Cardiology in the Young (2018), **28**, 616–618
doi:10.1017/S1047951117002785

Brief Report

Coronary artery spasm due to intravenous atropine infusion in a child: possible Kounis syndrome

Ana Castellano-Martinez,[1] Moises Rodriguez-Gonzalez[2]

[1]*Department of Pediatrics;* [2]*Department of Pediatric Cardiology, Hospital Universitario Puerta del Mar, Cadiz, Spain*

Abstract Coronary vasospasm can result from silent myocardial ischaemia to sudden death. There are many precipitant factors including different pharmacological agents. Kounis syndrome is defined by acute coronary syndromes associated with anaphylactic or anaphylactoid reactions. We report, to the best of our knowledge, the first paediatric case of Kounis syndrome due to intravenous atropine.

Keywords: Atropine; coronary vasospasm; Kounis syndrome; children

Received: 13 November 2017; Accepted: 23 November 2017; First published online: 10 January 2018

Coronary vasospasm is a myocardial ischaemic syndrome with a great clinical variability, from silent myocardial ischaemia to even sudden death.[1,2] Hyper-reactivity of coronary vascular smooth muscle precipitated by different factors seems to be the main pathophysiologic substrate.[1] Elevated cardiac enzymes and transient ischaemic electrocardiographic changes can suggest the diagnosis. Coronary angiography with provocative testing is the only certain method of diagnosing coronary vasospasm, but a negative test cannot always exclude it.[1] Patients must avoid known precipitating factors, and medical treatment with long-acting calcium antagonist is proposed when attacks are recurrent or prolonged. The prognosis of vasospasm-induced acute coronary syndrome remains excellent if it is short in duration.[2]

There are few cases of coronary vasospasm reported in the paediatric literature, usually with predisposing factors such as Erythematous Systemic Lupus[3]or Kawasaki disease.[4] Coronary vasospasm secondary to atropine is reported in only one adult patient.[5] We report, to the best of our knowledge, the first published case induced by atropine, probably secondary to a cardiac hypersensitivity, in a children.

Correspondence to: M. Rodriguez-Gonzalez, MD, Department of Pediatrics, Hospital Universitario Puerta del Mar, Ana de Viya Avenue 34, 11009 Cadiz, Spain. Tel: 34 956 00 27 00; Fax: 34 956002085; E-mail: moirogo@gmail.com

Case report

A 10-year-old boy underwent an upper endoscopy to complete a chronic abdominal pain study. Personal history revealed that he received a well-tolerated intravenous atropine infusion during the anaesthetic induction of the surgical resection of a cholesteatoma 2 years ago. Sedation with ketamine and midazolam with cardiorespiratory monitoring at the ICU was prepared. Previously, to infuse the sedative agents the patient received an intravenous bolus of atropine (0.1 mg/kg). Immediately the patient complained of chest discomfort with nausea and vomiting. He became pale, sweaty, and hypotensive (71/32 mmHg), with thoracic urticarial rash. Electrocardiographic monitor revealed severe bradycardia with ventricular escape rhythm (Fig 1a). Spontaneous circulation was restored and symptoms, including urticarial rash, disappeared spontaneously in ~30 seconds without any treatment. Endoscopy was interrupted and an immediate 12-lead electrocardiogram showed ischaemic changes (Fig 2). Troponin I was elevated (295 ng/L). One hour after the episode, electrocardiogram became normal without any treatment. Troponin I levels were normalised in 24 hours (12 ng/L) and the patient remained asymptomatic. An acute myocardial ischaemic event work-up, including 24-hour Holter-ECG, ergometry, two-dimensional-Doppler echocardiography, cardiac angioMRI, and cardiac angioCT, was performed with

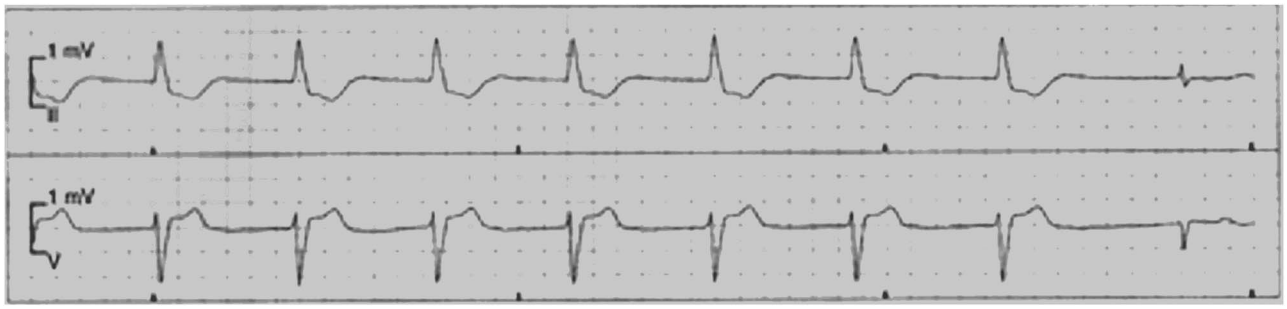

Figure 1.
Monitor ECG showing ventricular escape rhythm at 41 beats per minute.

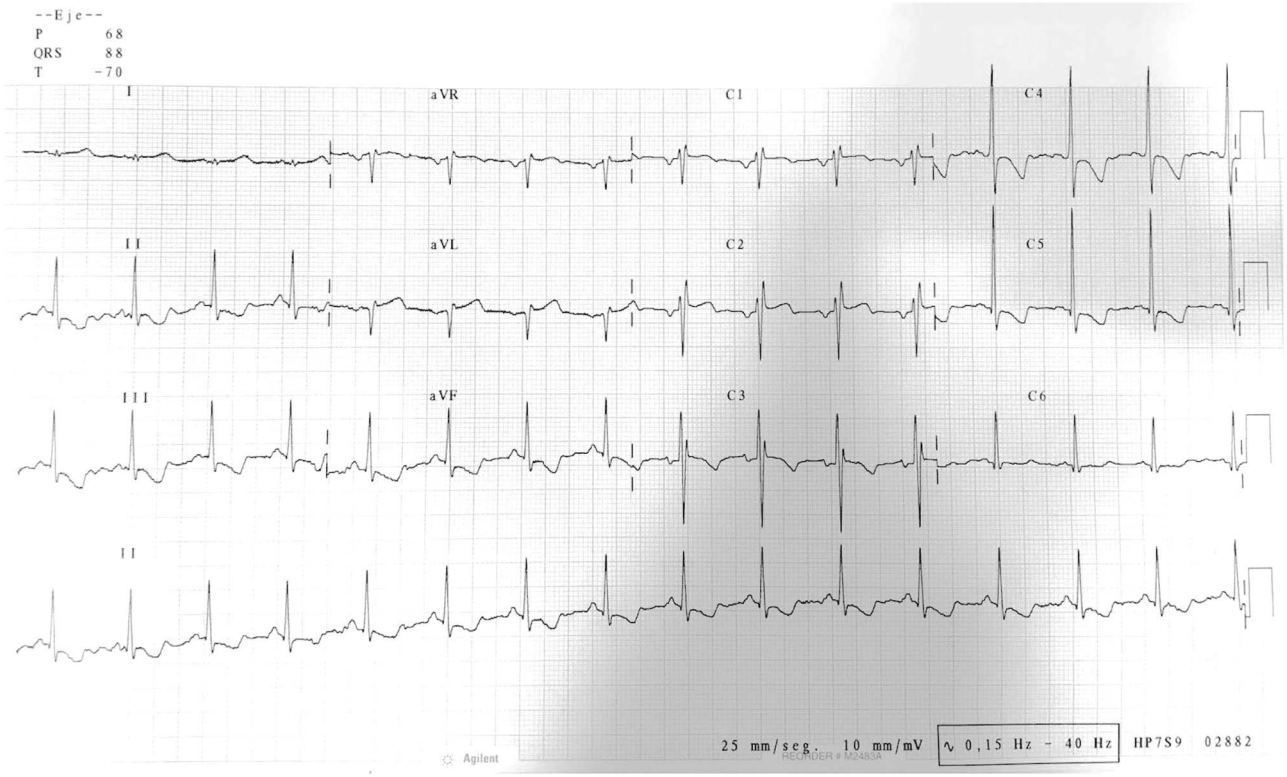

Figure 2.
12-leads ECG performed after resuscitation showing ischaemic changes in precordial left and inferior leads (ST-segment depression and inverted T-wave in leads II, III and aVF).

normal results. Because of the abrupt onset of the urticarial rash and the documented myocardial ischaemic event immediately after the atropine infusion without the administration of any other drugs, the possibility of a previous sensitisation to atropine, and the complete and spontaneous recuperation with a normal cardiac study, we thought that the most consistent explanation was a coronary vasospasm triggered by atropine in the context of an allergic reaction. Thus, the patient was discharged with the diagnosis of a possible type I Kounis syndrome with the recommendation to use glycopyrrolate as an alternative to atropine in case of needing anti-cholinergic medication.

Discussion

Kounis syndrome was described as "the concurrence of acute coronary syndromes with conditions associated with mast cell and platelet activation involving interrelated and interacting inflammatory cells in the setting of allergic or hypersensitivity and anaphylactic or anaphylactoid insults".[6] Of the three variants described, the type I – normal coronary arteries with no predisposing cardiovascular factors – is the most frequent in children.[6,7] There are numerous pharmacological triggers described, but to the best of our knowledge this is the first case reported of a paediatric Kounis syndrome triggered by atropine.

https://doi.org/10.1017/S1047951117002785 Published online by Cambridge University Press

Kounis syndrome could be infrequently recognised in clinical practice and under-reported in the literature. The diagnosis should be suspected when patients have signs of systemic allergic reactions associated with clinical, electrocardiographic, and laboratory findings of acute and transient myocardial ischaemia. A complete cardiac imaging work-up is necessary to delineate the normal coronary anatomy and to assess myocardial perfusion.[1,2] Although coronary angiography is the gold standard for this purpose, we decided to avoid this invasive technique in our patient because of the low probability that he had a coronary artery disease after the broad non-invasive work-up performed. Elevated serum levels of histamine, tryptase, and IgE are observed in Kounis syndrome, and it can lead to diagnosis if increased serum levels are detected in this context.[8] We did not determine this because we did not think about the possibility of Kounis syndrome in first instance. Anyway, it is reported that serum histamine and tryptase levels do not necessarily correlate in patients presenting with anaphylaxis – sensitivity of 73% and specificity of 98%.[8–10] Skin prick and intradermal tests are helpful for the diagnosis of immediate drug hypersensitivity reactions; however, the chronology of the symptoms was compatible with atropine hypersensitivity reaction and, following the recommendations of the International Consensus on drugs allergy,[10] they were avoided in our case because of the severe life-threatening reaction and the possibility of an equally effective and structurally unrelated safe alternative (glycopyrrolate). Regardless, moderate to low sensitivity and predictive values of skin tests for most of the drugs have been reported, and thus a negative value does not exclude the imputability of the drug.[8,10]

Therapeutic management of Kounis syndrome is a challenge. Mast cell stabilisers, steroids, and histamine antagonists are recommended as potential treatment options for the allergic event, even like prophylactic agents before anaesthesia induction of patients with an atopic or Kounis syndrome history.[1,2,6,7] However, the most important thing is the prevention identifying and avoiding the precipitant agent. In our case, no treatment was necessary because of the short duration of the episode and the spontaneous recuperation with any sequels.

The diagnosis of Kounis syndrome due to atropine is not a certainty in our patient. Thus, atropine by itself has a sympathetic activity that could contribute to the provocation of the CAS. However, because of the reasons mentioned above, we thought that our patient fitted well with possible type I Kounis syndrome as the most probable diagnosis.

Conclusions

Kounis syndrome is rare but can occur in the paediatric population. A quick recognition of the trigger agent is the better treatment. Reporting new cases could help increase the recognition of this condition and to discover unknown factors implicated, such as atropine in our case.

Acknowledgement

We thank Dr. Guitart-Martinez and Dr. Hernandez-Gonzalez for their collaboration in diagnosis and management of the patient.

Authors' contributions: C.-M. conceptualised and designed the study, drafted the initial manuscript, and approved the final manuscript as submitted. R.-G. conceptualised and designed the study, drafted the initial manuscript, and approved the final manuscript as submitted.

Financial Support

This research received no specific grant from any funding agency, commercial or not-for-profit sectors.

Conflicts of Interest

None.

References

1. Ming-Jui H, Hu P, Ming-Yow H. Coronary artery spasm: review and update. Int J Med Sci 2014; 11: 1161–1171.
2. Miwa K, Nakagawa K, Yoshida N, et al. Lipoprotein (a) is a risk factor for occurrence of acute myocardial infarction in patients with coronary vasospasm. J Am Coll Cardiol 2000; 35: 1200–1205.
3. Jasmin R, Ng C-T, Sockalingam S, et al. Myocardial infarction with normal coronaries: an unexpected finding in a 13-year-old girl with systemic lupus erythematosus. Lupus 2013; 22: 1518–1522.
4. Subramanian S, Gaum WE. Acute myocardial infarction caused by transient coronary vasospasm in a child with Kawasaki disease and no coronary aneurysms. Pediatr Cardiol 2010; 31: 875–877.
5. Lee J, Seok J, Kim Y, et al. Atropine injection followed by coronary artery spasm with ventricular tachycardia during spinal anesthesia. Korean J Anesthesiol 2013; 65: 66–70.
6. Kounis NG. Kounis syndrome: an update on epidemiology, pathogenesis, diagnosis and therapeutic management. Clin Chem Lab Med 2016; 54: 1545–1559.
7. Biteker M, Duran NE, Biteker F, et al. Kounis syndrome: first series in Turkish patients. Anadolu Kardiyol Derg 2009; 9: 59–60.
8. Ebo DG, Leysen J, Mayorga C, et al. The in vitro diagnosis of drug allergy: status and perspectives. Allergy 2011; 66: 1275–1286.
9. Demoly P, Adkinson NF, Brockow K, et al. International consensus on drug allergy. Allergy 2014; 69: 420–437.
10. Brockow K, Garvey LH, Aberer W, et al. Skin test concentrations for systemically administered drugs – an ENDA/EAACI Drug Allergy Interest Group position paper. Allergy 2013; 68: 702–712.