tool was located on the longitudinal axis in the main pulmonary artery and did not affect pulmonary flow. Because of the embolization of the device, percutaneous or surgical removal was indicated (3). In our case, percutaneous removal was not an option because of the chronic embolization of the device in the main pulmonary artery. Thus, we recommended surgery for our patient.

Conclusion

Device embolization, the most common complication of percutaneous closure of ASD, can occur in the late postoperative period. Different clinical presentations are possible depending on the location where the device is embolized. Rarely, patients may be asymptomatic. Individuals with a high risk of embolization should be followed up more frequently and for a longer time using echocardiography.

Informed consent: The informed consent was obtained from the patient.

References

1. Clark EB. Epidemiology of congenital cardiovascular malformations. In: Emmanouilides GC, Riemenschneider TA, Allen HD, et al., editors. Heart disease infants, children, and adolescent including the fetus and young adult. 5th ed. Baltimore: Williams & Wilkins; 1995. pp. 60–70.
2. Knepp MD, Rocchini AP, Lloyd TR, Aiyagari RM. Long-term follow up of secundum atrial septal defect closure with the Amplatzer septal occluder. *Congenital Heart Dis* 2010; 5: 32–7.
3. Chessa M, Carminati M, Butera G, Bini RM, Drago M, Rosti L, et al. Early and late complications associated with transcatheter occlusion of secundum atrial septal defect. *J Am Coll Cardiol* 2002; 39: 1061–5.
4. Chiappini B, Gregorini R, Di Eusanio M, Ciocca M, Villani C, Minuti U, et al. Embolization of an Amplatzer atrial septal closure device to the pulmonary artery. *J Card Surg* 2008; 23: 164–7.
5. Berdat PA, Chatterjee T, Pfammatter JP, Windecker S, Meier B, Carrel T. Surgical management of complications after transcatheter closure of an atrial septal defect or patent foramen ovale. *J Thorac Cardiovasc Surg* 2000; 120: 1034–9.
6. Sinha A, Nanda NC, Khanna D, Dod HS, Vengala S, Mehmood F, et al. Morphological assessment of left ventricular thrombus by live three-dimensional transthoracic echocardiography. *Echocardiography* 2004; 21: 649–55.
7. Misra M, Sadiq A, Namboodiri N, Karunakaran J. The 'aortic rim' recount: embolization of interatrial septal occluder into the main pulmonary artery bifurcation after atrial septal defect closure. *Interact Cardiovasc Thorac Surg* 2007; 6: 384–6.
8. Mashman WE, King SB, Jacobs WC, Ballard WL. Two cases of late embolization of Amplatzer septal occluder devices to the pulmonary artery following closure of secundum atrial septal defects. *Catheter Cardiovasc Interv* 2005; 65: 588–92.

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Fatal anaphylactic reaction due to ferric carboxymaltose: A case report

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Introduction

Iron-deficiency anemia is most frequently related with insufficient nutrition. However, it is also encountered in chronic diseases including chronic renal failure (CRF) and congestive heart failure (CHF). Oral or intravenous (IV) iron replacement is recommended for its treatment (1, 2). IV administration is the preferred route in CRF and CHF, where intestinal mucosal edema and diminished gastrointestinal blood flow limit absorption of oral iron. Although IV route may cause hypersensitivity reaction (HSR), it is generally safe. The report of the European Medicines Agency declares that IV-iron treatment has a high benefit/risk ratio (3).

Ferric carboxymaltose (FCM) is a nondextran third-generation IV-iron preparation which has the advantage of normalizing hemoglobin and replenishing iron stores over a short period of time because it can be administered fast and in high doses (4). It has been approved and presented to the market in 2007 in Europe and in 2012 in Turkey (5). Clinical research has shown that it is generally well tolerated and has low serious HSR risk ($\geq 1/10.000$ to $< 1/1.000$) (1, 4, 6, 7). Evaluation of safety reports discloses that there are four cases of death related to FCM (5, 8). To our knowledge, this is the first case of death related to FCM in Turkey and the fifth case of fatal anaphylactic reaction (AR) in the literature.

Case Report

A 74-year-old male patient who had a history of diabetes, hypertension, CRF, and coronary artery disease presented to the emergency service of our hospital with shortness of breath. On admission, since he had hypertension (190/110 mm Hg) and lung

edema, he was given IV furosemide and nitrate infusion, and noninvasive ventilation was started. He was on long-acting insulin, lercanidipin, isosorbid mononitrate, and nebivolol due to his chronic diseases. The next day, he was moved to the coronary intensive care unit because of an increase in cardiac enzymes. Echocardiography showed a left ventricular ejection fraction of 40%, anterolateral hypokinesia, and slight mitral and tricuspid insufficiency. Angiography showed various stenoses in his coronary arteries and right renal artery, for which percutaneous intervention was planned.

IV-iron treatment was planned due to his iron-deficiency anemia (Table 1). After his signs of heart failure regressed and he became generally stable, FCM (Ferinject®, 1000 mg/15 min) infu-

sion was started. He had no history of drug allergy or any allergic disease. Thirty seconds after the beginning of infusion, when the patient felt faint, infusion was stopped immediately. When respiratory distress (dyspnea and stridor) developed within a few minutes, IV prednisolone and an antihistaminic medication were administered. Despite treatment efforts, angioedema developed, which was followed by respiratory arrest. He was intubated using a video laryngoscope. When cardiac arrest developed shortly after, CPR was started, and IV atropine and IV adrenaline were given. CPR was stopped after 50 min of unresponsiveness.

Discussion

It is shown that iron deficiency worsens prognosis in patients with CRF and CHF. Therefore, IV FCM is recommended in the treatment of these symptomatic patients to decrease their symptoms and restore their exercise capacity (2, 4, 9).

IV-FCM treatment related fatal HSR is very rare, and the incidence is not increased in the presence of CHF or CRF (5, 8, 9). Retrospective evaluation of EudraVigilance drug safety database (2014–2017) revealed 121 FCM-related serious HSR, of which only one was fatal (5).

The factors which increase the incidence of HSR related to IV-iron administration are history of drug sensitivity, history of immune/inflammatory/allergic disease, mastocytosis, and high infusion rate (3). However, these factors were not present in our case. Causality relationship between the drug administration and AR was evaluated using the Naranjo Score (10), which was found to be "six" and interpreted as "probable" (Table 2). The presence of previous lung edema might have caused rapid decompensation after the occurrence of anaphylaxis. The presence of several comorbidities might have also influenced the develop-

Table 1. Various laboratory findings of our patient before ferric carboxymaltose infusion

	Patient values	Normal range
Hemoglobin (g/dL)	9.4	13.5-17.5
Transferrin saturation (%)	3.76	15.0-50.0
Iron (µg/dL)	12	70.0-180.0
BUN (mg/dL)	39.6	8.0-23.0
Serum creatinine (mg/dL)	2.05	0.67-1.17
e-GFR (CKD-EPI)	30.99	90.0
Uric acid (mg/dL)	9.61	3.5-7.2
Albumin (g/dL)	3.35	3.5-5.2
CRP (mg/L)	15.3	0.2-5.0
hs troponin I (ng/mL)	293.4	14.0-42.9
HbA1c (%)	9.0	4.0-6.0

BUN - blood urea nitrogen, e-GFR - estimated-glomerular filtration rate, CRP - C-reactive protein

Table 2. The evaluation of causality relationship between the drug and anaphylactic reaction which developed after ferric carboxymaltose administration in our patient using the Naranjo Scale

Question	Yes	No	Do not know	Score
1. Are there previous conclusive reports on this reaction?	+1	0	0	+1
2. Did the adverse event appear after the suspected drug was administered?	+2	-1	0	+2
3. Did the adverse event improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0	0
4. Did the adverse event reappear when the drug was readministered?	+2	-1	0	0
5. Are there alternative causes that could on their own have caused the reaction?	-1	+2	0	+2
6. Did the reaction reappear when a placebo was given?	-1	+1	0	0
7. Was the drug detected in blood or other fluids in concentrations known to be toxic?	+1	0	0	0
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	0
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0	0
10. Was the adverse event confirmed by any objective evidence?	+1	0	0	+1
Total Score: 6				

Total Score ≥9: definite; 5 to 8: probable; 1 to 4: possible; ≤0: doubtful

ment of serious HSR. Indeed, comorbidities have been reported to increase the risk of HSR by at least 2.8 times, regardless of the type of IV-iron formulations (6).

Conclusion

It should be kept in mind that fatal AR related to FCM administration may develop, although rare. Therefore, FCM should be administered in centers where emergency treatment can be delivered by healthcare personnel who can evaluate and manage AR. It should be known that every administration bears AR risk, even if the previous treatment was well tolerated.

References

1. Friedrisch JR, Cançado RD. Intravenous ferric carboxymaltose for the treatment of iron deficiency anemia. *Rev Bras Hematol Hemoter* 2015; 37: 400-5. [CrossRef]
2. Gafter-Gvili A, Schechter A, Rozen-Zvi B. Iron deficiency anemia in chronic kidney disease. *Acta Haematol* 2019; 142: 44-50. [CrossRef]
3. EMA-CHMP. Assessment report for: iron containing intravenous (IV) medicinal products EMA/549569/2013,2013 (last accessed 10 February 2020). Available at; URL: http://www.ema.europa.eu/docs/en_GB/document_library/Referrals-document/IV_iron_31/WC500150771.pdf
4. Scott LJ. Ferric Carboxymaltose: A Review in Iron Deficiency. *Drugs* 2018; 78: 479-93. [CrossRef]
5. Ehlken B, Nathell L, Gohlke A, Bocuk D, Toussi M, Wohlfeil S. Evaluation of the reported rates of severe hypersensitivity reactions associated with ferric carboxymaltose and iron (III) isomaltoside 1000 in Europe based on data from EudraVigilance and VigiBase™ between 2014 and 2017. *Drug Saf* 2019; 42: 463-71. [CrossRef]
6. Mulder MB, van den Hoek HL, Birnie E, van Tilburg AJP, Westerman EM. Comparison of hypersensitivity reactions of intravenous iron: iron isomaltoside-1000 (Monofer®) versus ferric carboxy-maltose (Ferinject®). A single center, cohort study. *Br J Clin Pharmacol* 2019; 85: 385-92. [CrossRef]
7. Ferinject (ferric carboxymaltose). Uptating 13 November 2019. (last accessed 10 February 2020). Available at; URL: <https://www.medicines.org.uk/emc/product/5910/smpc>
8. FDA-CDER. Injectafer (VIT-45, ferric carboxymaltose injection; FCM) for the treatment of iron deficiency anemia. Updated clinical safety information (last accessed 10 February 2020). Available at; URL: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2013/2035650rig1s000MedR.pdf
9. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, et al.; Authors/Task Force Members; Document Reviewers. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur J Heart Fail* 2016; 18: 891-975. [CrossRef]
10. LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Adverse Drug Reaction Probability Scale (Naranjo) in Drug Induced Liver Injury (last accessed 10 February 2020). Available at; URL: <https://www.ncbi.nlm.nih.gov/books/NBK548069/>

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Misinterpretation of dual atrioventricular nodal non-reentrant tachycardia as ventricular tachycardia and implantation of implantable cardioverter-defibrillator followed by inappropriate shocks

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Introduction

A double ventricular response to a single atrial beat is defined as “double-fire,” and this forms the basis of dual atrioventricular (AV) nodal non-reentrant tachycardia (DAVNNT), which can mimic several other arrhythmias and lead the clinicians to misdiagnose and mismanage it. DAVNNT was first described in 1975 by Wu et al. (1). Until date, overall, 77 cases have been reported (2, 3) as DAVNNT, with tachycardia-induced cardiomyopathy developing in only few of these patients. To our knowledge, only few patients have been treated with implantable cardioverter-defibrillator (ICD) because of misinterpreting DAVNNT as VT.

Case Report

A 58-year-old female experienced her first palpitation 18 years ago, but it became persistent over the years. Physicians detected wide QRS tachycardia on her surface electrocardiography (ECG), which was recorded 8 years ago. An electrophysiological study was performed 5 years ago in sinus rhythm, but no tachycardia could be induced. Her coronary arteries were normal, but left ventricular ejection fraction (LVEF) was 35% on transthoracic echocardiography. Hence, ICD was implanted because of decreased left ventricular function and the previously documented wide QRS tachycardia. Nonetheless, the patient remained symptomatic despite antiarrhythmic medication and ICD. She was referred to our university's arrhythmia department because of her increased ongoing complaints. Notably, the patient informed that her symptoms disappeared during ex-