Torsades de pointes secondary to intravenous haloperidol after coronary bypass grafting surgery

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Purpose: Postoperative delirium occurs in about 2% of patients undergoing major cardiac surgery including coronary artery bypass grafting surgery (CABG). Haloperidol (Sabex, Boucherville, Canada) is a drug commonly used in the intensive care unit for the treatment of delirium and is usually considered safe even at high doses and is rarely implicated in the development of malignant ventricular arrhythmias such as torsades de pointes. The purpose of this study is to report such a complication of use of haloperidol after myocardial revascularization.

Clinical features: The patient reported underwent uneventful triple bypass surgery. Administration of large intravenous doses of haloperidol was necessary for control of psychomotor agitation due to delirium. Torsades de pointes occurred in the absence of QT prolongation on the third postoperative day following use of the drug with no other obvious etiological factor.

Conclusion: Awareness of this rare complication is key to judicious use of this drug in the post CABG patient in whom such an arrhythmia may have very deleterious consequences because of the underlying cardiac condition.

Objectif : Le délire postopératoire survient chez environ 2 % des patients qui subissent une intervention cardiaque importante, y compris le pontage aortocoronarien. L'halopéridol (Sabex, Boucherville, Canada) sert habituellement à traiter le délire à l'unité des soins intensifs et est généralement sécuritaire même à de fortes doses. Il est rarement impliqué dans le développement d'arythmies ventriculaires malignes comme les torsades de pointes. L'objectif de la présente étude est de faire état d'une telle complication liée à l'usage d'halopéridol après une revascularisation myocardique.

Éléments cliniques : Le patient en question a subi sans problème un triple pontage coronarien. L'administration d'importantes doses intraveineuses d'halopéridol a été rendue nécessaire pour contrôler l'agitation psychomotrice causée par le délire. Les torsades de pointes sont survenues en l'absence de prolongation QT le troisième jour postopératoire après avoir utilisé le médicament. Il n'y avait pas d'évidence d'autre facteur étiologique.

Conclusion : Quand on utilise l'halopéridol, il faut savoir que l'arythmie ventriculaire est une complication rare qui peut se présenter chez un patient qui a subi un pontage aortocoronarien et qu'elle pourrait avoir des conséquences graves, étant donné l'état cardiaque sous-jacent.

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THE purpose of this study is to report torsades de pointes arrhythmia following the use of haloperidol after myocardial revascularization. Since postoperative delirium is a frequent complication of major cardiac surgery which often necessitates pharmacological control of psychomotor agitation, the diagnosis, management and prevention of this complication is discussed.

A 64-yr-old woman underwent triple coronary artery bypass grafting surgery for class 2 angina for a three vessel disease with moderate left ventricular dysfunction. She had a history of tobacco smoking, obesity and hypertension treated with nifedipine and enalapril. The immediate postoperative period was uneventful with no evidence of myocardial infarction, arrhythmia, heart failure or stroke. The first postoperative electrocardiogram (ECG) 30 min after surgery was normal including a Q-T interval of 372ms (QTc of 418msec). Weaning from mechanical ventilation was delayed until the third postoperative day because of hypoxemia from shunting secondary to atelectasis. Concurrently, she began presenting symptoms of delirium with aggressive and paranoid behaviour. The trachea was extubated and blood gas analyses thereafter were normal. Intravenous haloperidol was administered to control psychomotor agitation that hindered chest physiotherapy. A total of 175 mg was used over 14 hr. After a few premature ventricular complexes, a long-short sequence was followed by an R on T phenomenon (Figure 1), a 29 beat sequence of wide complex ventricular tachycardia with polymorphous configuration of torsades de pointes developed (Figure 2). She converted back to sinus rhythm spontaneously, haloperidol was discontinued and 2 g of magnesium sulfate were administered intravenously. At that time, the ECG was unchanged compared with the first postoperative ECG. The QT interval was 356msec (QTc 413msec). Calcium and potassium concentrations were within the normal range. Plasma magnesium concentrations, obtained during and shortly after surgery, were normal. Concurrent medication included: sucralfate, furosemide, lorazepam, enalapril, nifedipine, metoclopramide and salbutamol. There was no recurrence of ventricular complexes or arrhythmias following cessation of haloperidol. She subsequently recovered uneventfully and was discharged on the 10th postoperative day.

FIGURE 1 Rhythm strip showing premature ventricular contractions (stars) and R on T phenomenon (arrows) occurring prior to the torsades de pointes episode.

FIGURE 2 Wide complex ventricular tachycardia with torsades de pointes configuration. The arrow indicates an R on T phenomenon and a variable T wave morphology. The long interval (LI) and short interval (SI) sequence precedes the next torsades de pointes.

Discussion

The arrhythmia observed in this patient had the typical aspect of torsades de pointes: the ventricular rate was irregular at about 250 bpm with a wide QRS complex of varying rate that twisted around the isoelectric line with alternating electrical polarity (beginning of Figure 2). The torsades de pointes sequence was preceded by a pause then followed by a premature beat occurring on the T wave of the previous beat ® on T phenomenon). This was referred to as the pause-dependent "long-short" initating sequence.

Antipsychotic drugs are usually considered to be safe and are frequently used in the intensive care unit (ICU) for the treatment of delirium. Haloperidol a butyrophenone, is the most commonly used antipsychotic in the ICU. Apart from mild hypotension through an alpha-blocking action and the neuroleptic malignant syndrome, butyrophenone does not cause any hemodynamic alterations.[1] However, there have been reports of major cardiac arrhythmias in patients receiving psychotropic; drugs and some authors have suggested that the use of haloperidol was directly related to the genesis of torsades de pointes.[2–10] Initially described during haloperidol overdoses,[2] torsades de pointes appeared following conventional doses of haloperidol .[3,4] Wilt *et al.* observed this type of arrhythmia in four women who received large doses of intravenous haloperidol.[5] In Kay's series of 32 patients and Di Salva's, torsades de pointes occurred mostly in patients with underlying heart disease,[6,7] most frequently ischemic heart disease, in 53% of patients in some series[6] but it is also described in patients with liver diseases[8,9] and in critically ill patients.[10] It has also been described with doses as small as 4 mg.[11] In more than 90% of patients, the initiating

event is a premature ventricular beat occurring following an R on T phenomenon as observed in this report. Most patients also show a long-short cycle length sequence, as in Figure 2. Appearance of a labile T wave following a post-extrasystolic pause configuration is a warning sign preceding torsades de pointes, and was present in this patient (Figures 1,2). The Q-T interval (356 msec) during the arrhythmia, is not considered to be prolonged[1,2] and was unchanged from the first postoperative days. A new and significant flattening of the T wave was present the day prior to the arrhythmia compared with the first postoperative ECG. These abnormalities of the Q-T interval and T wave illustrate the pathophysiology of torsades de pointes which is due to abnormal and prolonged ventricular repolarization.[1,3] Animal models have shown a concentration dependency prolongation of the QT interval with the use of antipsychotics.[1,4] Droperidol which is a butyrophenone can also prolong the QT interval but so far has not been associated with the development of torsades de pointes.[1,5]

Torsades de pointes arrhythmias are classified as pause-dependent and adrenergic-dependent types.[1,3] The former, related to drugs and electrolyte abnormalities that prolong the Q-T interval, is best treated by removing the cause and by agents or maneuvers, such as pacing, isoproterenol or magnesium, that increase conduction velocity and shorten the Q-T interval. The latter type, of familial origin, is best treated with beta-adrenergic blocking agents or left stellate ganglion block. In the present case, the torsades de pointes observed was of the pause-dependent type. The large dose of haloperidol administered was the most likely cause of torsades de pointes in the case presented in this report since there was no recurrence of rhythm disturbances after haloperidol withdrawal. Hypomagnesemia could not be completely ruled out as the cause of this life-threatening tachyarrythmia. However, plasma magnesium concentrations were normal 72 hr earlier and there were no recurrences despite administration of a suboptimal dose of magnesium for replenishment of stores. Considering that magnesium deficiency is usually treated with doses of 5 g per day for three to five days. Moreover, if magnesium deficiency were the primary cause of torsades in this case, we would have expected an associated hypokalemia, progressive Q-T prolongation or recurrence following the initial therapy. In the absence of hypokalemia, there is some controversy as whether hypomagnesemia is arrythmogenic. Finally, most cases of magnesium deficiency-related torsades de pointes occur in chronically malnourished patients and are not reversed by the sole administration of 2 g of magnesium sulfate. The combination of ischemic heart disease, electrolyte abnormality and haloperidol operating simultaneously cannot be excluded in the pathogenesis of this arrhythmia. However, the time-sequence and the high cumulative amount of haloperidol administered and development of torsades de pointes argues for a link of causality.

In summary, delirium after CABG surgery requiring treatment with antipsychotic drugs is frequent. The administration of haloperidol in large amounts in this setting mandates use of caution because of the risk of inducing torsades de pointes in patients susceptible to myocardial electrical instability. This type of drug related complication can occur without the warning sign of a prolonged QT interval and should be promptly recognized and treated since the consequences of such an arrhythmia may be extremely deleterious in patients with an already compromised myocardial function and reserve.

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