

Complete atrioventricular block after self-ingestion of *Nerium oleander* for relief of hemorrhoidal complaints

Hemoroit yakınmaları nedeniyle zakkum kullanan bir hastada tam atriyoventriküler blok

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Summary - *Nerium oleander* is a plant native only in the Mediterranean region, but it can also be cultivated worldwide, particularly in warm areas. Biologically active oleander compounds may be used for therapeutic purposes. However, when used for self-medication, it may cause serious problems including death. We present a 30-year-old otherwise healthy man who developed complete atrioventricular block after taking a syrup of *N. oleander* leaves for self-medication to relieve hemorrhoidal complaints. The patient was treated by oral administration of charcoal combined with sodium sulfate as well as electrolyte solutions and transient use of an external cardiac pacemaker. The atrioventricular block reverted to sinus rhythm in 30 hours and he was discharged in good hemodynamic status and general condition.

Özet - Zakkum (*Nerium oleander*), her ne kadar Akdeniz bölgesine özgü bir bitki olsa da, bilhassa ılıman bölgelerde olmak üzere tüm dünyada yetiştirilebilir. Biyolojik olarak aktif olan oleander bileşenleri terapötik amaçlarla kullanılabilir. Ancak, bitkisel tedavi amaçlı kişisel kullanımı, ölüm dahil birçok ciddi soruna yol açabilir. Bu yazıda, hemoroit yakınmaları nedeniyle kişisel bitkisel tedavi amacıyla zakkum yapraklarından hazırladığı şurubu içtikten sonra tam atriyoventriküler blok gelişen, 30 yaşında, başka sağlık sorunu olmayan bir erkek hasta sunuldu. Hastaya sodyum sülfat ile birlikte ağızdan kömür tedavisi, elektrolit sıvı desteği ve geçici kalp pili tedavisi uygulandı. Atriyoventriküler blok 30 saat sonra sinüs ritmine döndü ve hasta hemodinamik ve genel durumu düzelmiş şekilde taburcu edildi.

Nerium oleander is an evergreen plant native only in the Mediterranean region, but it can also be cultivated worldwide, particularly in warm areas. Biologically active oleander compounds exhibit insecticidal, antimycotic, cardiac properties, and recently have been proposed for oncologic therapeutic purposes.^[1] Many people consider it useful and thus use it in the context of herbal therapy. However, it may also have many side effects including cardiac effects that may be lethal. We report on a patient who presented to our hospital with bradycardia and atrioventricular block after usage of oleander leaves for treatment of hemorrhoid.

CASE REPORT

A 30-year-old man was admitted to our emergency service with nausea, vomiting, atypical chest pain,

malaise, and lightheadedness. He had no history of cardiometabolic diseases and was not on any medication including negative inotropic agents. His heart rate was 35 bpm and blood pressure was 140/100 mmHg. The rest of the cardiac examination and other system examinations were unremarkable. The electrocardiogram revealed complete atrioventricular block with atrial fibroflutter (Fig. 1a). Laboratory findings including electrolytes, inflammation markers, liver enzymes, creatinine, blood count, and cardiac enzymes were normal. Upon questioning the patient on the possible etiology of the condition, he explained that, on an advise of an herbalist to treat his hemorrhoid, he had drunk a homemade syrup of *N. oleander* leaves (a mid-size package of leaves boiled in water) for eight hours before admission. The patient was treated by oral

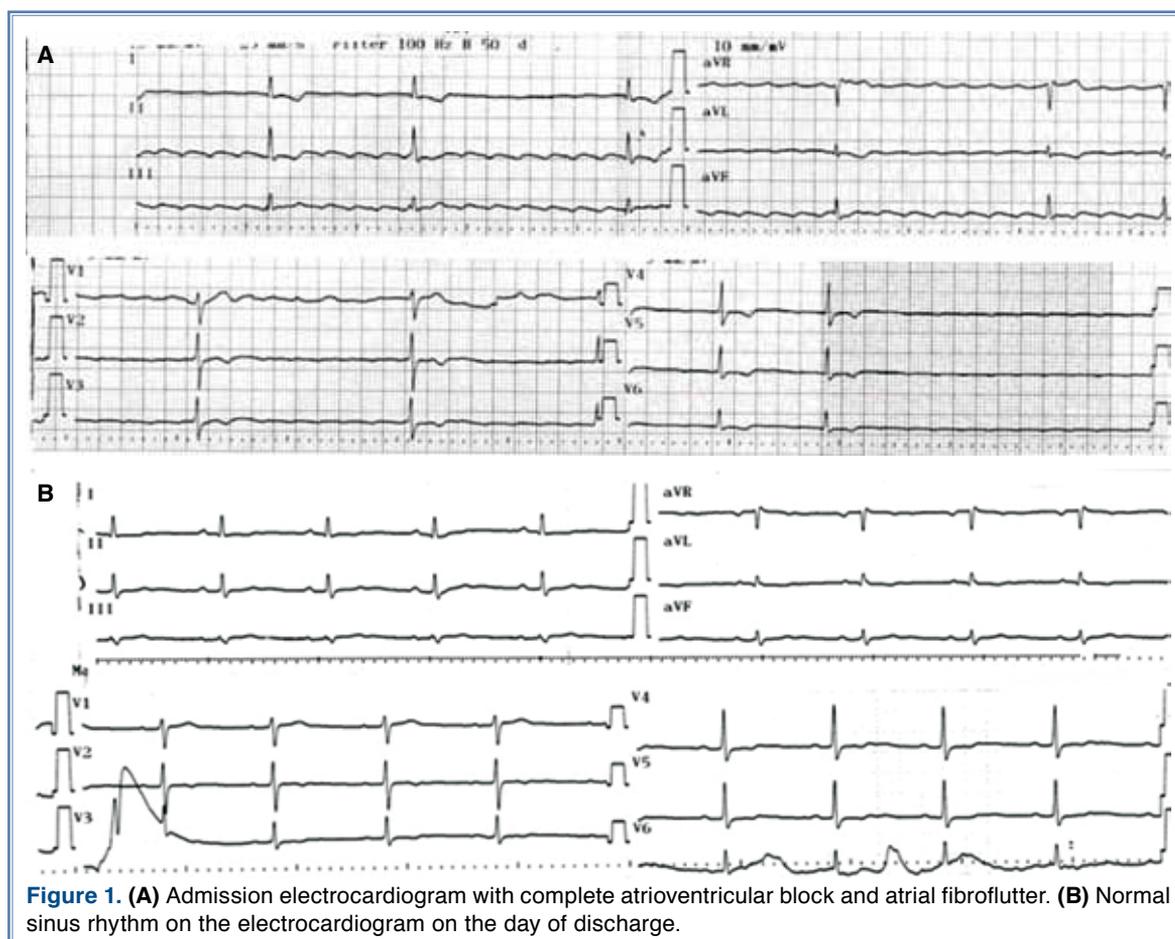
Abbreviation:

AV Atrioventricular block

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administration of charcoal combined with sodium sulfate as well as electrolyte solutions. An external cardiac pacemaker was temporarily attached because of the complete AV block and bradycardic episodes. The AV block reverted to sinus rhythm in 30 hours. The patient's hemodynamic status and general condition improved and he was discharged on Day 6. Delayed discharge was due to the close follow-up of atrial extra systoles that occurred in decreasing frequency. At the first follow-up visit 10 days later, he was free of cardiac symptoms with normal sinus rhythm on the electrocardiogram (Fig. 1b). The patient was referred to the gastroenterology department for his hemorrhoid.

DISCUSSION

Oleandrin was formerly used as a cardiac tonic and diuretic, and its extracts are still used in homeopathy.^[2] All parts of this plant, including the sap, either fresh, dried or boiled, are toxic. Oleander leaves and seeds contain more than 30 different cardiac glycosides (e.g. oleandrin, oleandrogenin, desacetyloleandrin,

glucosyloleandrin, gentiobiosyloleandrin, nerigoside, odorosides, oleasides) at various concentrations. A dose of 5 to 15 leaves of oleandrin may be lethal for adults, but in children a single leaf may be lethal.^[3] Parts of the plant can be ingested accidentally, used in suicide attempts^[4] or for therapeutical aims,^[5] leading to oleander poisoning. The first signs are gastrointestinal discomfort, nausea, and vomiting, followed by neurological symptoms that include weakness, mental confusion, and cardiac involvement that presents as cardiac arrhythmias (atrial and ventricular ectopic arrhythmias) and conduction disturbances (sinoatrial and AV node conduction disturbances) usually manifesting as bradycardia which may progress to AV block and asystole. In some cases, ectopic beats may be followed by ventricular tachycardia and fibrillation. The triad of gastrointestinal distress, circumoral erythema and cardiac dysrhythmia should alert to the possibility of *N. oleander* poisoning.^[6]

Nerium oleander produces typical clinical signs of cardiac glycoside poisoning. The physiological action of cardenolides are attributed to their binding to the

Na⁺/K⁺-sensitive membrane-bound enzymes, thereby disturbing the Na⁺/K⁺ transport and leading to increased intracellular Ca²⁺ levels. Intoxication rates are higher in tropic and subtropic regions of the world. In a study of 170 cases in Sri Lanka, it was reported that the majority of the cases were due to suicide attempts;^[7] however, in recent years, herbal medication has also become an important source for plant poisoning including that associated with *N. oleander*.^[8] In all cases of plant poisoning, the identification of the plant involved is the first and most important diagnostic step especially if the patient arrives early after ingestion of the plant, before the onset of systemic symptoms other than vomiting. Measurement of digitalis glycoside levels is important and of prognostic value since the AV block is reversible, but it should not be forgotten that antibody-based digoxin assays may cross-react with other cardiac glycosides nonquantitatively so chromatographic techniques can be used in the specific diagnosis. Patients with cardiovascular illness, those who ingest more than 0.5 mg/kg of oleander leaves and/or those who arrive late to hospital are at highest risk. Serum potassium concentrations are of prognostic importance, as in digoxin intoxication.^[9] The presence of hyperkalemia in the initial stage of intoxication worsens the prognosis because deaths from ingestion of *N. oleander* occur due to dysrhythmias.^[6]

Because of the chemical and pharmacological similarities between digitalis and oleandrin, the treatment is similar, as well.^[5] Thus, treatment should aim at gut decontamination by means of emesis or lavage, correction of electrolyte imbalance, correction of severe bradycardia with atropine or electrical pacing, corrections of ventricular dysrhythmias, and administration of digoxin-specific antibody (Fab) fragments if available.^[10] Forced diuresis, hemoperfusion, and hemodialysis are not effective methods for improved digoxin elimination.

In conclusion, clinicians must include oleander poisoning in the differential diagnosis of bradyarrhythmias, particularly in children and young people without known cardiovascular disease, in areas where this plant either is used as a herbal medicine or is known as poisonous. In addition, *N. oleander* intoxication might be considered highly probable for similar

patients with conduction abnormalities in the presence of permanent disappearance of the AV block and the absence of a convincing alternative diagnosis during hospitalization. In the context of public awareness, people should be warned about the appropriate use of herbal therapies which might be useless, harmful, and sometimes lethal.

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REFERENCES

1. Mekhail T, Kaur H, Ganapathi R, Budd GT, Elson P, Bukowski RM. Phase 1 trial of Anvirzel in patients with refractory solid tumors. *Invest New Drugs* 2006;24:423-7.
2. van Wyk BE, van Heerden FR, van Oudtshoorn B, editors. *Poisonous plants of South Africa*. Pretoria; Briza Publications; 2002. p. 156-7.
3. Shaw D, Pearn J. Oleander poisoning. *Med J Aust* 1979;2:267-9.
4. Pietsch J, Oertel R, Trautmann S, Schulz K, Kopp B, Dressler J. A non-fatal oleander poisoning. *Int J Legal Med* 2005;119:236-40.
5. Wojtyna W, Enseleit F. A rare cause of complete heart block after transdermal botanical treatment for psoriasis. *Pacing Clin Electrophysiol* 2004;27:1686-8.
6. IPCS International Programme on Chemical Safety. *Nerium oleander L.* Available from: <http://www.inchem.org/documents/pims/plant/pim366.htm>.
7. Saravanapavanathan N, Ganeshamoorthy J. Yellow oleander poisoning-a study of 170 cases. *Forensic Sci Int* 1988; 36:247-50.
8. Altan E, Bitik B, Kalpakçı Y, Doğan E, Altundağ K. Probable hepatotoxicity related to Nerium oleander extract in a patient with metastatic synovial sarcoma of the knee. *J Altern Complement Med* 2009;15:113.
9. Gupta A, Joshi P, Jortani SA, Valdes R Jr, Thorkelsson T, Verjee Z, et al. A case of nondigitalis cardiac glycoside toxicity. *Ther Drug Monit* 1997;19:711-4.
10. Shumaik GM, Wu AW, Ping AC. Oleander poisoning: treatment with digoxin-specific Fab antibody fragments. *Ann Emerg Med* 1988;17:732-5.

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Anahtar sözcükler: Kalp bloku/etyoloji; Nerium/zehirlenme; bitki zehirlenmesi; bitki, toksik.