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## LETTERS TO THE EDITOR

### HYPOGLYCAEMIA ASSOCIATED WITH CLOMETHIAZOLE INTOXICATION

Dear Editor,

Acute intoxications are a frequent cause for consultation at emergency departments, and medications, ethyl alcohol and other abused substances are the products most frequently involved<sup>1</sup>. Among medication intoxications, psychotropic drugs are among the most common, including clomethiazole. This is drug with hypnotic, anxiolytic and sedative properties, commonly used in chronic alcoholics<sup>2,3</sup> and widely prescribed in Spain<sup>4</sup>. The most frequent side effect of clomethiazole use is nasal congestion and, to a lesser extent, conjunctive irritation and gastrointestinal problems. In some patients it has exceptionally produced anaphylactic reaction, paradoxical excitement or mental confusion. In the event of overdose, the most significant toxic effects are coma, respiratory depression, low blood pressure and hypothermia.

Having observed a patient with hypoglycaemia associated with clomethiazole intoxication and not having found this association previously described, we have considered a report on the case to be of interest.

Woman aged 29 was referred to A&E due to ingestion of 12-15 capsules of 192 mg clomethiazole following a family argument. No concomitant ingestion of alcohol or other medication. Diagnosed with borderline personality disorder, she had had alcohol dependence currently in full remission and was receiving treatment with several psychotropic medications, including clomethiazole. She was not diabetic nor had access in the home to insulin or oral anti-diabetic medication. The outpatient emergency unit that brought her to the hospital detected asymptomatic hypoglycaemia (59 mg/dL). Upon arrival at the A&E she was conscious but drowsy. Blood pressure was 102/53 mmHg, heartbeat at 92 beats/min, respiratory frequency at 16 breaths/min, body temperature of 36.5°C, 95% oxygen saturation by pulsioxymetry and in basal conditions and a new capillary glycaemia of 55 mg/dL. Physical exploration was normal, except for the aforementioned drowsiness. Continuous intravenous perfusion of dextrose 10% solution was begun immediately, to which perfusion of plasma expanders was subsequently added due to low blood pressure (80/50 mmHg). New glycaemia readings were obtained after 1 hour (106 mg/dL) and 4 hours (142 mg/dL, following 25 g. glucose perfusion), after

which glucose administration was stopped. Two hours later the blood glucose was 129 mg/dL. The haemogram, hepatic and renal profiles, the acid alkaline balance and the ECG were normal. Following the complete normalization and stabilisation of blood pressure and level of consciousness, a psychiatric assessment was carried out, after which the patient was discharged.

A bibliographic search on Pubmed performed in September 2007 using "chlormethiazole" and "hypoglycaemia" as key words did not yield any documentation related to intoxication, overdose or clomethiazole therapy with hypoglycaemia. The same result was obtained from the Spanish Medical Index with the terms "clometiazol" and "hipoglucemia".

The hypoglycaemias most frequently treated in the A&E are those of diabetic patients that are on insulin therapy or oral anti-diabetic medication. Other possible causes for hypoglycaemia include insulinomas, mesenchymatous tumours, terminal or extreme malnourishment stages, endocrine deficiencies, alcohol consumption, severe hepatocellular failure and postprandial reactive hypoglycaemia disorders. Excessive adrenalin secretion can lead to sudden onset hypoglycaemias. None of these circumstances seemed to manifest in the case herein described. Furthermore, normal blood glucose counts had been recorded (121 and 146 mg/dL) on two previous occasions that she had presented at the A&E for other reasons.

The cause for this hypoglycaemia induced by clomethiazole cannot be established with certainty. The literature mentions the inhibitory effect on adenylyl cyclase of some psychotropic drugs such as haloperidol, bromperidol, chlorprothixene and lithium<sup>5</sup>. This inhibition reduces the cyclic AMP acting as a second messenger in reactions mediated by counter-regulating hormones such as glucagon, cortisol or catecholamines, that reduces the hyperglycaemic capacity of such hormones. If clomethiazole acted in a similar manner, it could be explained by this action mechanism. Another possible explanation could be associated with the inhibitory effect of clomethiazole on ATP fragmentation, reducing metabolism in the hippocampus and its response to hypoglycaemia<sup>6</sup>.

In light of the above, we recommend that blood glucose concentrations in all patients with clomethiazole overdoses or intoxications be monitored for several hours.

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**Minerva MAS-HEREDIA,  
Mireia DALMASES-CLERIES,  
Santiago NOGUÉ-XARAU,  
Òscar MIRÓ**

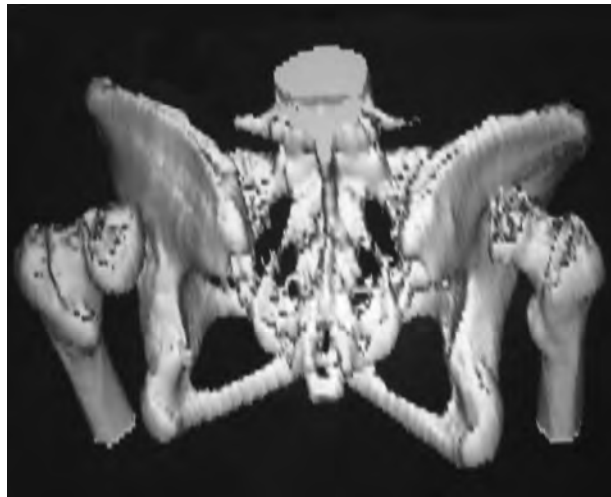
*Emergency Dept. Hospital Clínic. Barcelona, Spain.*

## CONGENITAL BILATERAL HIP DISLOCATION IN ADULTS

### Dear Editor,

Congenital hip dislocation occurs in 3.5% of newborns with a higher prevalence among female Caucasians (80%) and a certain hereditary component. The dislocation may be unilateral or bilateral, with breech birth considered to be a predisposing factor. Newborns must be subjected to a meticulous hip exploration, especially if the newborn is female, has a relevant family history or was a breech birth. Ortolani and Barlow screening manoeuvres for infants attempt to show the projection of the dislocated hip<sup>1,2</sup>.

We present the case of a 26-year-old patient of South American origin with no relevant clinical history, presenting at the A&E with a limp and exacerbation of chronic lower back pain. She presented with a Trendelenburg gait, limp in left limb, and no limp in monopodal support or hopping. Lumbar spinal palpation was not painful, although an increase in right paravertebral muscle tone was observed, no limb dysmetry, hip flexion was 90°



**Figure 1.** Reconstruction of 3D CT scan: bilateral hip dislocation.

and normal abduction. The muscular balance of the lower limbs was 4/5 and no neurological alterations were observed (preserved sensitivity, negative Lassègue and Bragard, osteotendinous reflexes present and symmetrical).

A pelvis and lumbar spine radiography was performed, followed by a 3D CT scan in the rehabilitation rooms (Figure 1), achieving a diagnosis of congenital bilateral hip dislocation. She was treated with non-steroidal anti-inflammatories (NSAIDs), myorelaxants and a cane to relieve the weight on the left limb, in addition to strengthening and flexing lumbar spine exercises.

Gait alterations<sup>3</sup>, vertebral alignment<sup>4</sup> and onset of early osteoarthritis are the most frequent complications found in patients with congenital unilateral or bilateral hip dislocation. The most relevant characteristics of this case include the presence of non-traumatic bilateral hip dislocation in an adult, the absence of any previous symptoms and the low number of cases in the medical literature.

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**Ignacio GÓMEZ OCHOA<sup>1</sup>,  
Pilar LÓPEZ LAHOZ<sup>2</sup>,  
José Manuel ESQUIVEL NESTAL<sup>3</sup>,  
Ana BUENAFÉ RAMOS<sup>3</sup>**

<sup>1</sup>Rehabilitation Service. Hospital Clínico Universitario Lozano Blesa. Zaragoza, Spain.

<sup>2</sup>Emergency Service 061 Aragón, Spain.

<sup>3</sup>Rehabilitation Service.

Complejo Hospitalario La Mancha Centro. Alcázar de San Juan. Ciudad Real, Spain.

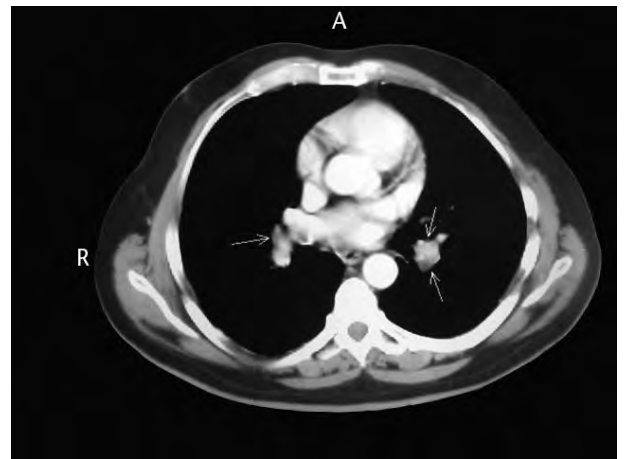
## SYNCOPE AS MODE OF PRESENTATION OF PULMONARY THROMBOEMBOLISM

Dear Editor,

Pulmonary thromboembolism (PTE) often presents with non-specific symptoms that hinder diagnosis and early treatment. The annual incidence of lung embolism is 1 to 2 cases per 1000 people and is the cause of 5-6% of hospital deaths<sup>2</sup>. Recurrence of properly treated thromboembolic disease ranges from 5 to 10% per annum. As is the case with the first episode, recurrent pathogenesis is multifactorial and risk depends on the severity and number of hereditary and acquired factors. Here we present a case of syncope as a mode of presentation of PTE.

Male patient aged 57 years with a history of diabetes mellitus, dyslipemia, high blood pressure and ischaemic cardiomyopathy presenting at the A&E for a sudden loss of consciousness with a fall to the ground and head trauma. The patient reported having had effort dyspnoea over several weeks with no other symptoms. Basic examination showed an incised-contused wound on the left suprascapular region. The patient was eupneic at rest with no neurological focality being observed. Haemogram and biochemistry did not show alterations; D-Dimer was 1,094 ng/ml and arterial gasometry yielded pH 7.5, pO<sub>2</sub> 61 and pCO<sub>2</sub> 36. The electrocardiogram showed a sinus rhythm with no alterations and chest radiography was normal. In thoracic CT scan (Figure 1) repletion defects in peripheral regions of both pulmonary arteries and in the descending branch of the left pulmonary artery indicative of pulmonary thromboembolism were observed. Anticoagulant therapy was commenced with a favourable evolution.

Syncope is not a frequent mode of presentation for PTE. It has been described as the initial



**Figure 1.** Chest CT scan. Repletion defects in peripheral regions of both main pulmonary arteries and in the descending branch of the left pulmonary artery related to a pulmonary embolism. Anticoagulant treatment was begun with a favourable outcome.

presentation in 13-30% of cases. It is usually associated with a massive lung embolism<sup>3</sup>.

An occlusion of the pulmonary vascular area above 50% produces failure of the right ventricle, reduced filling pressure of the left ventricle with decreased cardiac output, hypotension, reduction in cerebral blood flow and syncope. Another mechanism associated with PTE involves the onset of arrhythmia associated with right ventricular overload. In the third mechanism, the embolus can trigger a vaso-vagal reflex leading to a neurogenic syncope.

PTEs that begin with a syncope are often massive and accompanied by acute cor pulmonale and hypotension.

Patients who begin with syncope have no increased risk of death and/or recurrence<sup>4</sup>. Treatment and duration of normally accepted secondary prophylaxis are not associated with a worse prognosis in patients whose PTE commences with syncope.

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**José Javier QUEROL GUTIÉRREZ<sup>1</sup>,  
Leopoldo DOMÍNGUEZ PÉREZ<sup>2</sup>,  
Juan Carlos QUEROL GUTIÉRREZ<sup>1</sup>,  
Noelia VÁZQUEZ FUENTES<sup>1</sup>,  
María del Mar SERRA ZAMORA<sup>1</sup>**  
<sup>1</sup>*Emergency Dept.* <sup>2</sup>*Pneumology Dept.*  
*Hospital Ingesa de Ceuta, Spain.*

## UPPER AIRWAY OBSTRUCTION OF INFECTIOUS ORIGIN IN ADULTS

### Dear Editor,

Acute laryngotracheitis, stridor or laryngeal croup is a frequent cause of obstruction of the upper airways in children, accounting for 15-20% of upper respiratory infections with a greater or lesser clinical involvement. The aetiology thereof is viral infection, whereas bacterial infections are fairly infrequent<sup>1</sup>. In adults it is rare, but may be the cause of severe respiratory failure<sup>2</sup>. Here we present two cases of upper airway obstruction of infectious origin requiring artificial ventilation support.

The first case refers to a 45-year-old male with a background of pulmonary tuberculosis diagnosed two months previously for which he was being treated with antituberculostatics and no known allergies to medication. He presented at the A&E with laryngeal stridor and dyspnoea with dysphonia over the course of 2 hours. The previous night he reported cough and odinophagia, and one hour before the onset of the current symptoms he had taken paracetamol. The exploration showed tachypnea, ventilatory effort with laryngeal stridor and respiratory silence on pulmonary auscultation. Complementary tests showed respiratory failure with hypercapnia and acidosis that did not improve after a first administration of bronchodilators, high dosage corticoids and adrenalin. Chest radiography was normal. An emergency bronchoscopy showed purulent laryngotracheobronchitis with significant oedema in the vocal cords, larynx and subglottic apparatus. The epiglottis was conserved. Orotracheal intubation and mechanical ventilation were performed and amoxicillin clavulanate, bronchodilators, corticoids and adrenalin were administered. Samples taken for conventional cultures as well as for *Mycobacterium tuberculosis* were negative. The patient evolved well, was extubated after 4 days and had good subsequent functional recovery.

The second case involved a male 46-year-old smoker, who presented sudden dyspnoea over 2 hours as part of a viral respiratory infection of the upper airways over pre-

vious days, for which he was being treated with dextromethorphan and ibuprofen. Upon arrival at the A&E he presented laryngeal stridor, shawl sign cervical oedema and uvula oedema with oropharyngeal obstruction, tachypnea and ventilatory stress. Analysis showed acute respiratory failure with hypercapnia and acidosis. Following an initial treatment with corticoids, bronchodilators and adrenalin, the poor evolution of the patient required an emergency tracheostomy given the impossibility of orotracheal intubation. Surgical exploration showed oedematous epiglottitis. The patient was referred to the ICU for ventilatory support with a diagnosis of acute epiglottitis. Respiratory secretion cultures, including *Haemophilus influenza* yielded negative results. The patient evolved favourably and is currently asymptomatic.

Acute obstruction of the upper airways of an infectious origin is frequent at a paediatric age. In fact, acute epiglottitis due to type B *H. influenza* has been reduced by 95% thanks to systematic vaccination since infancy<sup>3</sup>. There are fewer data available for adults, although it is a high cause of mortality. The percentage of infectious causes ranges from 45-61% of positive pharyngeal cultures, mainly *H. influenza* – which causes between 12-26% of bacteriaemias, – pneumococci, staphylococci, streptococci and *Candida albicans*. The role of viruses has not been established, although some herpes cases<sup>4,5</sup> have been described. Most patients present odinophagia, pharyngeal secretion and dyspnoea as initial symptoms. Paradoxically, fewer than 50% present classic stridor. Forty-four percent of patients present normal oropharyngeal exploration, with diagnosis often requiring direct laryngoscopy<sup>2,5</sup>. Simple radiography of side of the neck often shows luminal narrowing with tumefaction of soft tissue or an emphysematous epiglottitis. However, the radiography may also be normal<sup>4</sup>. Clinical management of upper airway obstruction of any aetiology includes ensuring the airway with intubation or even tracheostomy if required, adrenalin nebulisations and corticoidal anti-inflammatories. Steroids are used for their anti-inflammatory effects, although there is no clear evidence as to their efficacy<sup>4</sup>. Antibiotics are to be administered if bacterial origin is suspected<sup>2,6</sup>.

The cases presented herein began with stridor and both presented an underlying infection of an apparently viral origin, in light of negative bacterial cultures including *H. influenza*. Both required invasive mechanical ventilation, despite administration of all aforementioned treatments. In the first case the epiglottis was conserved and was diagnosed as subglottitis, and the second was deemed to be a bacterial epiglottitis. Both evolved favourably and normal life was resumed within one month.

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**Pablo Javier MARCHENA YGLESIAS,  
Ignasi GARCÍA GONZÁLEZ**

*Emergency Dept. -Internal Medicine. Hospital General de L'Hospitalet. L'Hospitalet de Llobregat. Barcelona, Spain.*

## PRIMARY CARE HOSPITAL REFERRAL

### Dear Editor,

In light of the review carried out by Márquez Cabeza et al.<sup>1</sup> on the differences between causes for consultation among patients presenting at the A&E by referral or on own initiative, we believe our experience in terms of Primacy Care (PC) referral patients may be of interest.

The last 20 years have shown a gradual increase in emergency care demand, both in-hospital and outpatient<sup>2</sup>. A&E departments are the vertex of the emergency medical attention pyramid, where patients receiving care from the many points of healthcare network and those presenting on their own initiatives all converge<sup>3</sup>. The amount of PC-referred visits proves that there are certain pathologies that cannot be treated in an outpatient mode<sup>4</sup>.

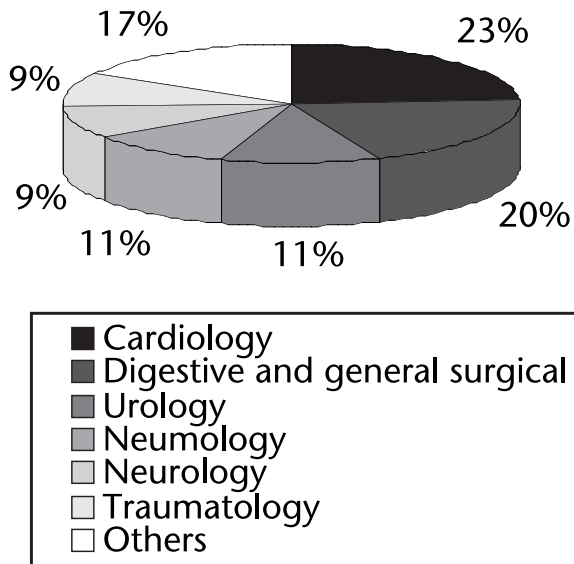
In an attempt to analyse the reasons for consultation of PC-referred patients, we studied the visits over a 2-week period during the winter of 2007. Our A&E department attended 2,284 patients. Saturdays and Sundays were excluded from the study in order to avoid possible biases of weekend dynamics at the A&E, as well as paediatric, gynaecological and ophthalmologic causes. PC-referred pathologies accounted for 5.9% (135/2284). The mean age of the referred patients was 46.5 years, and 51% were male with 94% of patients being from Primary Care Centres (PCC) in our catchment area; 70.37% of the

cases were referred from outpatient A&E centres. The days on which the highest number of PC referrals took place were Mondays and Tuesdays (22.2% and 28.1% respectively). In terms of specialty, the most frequent causes for consultation were cardiologic (23.7%), digestive and general surgical intervention (19.3%) and urology (11.1%) (Figure 1). According to the Spanish Triage System (Andorran Triage Model in Catalonia), which includes 5 levels of useful, valid and reproducible prioritization<sup>5</sup>, 46.7% of patients were classified as third level prioritization. 36% of visits were performed at emergency level 1. No complementary exploration was performed and no specific treatment was prescribed for 20% of patients; most of these referrals were made by outpatient emergency centres. A total of 69.9% was sent home with GP control and 23.7% was admitted to different hospital departments. Appropriateness of referral was assessed according to whether PCC belonged to the catchment area of our hospital and whether the pathology qualified for emergency attention in terms of complementary explorations and specific treatment<sup>6</sup>. According to these criteria, 65% of PC-referred visits were appropriate.

The number of PC-referred visits attended at A&E departments is minimal, thereby demonstrating the good response capacity of PCs to the gradual increase in emergency medical care at all levels of the healthcare system<sup>7</sup>. In most cases, necessary complementary explorations or specific treatments require hospital care. Requests for diagnostic tests are unavoidably influenced by clinical practice style which, in A&E departments - where there is often a preference for parallel testing - can lead to over assessment of the appropriateness of referrals<sup>8</sup>. Approximately one quarter of referred patients are admitted, either via conventional hospital admission or by any of healthcare alternatives (home hospitalisation, short stay emergency admission). In general, we are able to conclude that, in accordance with the study of Márquez et al., PC is indeed a good emergency filter<sup>9</sup>, and referred patients are those truly requiring hospital care.

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**Figure 1.** Motivos de consulta por aparatos.

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**Cristina CABEZA CAIXELÓS,**  
**Cristina CAPDEVILA AGUILERA,**  
**Leonor CUADRA LLOPART,**  
**Dolores SERRA ARTIGAS**  
*Emergency Department. Hospital Mútua  
de Terrassa, Barcelona, Spain.*

## CHEST INJURY BY FIRE ARM

**Dear Editor,**

Injuries caused by fire arms are defined as contuse lesions caused by the physical and chemical actions of the gunshot bullet or projectile and concurrent elements, plus neofor-med effects from the gunshot.

In recent years, the incidence of this type of injury has increased all over the world due to many factors (exhibition of violence in the media, easy access to fire arms, proliferation of hunting sports and warfare videogames)<sup>1,2</sup>. Of all body areas, the chest is one of the most affected by violent trauma. Nevertheless, in terms of aetiopathogenesis, cold steel wounds are the most frequent cause of open chest wounds with a much higher incidence than gunshot wounds<sup>3-6</sup>.

Mortality from chest trauma is variable<sup>7</sup>, ranking at 13.4% in penetrating trauma, although in some series this is higher and depends on the severity of the affected structures and type of bullet. Pulmonary contusion in penetrating injuries is the result of high-velocity bullets that enter a few centimetres away from the lung<sup>5,8</sup>.

Extraction of the bullet is controversial<sup>9</sup>, as in many cases extraction is associated with more significant complications beyond the mere location of the bullet. According to Watt<sup>10</sup>, there are two indications for missile extraction: "symptomatic" missile, that is, intra-joint location, causing sepsis or abscess, migration, embolism or lead intoxication; and extraction during surgical exploration.

We present the case of a 30-year-old male with a gunshot injury (pistol) entering the outer side of the left shoulder producing a humeral diaphysary fracture and lodging in the thoracic cavity, adjacent to the posterior arc of the eighth left rib (Figure 1), causing a small apical pneumothorax and pulmonary contusion focus with areas of subcutaneous emphysema. The bone fracture observed on the humerus (Figure 2) exhibited typical characteristics of a pistol bullet: drill-hole fracture of cortical bone combined with spiroidal fracture at a certain distal distance from the bone fracture caused by the bullet, as opposed to bone lesions caused by rifles and higher calibre pistols where a greater degree of comminution is observed. The patient remained stable at all times, both from a haemodynamic and respiratory perspective, leading to the implementation of conservative treatment and admission into intensive care.



**Figure 1.** Radiography showing bullet lodged in chest cavity.



**Figure 2.** Radiography showing fracture in humerus.

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José Ramón IBARRECHE MARCOS<sup>1</sup>,  
Francisco Javier GIL MARTÍN<sup>1</sup>,  
Amaia PÉREZ ORDÓÑEZ<sup>2</sup>,  
Guadalupe DELGADO BARTOLOMÉ<sup>1</sup>,  
Iñaki SALEGUI ETXEBESTE<sup>1</sup>,  
Nieves PELÁEZ CORRES<sup>1</sup>

<sup>1</sup>*Emergentziak. Osakidetza.* <sup>2</sup>*Anaesthesia and Resuscitation Dept. Hospital Cruces. Barakaldo, Bizkaia, Spain.*

## FIBRINOLYSIS DURING CARDIOPULMONARY RESUSCITATION, A ROUTINE MEDICAL PRACTICE?

### Dear Editor,

Massive pulmonary thromboembolism (PTE) is a life-threatening disease that often leads to cardiorespiratory arrest (CRA). Here we present the case of intra-hospitalary CRA secondary to massive PTE in which systemic fibrinolysis was used during cardiopulmonary resuscitation (CPR) manoeuvres.

A 60-year-old female presented with a history of left hemicolectomy due to stenosing neoplasia in the sigma. She had been admitted to hospital for 12 hours for study of right deep vein thrombosis over 15 days and had not received prior antithrombotic prophylaxis.

Coincidental with mobilisation, the patient developed a loss of consciousness with agonic respiration. CRA was confirmed and CPR was immediately begun. Electrocardiographic monitoring was compatible with electromechanical dissociation. Advanced CPR was performed for 45 minutes until an effective pulse was achieved.

Upon arrival at the ICU, the patient was sedated and connected to mechanical ventilation, blood pressure was 90/60 mmHg, cardiac frequency 150 bpm in atrial fibrillation and oxygen arterial saturation was 90% with FiO<sub>2</sub>

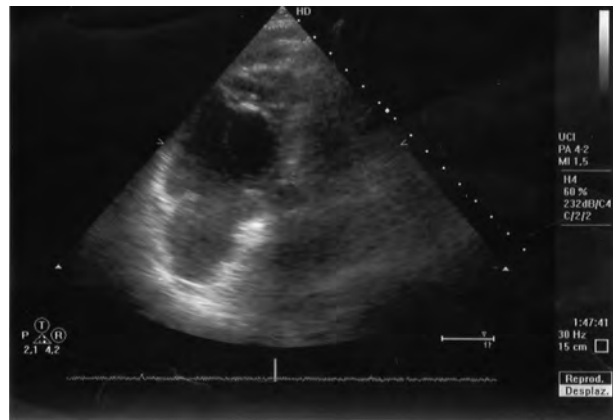
at 100%. Treatment included perfusion of high dosage dobutamin and noradrenalin; 200 ml of saline solution had been previously administered. Cardiorespiratory auscultation showed no findings of interest. ECG showed complete blockage of the right branch of the bundle of His not present in previous ECGs. Chest radiography was anodyne. An urgent ecocardiogram was performed revealing a significant enlargement of right cavities, dilation of suprahepatic veins and an estimated systolic pressure in pulmonary artery of 45mmHg.

Fifteen minutes after admission to the ICU a loss of pulse again occurred, with sinus bradycardia of 40 bpm. Adrenalin with 21 mg and sodium bicarbonate (1 mEq/Kg) were again administered and CPR manoeuvres were begun for a period of 5 minutes, after which spontaneous pulse was resumed. After this episode, haemodynamic instability persisted with an arterial pressure of 80/60 mmHg and arterial oxygen saturation of 70% (high FiO<sub>2</sub>). In light of a suspected PTE, performance of thrombolysis was decided during resuscitation. Tenecteplase (Metalyse®) 6000 U was intravenously administered together with anticoagulants via subcutaneous enoxaparin.

Over the next few hours, a clear haemodynamic improvement was observed, enabling removal of vaso-active medication. The patient spontaneously recovered sinus rhythm. An eco-Doppler of lower limbs was performed, revealing deep vein thrombosis in the common femoral vein together with thrombosis of right popliteal vein. Control ecocardiogram showed normalisation of the overload pattern of the right ventricle. The patient progressed well and was extubated after 72 hours with no sequels. On the fourth day of admission she was sent to the ward with acenocumarol anticoagulant treatment.

Systemic fibrinolysis is considered a first line treatment in cases of cardiogenic shock and/or onset of several right ventricular dysfunction in the context of massive PTE<sup>1,2,10</sup>. The fibrinolytic agent of choice is alteplase.

In the case of fibrinolysis administered during CPR, there are fewer studies<sup>3,6</sup>. Observation of isolated cases and small series suggest the benefits of this treatment<sup>4</sup>. Nevertheless, a prospective<sup>3</sup> randomised study of 223 CPR patients failed to show significant differences in mortality with respect to the use of fibrinolysis during CPR. The most recent resuscitation guidelines indicate that fibrinolysis may be used during CPR in cases of pulmonary embolism that fails to respond to CPR<sup>5,7</sup>. In this case, PCR should be prolonged for 60 to 90 minutes. In our case TNK was used as a fibrinolytic agent instead of r-TPA due to the ease of administration of this treatment during active CPR.



**Figure 1.** Ecocardiograma en el que se aprecia dilatación de las cavidades derechas.

To summarise, scientific evidence in the literature and normal clinical practice recommend the routine use of thrombolysis in cardiopulmonary resuscitation manoeuvres, as this treatment can be effective in individual cases, particularly in the event of suspected massive PTE.

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**RICARDO SALAS DE ZAYAS**

*Hospital Universitario San Juan. San Juan,  
Alicante, Spain.*