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CLINICAL REPORT

Acute coronary syndrome as the first manifestation of essential thrombocythaemia: A challenge for cardiologists☆

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Abstract We present the case is presented of an acute coronary syndrome in a 30-year-old patient with essential thrombocythaemia. Acute coronary syndromes occur in 9% of cases in these patients, and their management constitutes a challenge for the cardiologist, specifically in terms of choosing the most appropriate antiplatelet therapy and its duration, taking into account that these patients have a high thrombotic risk, as well as a considerable haemorrhagic risk.

PALABRAS CLAVE
Síndrome coronario agudo;
Tratamiento antiagregante;

Síndrome coronario agudo como primera manifestación de trombocitemia esencial: un reto para los cardiólogos

Resumen Presentamos el caso de un síndrome coronario agudo en un paciente de 30 años con trombocitemia esencial. Los síndromes coronarios agudos ocurren en el 9% de los casos en estos

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Trombocitemia esencial

pacientes, y su manejo constituye todo un reto para el cardiólogo, en concreto, en cuanto a la elección del tratamiento antiagregante más adecuado y su duración, considerando que estos pacientes tienen por una parte un elevado riesgo trombótico y, además, un riesgo hemorrágico no despreciable.

A 37 year-old male, smoker of 30 cigarettes per day. He consulted due to resting thoracic pain that had evolved over 1 h. An electrocardiogram showed raised ST in the lower face. Echocardiogram showed no alterations in segment contractility with conserved left ventricle ejection fraction. Cardiac catheterisation was performed, showing a severe thrombotic lesion at the level of the distal right coronary artery, implanting 2 metal stents. In the analytical results thrombocytosis stood out, with a platelet count of 905,000/mm^3. Blood smear findings, together with the presence of a mutation in gene JAK2 V617F, confirmed the diagnosis of essential thrombocythaemia (ET). Subsequent clinical evolution was favourable, and the patient was discharged with dual antiaggregant treatment with acetylsalicylic acid (ASA) and prasugrel (which was maintained for one year), beta-blockers and statins, as well as hydroxyurea, with which the platelet count fell to 600,000/mm^3 at 3 months and normalised at 6 months. After 5 years the patient has not suffered any further thrombotic complications and has maintained normal platelet counts.

ET is a chronic clonal myeloproliferative neoplasm, characterised by persistent thrombocytosis and megakaryocytic hyperplasia. It is a rare disorder, with an incidence of 1–2.5 cases per 100,000 individuals/year. The majority of cases are diagnosed between the ages of 50–60 years old, without any difference according to sex, and there is a second peak of incidence at 30 years old, with a 2:1 predominance in this case of women.

The 2016 World Health Organisation diagnostic criteria for ET include a platelet count higher than 450,000/mm^3, megakaryocytic proliferation, having ruled out other myeloproliferative disorders and having proven that the JAK2 mutation or another clonal marker is present, without evidence for reactive thrombocytosis.[1]

In approximately half of cases the patients are asymptomatic at the moment of diagnosis. Patients with ET are at high risk of arterial as well as venous thrombosis, of which the former is more frequent. They are also at higher risk of haemorrhage, especially those with very high platelet counts, above 1,000,000/mm^3. Bleeding does not occur in these patients due to platelet dysfunction, as it is associated with the appearance of an alteration in the von Willebrand factor (vWF), which is characterised by the loss of large vWF multimers.[2]

The vasomotor symptoms of this disease due to involvement of the microcirculation include Raynaud's phenomenon, erythromelalgia, visual and auditory disorders, cephalalgia and nausea, among others. The thrombotic events include ictus, coronary ischaemia, arterial and retinal venous blockages, pulmonary embolism, hepatic or portal thrombosis, deep vein thrombosis and digital ischaemia. Acute coronary syndromes occur in 9% of patients, with multiple pathogenic mechanisms such as coronary thrombosis, vasospasm and atherosclerosis.

Manifestations involving haemorrhage are generally slight (epistaxis, gingivorrhagia), while intramuscular or gastrointestinal bleeding is not common.

The factors which are associated with a high risk of arterial thrombosis in ET include age greater than 60 years old, a previous history of thrombosis, the existence of cardiovascular risk factors or the presence of JAK2 mutation.[3] Nevertheless, and paradoxically, platelet number does not seem to be a good predictor of thromboembolic events in these patients.

The JAK2 mutation is present in 50%–60% of cases of ET. It must be pointed out that this mutation has also been described in the general population and in patients with acute coronary syndrome (ACS) and peripheral arteriopathy, although at a low level of prevalence. Muendlein et al. found that the presence of this mutation in coronary patients does not lead to an increased risk of atherothrombotic complications in comparison with patients without the mutation.[4] However, it has been hypothesised that this mutation is associated with stent thrombosis,[5] so that further research is necessary in this area.

It is important to distinguish ET from cases of reactive thrombocytosis, given that clinical management is different. The latter is caused by high levels of erythropoietin and other cytokines such as interleukin-6. The most frequent causes of reactive thrombocytosis include surgery, infections, neoplasms and postsplenectomy, and one case has been described in patients with myocardial infarct.[6] The rate of thromboembolic events is higher in ET than it is in reactive thrombocytosis.

Although the association between the degree of thrombocytosis and thrombotic events has not been proven, interventions that reduce the number of platelets also reduce the incidence of thrombosis.

Hydroxyurea is the treatment of choice for high risk patients (with a history of thrombosis, haemorrhagic complications, platelet counts higher than 1,000,000/mm^3, or aged above 60 years old), as it is effective in preventing thrombotic complications. Nevertheless, the potential leukemogenic effect of this drug over the long term must be taken into account. Interferon-α and busulfan are available as second-line drugs.

Clinical guides do not stipulate how to manage ACS in patients with ET. As we pointed out above, in this entity there is a risk of thrombotic as well as haemorrhagic events, so that the antithrombotic treatment of these patients is a challenge. On the one hand, and due to an alteration in platelet function, these patients may not respond suitably to antiaggregant treatment. On the other hand, platelet antiaggregants may increase the risk of haemorrhagic complications, as these patients often have acquired von Willebrand syndrome. In general, patients with ET have a 3.4% thromboembolic risk, although this rises to 31.4% if they have already had a thrombotic event.

It is therefore still unclear which antiaggregant treatment is the most appropriate, as well as the optimum duration of the same in patients with ET who suffer an ACS. In our opinion, in these patients decision-making in general should be based on the fact that thrombotic events occur more frequently than haemorrhages, although special care should be taken in patients with very high platelet counts who have an increased risk of haemorrhage. Antiaggregant treatment with powerful antiaggregants such as prasugrel or ticagrelor should therefore last for less than one year. The recent commercialisation of a 60 mg dose of ticagrelor may be a therapeutic option for the longer term in this group of patients. In patients with very high numbers of platelets, early commencement with cytoreductive treatment to reduce the number of platelets may help to minimise the risk of haemorrhage due to antiaggregant therapy.

Respecting stent type, metal stents were implanted in our patient, as at the time the duration of dual antiaggregation required was less than in the case of pharmacoactive stents if complications with haemorrhaging had arisen. This has changed in the most recent guides on dual platelet antiaggregant treatment in coronary disease,[7] in which the decision on the duration of dual antiaggregation has to be dynamic and based on the clinical symptoms more than the type of stent implanted.

Likewise, it should be underlined that as there are differences between individuals in terms of platelet function in patients with ET, antiaggregant treatment is not equally effective in all patients. It may therefore be useful to evaluate platelet reactivity using P2Y12 reaction units to detect which antiaggregant is the most suitable, together with the dose that should be used.[8]

Another aspect to be taken into account is that low molecular weight heparin-induced thrombocytopenia may go undetected, given the high number of platelets in these patients.[9]

To conclude we are able to state that infrequent aetiologies must always be considered when faced with an ACS in young patients, including ET.

Conflict of interests

The authors have no conflict of interests to declare.

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