Luis Efren Santos-Martínez[a,*], Nielzer Armando Rodríguez-Almendros[a], César Antonio Flores-García[b], Patricia Soto-Márquez[c], Moisés Jiménez-Santos[d], Joel Estrada Gallegos[e] y Moisés Cuttiel Calderón-Abbo[f]

[a] *Unidad Médica de Alta Especialidad, Departamento de Hipertensión Pulmonar y Función Ventricular Derecha, Hospital de Cardiología del Centro Médico Nacional Siglo XXI, Instituto Mexicano del Seguro Social, Ciudad de México, México*
[b] *Unidad Médica de Alta Especialidad, Departamento de Patología, Hospital de Cardiología del Centro Médico Nacional Siglo XXI, Instituto Mexicano del Seguro Social, Ciudad de México, México*
[c] *Unidad Médica de Alta Especialidad, División de Auxiliares de Diagnóstico y Tratamiento, Hospital de Cardiología del Centro Médico Nacional Siglo XXI, Instituto Mexicano del Seguro Social, Ciudad de México, México*
[d] *Unidad Médica de Alta Especialidad, Departamento de Imagen Cardiovascular, Hospital de Cardiología del Centro Médico Nacional Siglo XXI, Instituto Mexicano del Seguro Social, Ciudad de México, México*
[e] *Unidad Médica de Alta Especialidad, Departamento de Hemodinámica, Hospital de Cardiología del Centro Médico Nacional Siglo XXI, Instituto Mexicano del Seguro Social, Ciudad de México, México*
[f] *Dirección General, Unidad Médica de Alta Especialidad, Hospital de Cardiología del Centro Médico Nacional Siglo XXI, Instituto Mexicano del Seguro Social, Ciudad de México, México*

[*] Autor para correspondencia. Avenida Cuauhtémoc N.º. 330 Colonia Doctores, Delegación Cuauhtémoc, CP 06720, Ciudad de México, México.
Correo electrónico: luis.santosma@imss.gob.mx (L.E. Santos-Martínez).

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Occult gastrointestinal disease unmasked by direct oral anticoagulants used for the prevention of atrial fibrillation

Enfermedad gastrointestinal oculta desenmascarada por anticoagulantes orales directos utilizados para la prevención de la fibrilación atrial

Nowadays, most patients with non-valvular atrial fibrillation (NVAF) patients, receive long-term anticoagulation for prevention of stroke or systemic embolism.[1,2] It is important to consider that many of them are elderly and frail patients who may have an increased risk of bleeding.[3,4] The use of any anticoagulants increase the risk of bleeding, especially gastrointestinal (GI) bleeding.[5,6] Interestingly, direct oral anticoagulants (DOACs) have shown lower risk of major bleeding, compared with traditional vitamin K antagonists (VKA).[7] When a GI bleeding appears in subjects under anticoagulation, our first reaction is to consider it as a complication or an adverse effect of anticoagulants. Herein we report four patients in which a lower GI bleeding under DOACs unmasked intestinal disease leading to proper treatment that ultimately permitted the continuation of DOAC.

We present the clinical characteristics of the four patients (Table 1) (males = 3), under anticoagulation because of NVAF, either paroxysmal ($n = 3$) or chronic, all the patients were older than 70 years, and had not received any previous oral anticoagulation. They presented lower GI bleeding between 1 and 6 months after the start of DOAC treatment, manifested by hematochezia. Only one patient had major bleeding requiring red blood cell transfusion (3 concentrates; 1500 mL). All were submitted to upper GI endoscopy and colonoscopy. One case needed a capsule endoscopy, because diagnosis was not obtained after conventional endoscopies. In two cases a colon malignancy was detected and surgical resection was performed without complications; specimen biopsies confirmed the diagnosis of adenocarcinoma. Patient 1 required a left hemicolectomy for a tumor localized at the splenic angle; he received chemotherapy with FOLFOX (Folinic acid, fluorouracil [5-FU], oxaliplatin) and Vectivix (panitumumab); after a two-year follow-up he is free from cancer. Patient 2 developed unexplained anemia, fecal occult blood test was positive, colonoscopy revealed a sigmoid colon neoplasia and a left hemicolectomy was performed. Pathology revealed a localized invasive adenocarcinoma and no further therapy was needed. In case 3 the diagnosis of jejunum angiodysplasia was established with a capsule endoscopy. The female patient had several tubulovillous adenomas; the smaller were resected in the same procedure and the largest, in a second colonoscopy.

Occult bleeding has been reported since the beginning of anticoagulant use.[8] Clemens et al. first report on the fact that the higher incidence of GI bleeding with the DOACs may also be related to pre-existing malignancies.[9] They reported the incidence of GI bleeding with DOACs, compared with warfarin: dabigatran 110 mg bid 1.42% versus 1.37%, dabigatran 150 mg bid 1.93% versus 1.37%, rivaroxaban 3.52% versus 2.68%, and apixaban 1.93% versus 1.59%. The incidence of GI bleeding cancer related was similar between analyzed DOACs (D110 [0.79%], D150 [0.61%], rivaroxaban [0.83%], and apixaban [0.69%]), interestingly, numerically higher compared with warfarin (0.37%; 0.73%; 0.57%, respectively). Their conclusion that anticoagulant-related GI bleeding may unmask pre-existing malignancies leading to increased detection of GI cancer is similar to what Michaels wrote in 1962: ''The probability of uncovering an occult malignancy in a patient with bleeding manifestations during anticoagulants is small. Since the chances of obtaining a cure

Table 1 Demographic and clinical characteristics of patients with intestinal bleeding associated with direct oral anticoagulants.

Patient	Age (years)	Gender	AF type	Final gastrointestinal diagnosis	DOAC
1	79	M	Paroxysmal	Colon cancer (adenocarcinoma)	Apixaban
2	76	M	Permanent	Colon cancer (adenocarcinoma)	Dabigatran
3	73	M	Paroxysmal	Jejunal angiodysplasia	Apixaban
4	81	F	Paroxysmal	Multiple tubulovillous adenomas	Apixaban

of cancer depend in part upon early diagnosis, it behoves physicians to follow all possible leads''. We want to stress their conclusion with our two cases of adenocarcinoma. Physicians must be aware of the risk of GI bleeding with DOACs use and look for occult GI bleeding intentionally. Taking into consideration the high prevalence of GI bleeding it could be a good practice to test for occult bleeding before and after start of DOAC treatment.

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Luis Colín*, Manlio F. Márquez

Departamento de Electrocardiología, Instituto Nacional de Cardiología ''Ignacio Chávez'', Ciudad de México, Mexico

* Corresponding author at: Departamento de Electrocardiología, Instituto Nacional de Cardiología ''Ignacio Chávez'', Ciudad de México, México Juan Badiano 1, Sección XVI, Tlalpan 14010, Mexico City, Mexico.
E-mail address: luiscolin@yahoo.com.mx (L. Colín).

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Miocardiopatía de Takotsubo: cuando las coronarias callan

Takotsubo myocardiopathy: When coronary arteries are silent

Caso clínico

Mujer de 65 años con antecedentes de hipertensión arterial y dislipidemia de 15 años de evolución en manejo farmacológico, exfumadora hace 2 años de 20 paquetes/año, quien hace 2 días experimentó un evento familiar que le ocasionó gran estrés emocional. Ingresó al servicio de urgencias por cuadro de dolor precordial opresivo intenso, con irradiación a espalda, de una hora de evolución y diaforesis. El examen físico no demostró hallazgos relevantes, mientras que el electrocardiograma (ECG) evidenció elevación del segmento ST en cara inferior y lateral alta (fig. 1).

La troponina I resultó elevada (2.86 ng/ml) y dadas las características del dolor se sugirió la posibilidad de un síndrome aórtico agudo, motivo por el cual se realizó una angiotomografía computarizada toracoabdominal cuyo resultado fue normal. Con la impresión diagnóstica de un infarto agudo de miocardio (IAM), la paciente fue llevada a coronariografía, donde se observaron coronarias sanas, sin lesiones ateromatosas obstructivas (figs. 2A y B). La ventriculografía demostró acinesia en los segmentos inferolateral basal y apical (figs. 2C y D), con una fracción de eyección del ventrículo izquierdo (FEVI%) estimada en el 35%. Una ecocardiografía realizada al ingreso confirmó los hallazgos de la ventriculografía y no reveló enfermedad valvular asociada.

Estos hallazgos fueron compatibles con una cardiomiopatía de Takotsubo. La paciente estuvo estable hemodinamicamente durante su estancia hospitalaria y se dio de alta con inhibidor de la enzima convertidora de angiotensina (IECA) y beta-bloqueador. Una nueva ecocardiografía realizada al mes del evento demostró mejoría de