Clostridium difficile causante de síndrome de distrés respiratorio agudo tras pancreatectomía total

Acute respiratory distress syndrome due to clostridium difficile after total pancreatectomy

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La diarrea nosocomial, que es la adquirida en el ámbito hospitalario, suele ser producida por Clostridium difficile. Sin embargo, en raras ocasiones puede ocasionar un síndrome de distrés respiratorio. Por ello, el diagnóstico de dicha patología es difícil si no se sospecha. El tratamiento se basa en el uso de antibiótico vía oral. Se expone el caso de una paciente de 66 años con dicha patología tras la realización de pancreatectomía total.

Resumen

La diarrea nosocomial, que es la adquirida en el ámbito hospitalario, suele ser producida por Clostridium difficile. Sin embargo, en raras ocasiones puede ocasionar un síndrome de distrés respiratorio. Por ello, el diagnóstico de dicha patología es difícil si no se sospecha. El tratamiento se basa en el uso de antibiótico vía oral. Se expone el caso de una paciente de 66 años con dicha patología tras la realización de pancreatectomía total.

Palabras clave: pancreatectomía, distrés, Clostridium.

ABSTRACT

Nosocomial (hospital-acquired) diarrhea is usually caused by Clostridium difficile. On rare occasions it can cause acute respiratory distress syndrome (ARDS). Therefore, this condition should be suspected in order to make a diagnosis. Treatment is based on oral antibiotics. We report the case of a 66-year-old female patient with ARDS secondary to Clostridium difficile colitis after total pancreatectomy.

Keywords: Pancreatectomy, distress, Clostridium
(UCI) con tratamiento antibiótico de amplio espectro: 4 4 g piperacilina/0,5 g tazobactam cada 6 horas.

Tras realización de estudio de extensión, la aparición de síndrome de distrés respiratorio agudo (SDRA), deposiciones diarreicas y cultivo con identificación de toxina de Clostridium difficile en cultivo de heces permitió que se iniciara tratamiento antibiótico con 500 mg c/12 horas de vancomicina oral y 500 mg c/8 horas de metronidazol intravenoso (IV) durante 12 días ante la sospecha de SDRA secundario a C. difficile. Tras 48 horas de tratamiento antibiótico, la paciente presentó mejoría clínica y radiológica evidente (Fig. 1).

Fue dada de alta al mes del tratamiento quirúrgico.

Anatomía patológica evidenció adenocarcinoma biliar moderadamente diferenciado con márgenes quirúrgicos amplios, sin afectación ganglionar.

La tríada diarrea, dolor abdominal y leucocitosis junto con la toma previa de antibióticos nos debe hacer sospechar una colitis por C. difficile. El desarrollo de megacolon tóxico secundario a dicho patógeno se debe a la translocación de la toxina de C. difficile en el sistema venoso portal.

Los factores de riesgo son edad avanzada, inmunosupresión, isquemia intestinal, desnutrición, tumores intestinales y la latencia entre el uso de antibiótico y diarrea.

Ante la sospecha de infección por Clostridium es importante realizar una tipificación molecular (con métodos genéticos y basados en la reacción en cadena de la polimerasa), cultivando dicho microorganismo.

Deberá realizarse en heces diarreicas, lo que permitirá identificar la cepa toxigénica. La prueba de inmunoenzimático (EIA) para las toxinas A y B de C. difficile es rápida pero menos sensible.

Existen pocos casos publicados por SDRA secundario a C. difficile, y ninguno de ellos era un paciente posquirúrgico (Tabla 1).

Un diagnóstico tardío contribuye a la rápida progresión de un síndrome de disfunción multiorgánica y SDRA.

Tras la pancreatectomía total, las complicaciones digestivas más frecuentes son la formación de abscesos, la hemorragia posquirúrgica y el retraso de vaciado gástrico. Desde el punto de vista respiratorio puede producirse SDRA, aunque secundario a C. difficile es excepcional.

El SDRA tiene una tasa de mortalidad del 40%, de ahí la importancia de un diagnóstico precoz e inicio inmediato de tratamiento. Las principales causas son neumonía y cuadros sépticos (> 80%).

El tratamiento de C. difficile se basa en el cese del tratamiento antibiótico. La principal opción terapéutica debe ser la ventilación mecánica y el tratamiento antibiótico con vancomicina oral durante 10-14 días (ante insuficiencia renal será sustituida por metronidazol oral).

En casos de enfermedad persistente o recurrente debemos administrar vancomicina oral (125

![FIGURA 1](image1)

Evolución radiográfica del síndrome de distrés respiratorio agudo (SDRA). A: estudio radiológico simple tras episodio de insuficiencia respiratoria hipoxémica. B: tras el diagnóstico de SDRA secundario a Clostridium difficile y tras usar antibiótico específico. C: tras resolución de cuadro SDRA.

| TABLA 1 | Casos publicados con síndrome de distrés respiratorio agudo secundario a Clostridium difficile |
|----------|-----------------------------------------------------------------------------------------------|
| Caso     | Publicación | Edad | Sexo | Síntomas                                      | UCI | Antibióticos                              | Megacolon tóxico | Éxito |
| Byl1     | 1996        | 78   | M    | Insuficiencia respiratoria                    | Sí  | Vancomicina oral e IV                      | No              | Sí    |
| Possamai4 | 1997       | 66   | F    | Diarrea, fiebre y dolor abdominal             | Sí  | Clindamicina IV + Metronidazol IV          | No              | No    |
| Dobson9  | 2002        | 69   | M    | Neumonía                                     | Sí  | Metronidazol IV                            | Sí              | No    |
| Eckel10  | 2002        | 62   | F    | Insuficiencia respiratoria                    | Sí  | Vancomicina oral + Metronidazol IV         | No              | Sí    |
| Jacob11  | 2004        | 38   | F    | Diarrea y síncope                            | Sí  | Vancomicina oral + Metronidazol IV         | No              | Sí    |
| Kim12    | 2014        | 83   | M    | Fiebre y tos                                 | Sí  | Vancomicina oral + Metronidazol oral       | No              | No    |
| Nuestro caso | 2016   | 66   | F    | Posoperatorio con insuficiencia respiratoria aguda hipoxémica | Sí  | Vancomicina oral + Metronidazol IV         | No              | No    |

M, masculino; F, femenino; UCI, unidad de cuidados intensivos; IV, intravenoso
Clostridium difficile is an anaerobic, spore-forming, gram-positive bacillus that produces asymptomatic colonization of the gastrointestinal tract. Clostridium difficile associated diarrhea can progress to toxic megacolon, sepsis, perforation, and even death. Acute respiratory distress syndrome (ARDS) due to Clostridium difficile is uncommon, particularly after abdominal surgery.

We report the case of a 66-year-old female patient who sought medical care at the emergency department due to fever, itching and jaundice for 72 hours. An endoscopic retrograde cholangiopancreatography (ERCP) reported a stricture in the middle third of the common bile duct suggestive of neoplasm (Bismuth I). The patient underwent bilateral sphincterectomy with metal stent placement. The biliary cytology was negative for malignancy.

A computed tomography (CT) scan revealed severe intrahepatic and extrahepatic bile duct dilation (13.5 mm) with concentric wall thickening at the caudal side of the common bile duct at the insertion of the cystic duct, suggestive of a tumor. The laboratory tests revealed total bilirubin 9.9 mg/dL (0.3-1.2), CA 19-9: 21.8 U/mL (< 37).

A diagnosis of cholangiocarcinoma was made, and the patient underwent scheduled surgery. A mass was found in the head, neck and uncinate process of the pancreas; the intraoperative biopsy reported distal bile duct carcinoma. Endotracheal suction was performed using a closed system. The surgical procedure lasted 4.5 hours and consisted of pancreatecoduodenectomy with lymph node resection and reconstruction with gastrojejunostomy and Roux-en-Y hepaticojejunostomy. During surgery, there was no need to administer vasoactive drugs or blood products. After surgery, orotracheal secretions were suctioned and the orotracheal tube was removed.

On postoperative day 4, the patient presented hyperglycemia, atrial flutter with high ventricular response (150 bpm), increased respiratory work and oxygen saturation of 65%. The chest X-ray showed bilateral pulmonary infiltrates and arterial blood gas test revealed hypoxemic respiratory failure. The patient was admitted to the intensive care unit (ICU) and was treated with broad-spectrum antibiotics: piperacillin 4 g/ tazobactam 0.5 g every 6 hours.

Due to the presence of acute respiratory distress syndrome (ARDS), diarrhea and stool tests positive for C. difficile toxin, a diagnosis of ARDS secondary to Clostridium difficile associated was made and antibiotic treatment was initiated with oral vancomycin 500 mg every 12 hours and 500 mg of intravenous (IV) metronidazole every 8 hours for 12 days. After 48 hours of antibiotic treatment, the patient evolved with clinical and radiological improvement and was discharged one month after surgery (Fig.1).

The pathology report demonstrated a moderately differentiated bile duct adenocarcinoma with wide surgical margins and negative lymph nodes. The triad diarrhea, abdominal pain and leukocytosis associated with treatment with antibiotics should raise the suspicion of Clostridium difficile associated colitis. The development of toxic megacolon secondary to Clostridium difficile is due to translocation of the germ toxin into the portal venous system.

Advanced age, immunosuppression, intestinal ischemia, malnutrition, bowel tumors and recent use of antibiotics are risk factors for Clostridium difficile associated colitis.

In case of suspecting an infection by Clostridium difficile, a polymerase chain-reaction-based (PCR) method should be performed for molecular typing. The sample is obtained from stools and cultured to identify Clostridium difficile toxin and the corresponding strain. The enzyme-linked immunosorbent assay (ELISA) for Clostridium difficile toxin A and B is rapid but less sensitive.

There are few case reports of ARDS secondary to C. difficile and none after a surgery (Table 1).

A late diagnosis contributes to rapid progression to MODS and ARDS.

The most common gastrointestinal complications after total pancreatectomy are abscesses, postoperative bleeding and delayed gastric emptying. The development of ARDS is feasible but is extremely rare due to Clostridium difficile associated colitis.

The mortality rate of ARDS is 40%, mainly due to pneumonia and sepsis (>80%); thus, early diagnosis and treatment is extremely important.

Once the diagnosis is made, antibiotics should be stopped. Mechanical ventilation is the main therapeutic option together with oral vancomycin...
for 10-14 days or oral metronidazole in case of renal failure. In case of persistent disease or recurrence, oral vancomycin (125 mg every 6 hours) or oral metronidazole (500 mg every 8 hours for 72 hours) should be administered. Intravenous metronidazole is indicated for critically ill patients or for those with inability to tolerate oral intake. Fecal microbiota transplantation has been described in refractory cases. Subtotal colectomy is indicated in case of lack of response to antibiotic therapy or toxic megacolon. Surgery is required in 65-71% of the cases. Multiple organ dysfunction syndrome and ARDS are sometimes inevitable. Recently, drotrecogin alfa and antiretroviral drugs have been used to treat ARDS and MODS. In conclusion, although ARDS secondary to Clostridium difficile associated colitis is rare, it should be included in the differential diagnosis of acute respiratory failure in patients with diarrhea in the postoperative period.

### FIGURE 1

X-ray evolution in acute respiratory distress syndrome (ARDS). A: plain X-ray after an episode of hypoxemic respiratory failure. B: after diagnosis of ARDS secondary to Clostridium difficile and after use of specific antibiotic. C: after resolution of ARDS

### TABLE 1

Publications of case reports with acute respiratory distress syndrome secondary to Clostridium difficile

| Case report | Publication | Age | Sex | Symptoms | ICU | Antibiotics | Toxic megacolon | Success |
|-------------|-------------|-----|-----|----------|-----|-------------|-----------------|---------|
| Byl⁷        | 1996        | 78  | M   | Respiratory failure | Yes | Oral and IV vancomycin | No               | Yes     |
| Possamai⁸   | 1997        | 66  | F   | Diarrhea, fever and abdominal pain | Yes | IV clindamycin + IV metronidazole | No | No     |
| Dobson⁹     | 2002        | 69  | M   | Pneumonia | Yes | IV metronidazole | Yes | No     |
| Eckel¹⁰     | 2002        | 62  | F   | Respiratory failure | Yes | Oral vancomycin + IV metronidazole | No | Yes    |
| Jacob¹¹     | 2004        | 38  | F   | Diarrhea and syncope | Yes | Oral vancomycin + IV metronidazole | No | Yes    |
| Kim¹²       | 2014        | 83  | M   | Fever and cough | Yes | Oral vancomycin + oral metronidazole | No | No     |
| Our case report | 2016    | 66  | F   | Postoperative with acute hypoxemic respiratory failure | Yes | Oral vancomycin + IV metronidazole | No | No     |

M, male; F, female; ICU, intensive care unit; IV, intravenous

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