Acute acalculous cholecystitis in patients with acute traumatic spinal cord injury

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Acute acalculous cholecystitis (AAC) is a very serious complication which can be found in patients with multiple serious traumatic lesions ('polytrauma'). Very few patients have been reported in the literature with an acute spinal injury and associated AAC. We report seven patients with polytrauma and acute spinal cord injury who developed AAC. All had no complaint of the principal warning symptom: right upper quadrant abdominal pain. All presented with a palpable mass in this site and the laboratory results were compatible with cholestasis. The diagnosis of AAC was confirmed both by ultrasound and CT scanning. We discuss the possible precipitating factors and the treatment. One hundred and ninety one patients were admitted to the Intensive Care Unit in our Hospital with SCI over a period of 2 years, all of these in the acute stage. AAC was diagnosed in seven patients among them. Our purpose is to call attention to this clinical condition which can complicate the outcome of patients with multiple trauma and acute spinal cord injury. To date AAC in this group of patients has been infrequently described in the available literature.

Keywords: acute acalculous cholecystitis; spinal cord injury; digestive complications

Introduction

Patients with a transverse spinal cord injury (SCI) in the acute stage can develop several complications. These are more frequent and severe in direct proportion to the level of the SCI, the higher the level the greater the seriousness. Digestive system complications are frequently observed, mainly in patients with a spinal cord lesion above T6, with subsequent total or partial denervation of the afferent branches of the sympathetic nervous system.¹

It is generally accepted that serious digestive system complications consist of upper digestive tract haemorrhage, non specific symptoms (nausea, sporadic vomiting, transitory abdominal pain, constipation, etc.). There are reports of other occasional serious conditions such as pancreatitis, diverticulitis, bouts of ulcerative colitis and hepatitis.^{2,3} In the medical literature we have only found five examples of acute acalculous cholecystitis (AAC) occurring in the acute stage of traumatic SCI.^{4–7}

This finding has focused our attention on AAC as it is a serious, potentially lethal condition and must not be overlooked in patients with multiple trauma if there is prolonged total parenteral nutrition. This situation was common in our patients.^{8–11} We consider it to be important to bring the condition to the notice of physicians looking after such SCI patients.

Material and method

We have retrospectively reviewed the records of 191 patients with traumatic SCI admitted for the first time to our Hospital during the 2 year period 1 November 1993 to 31 October 1995. Patients were admitted to the Intensive Care Unit at Paraplegics National Hospital, Toledo, Spain. This is a nationwide reference hospital for patients with spinal cord injuries. Among these 191 new admissions we diagnosed seven with AAC, six of whom met the confirming ecographic and one the CT scanning criteria for the diagnosis, in addition to the symptomatic and laboratory criteria compatible with the condition.^{8–12} Diagnostic criteria are shown in Table 1. The diagnosis of AAC was established on the synchronous presence of two ultrasound major criteria with one or more minor criteria in addition to the presence of the compatible clinical and/or laboratory findings. The sonographic Murphy sign is rarely reliable in a spinal cord injured patient because of the anesthesia below the level of the lesion.

Results

A total of 191 patients were studied, seven of whom had AAC. There were six males and one female, aged 17 to 72 years old, mean age 41.8 years old. All patients had a SCI from acute trauma. The level of the spinal cord lesion was cervical in three (C5, C7 and C8) and thoracic in four (T1, T2, T7 and T12). All presented with sensory and motor complete lesions,

grade A in the ASIA Impairment Scale (AIS). Likewise all had multiple associated traumatic lesions with scores of 29 to 38 in the Injury Severity Score (ISS)¹³ scale. This ISS scale median was 34.4 (serious to very serious traumatic lesions). In three patients (42.8%) the associated lesions included abdominal trauma, which demanded urgent surgical treatment in one patient (splenectomy). AAC was diagnosed from 8–82 days after the trauma (average of 33.1 days).

When AAC was diagnosed, four patients (57.1%) required mechanical ventilation and three (42.8%) sedation, including opiates (morphine chloride, meperidine and fentanyl). Five (71.4%) had total parenteral nutrition via a central venous line, one patient had nasogastric tube feeding and one patient mixed oral and tube feeding. Four patients presented stress upper digestive tract haemorrhage at the time of diagnosis or in the previous weeks.

The patient with a lower level SCI at T12 was the only one who complained of right upper quadrant abdominal pain. Three patients (42.8%) had a sensation of intense malaise not explained by their original illness.

The axillary temperature fluctuated from 37.7°C to 39.5°C (average: 38.8°C). Six patients (85.7%) had a steady fever of over 38.8°C. The heart rate fluctuated between 103–146 beats per minute, with an average of 112.3 per minute. Abdominal examination of all of the patients revealed a palpable mass in the right hypocondrium, painful to the patient who was hypersensitive at this level. The systolic blood pressure dropped to below 95 mmHg in only one patient. Shock was present in only one patient, who required vasoconstrictor amines for recovery.

The biochemical parameters of cholestasis were determined. We observed cholestasis (bilirubin

>2 mg/dl and alkaline phosphatase >190 UI/l) without disease of the gallbladder or biliary ducts in other 31 patients. In these patients the ultrasonography did not show evidence of AAC, and the biochemical abnormalities were imputed to intrahepatic cholestasis due to sepsis, drug toxicity or from total parenteral nutrition. Ultrasonography was carried out in total parenteral nutrition. Ultrasonography was carried out in another 21 patients for other reasons, without discovering AAC.

Urgent cholecystectomy was performed for two patients, and cholecystostomy for another. Two other patients underwent non-urgent cholecystectomy, and two had medical treatment. There were no fatalities. In the two patients where an urgent cholecystectomy was performed, the anatomopathological macroscopic and microscopic diagnosis was gangrenous cholecystitis. In the two patients with deferred cholecystectomy an inflammatory mass involving the gallbladder, duodenum and omentum was found during surgery.

Bile culture was positive in only one patient, for *Pseudomonas aeruginosa* and *Enterococcus*. The laboratory reports are detailed in Table 2. Sonographic and CT scanning findings are reported in Table 3.

Discussion

AAC has been described in association with major abdominal surgery, multiple serious trauma, and in patients with a prolonged serious illness and sepsis.^{8,14–16} In almost 90% of those with acute cholecystitis and severe multiple trauma the condition is acalculous.¹² Predisposing factors include diminished gastrointestinal motility with prolonged ileus, hyperalimentation, mechanical ventilation with positive end-

Table 1 Diagnostic criteria for acute acalculous cholecystitis

Clinical findings	<ul style="list-style-type: none"> –Fever > 38°C –Jaundice –Pain with tenderness and rigidity of the abdomen: right upper quadrant –Palpable mass in the right upper abdominal quadrant
Laboratory findings	<ul style="list-style-type: none"> –Leucocytosis > 12 000/mm³ –Serum glutamic oxalacetic and glutamic pyruvic transaminases in normal limits or mildly elevated –Alkaline phosphatase > 190 UI/l –Total bilirubin > 2 mg/dl –Serum amylase normal
Sonography criteria	<p><i>Major criteria</i></p> <ul style="list-style-type: none"> –Wall thickening > 3.5 mm –Distention of the gallbladder in length > 8 cm and in width > 4 cm (Hydrops) –Presence of bile sludge <p><i>Minor criteria</i></p> <ul style="list-style-type: none"> –Sonolucent intramural layer (intramural edema) –Pericholecystic fluid in the absence of ascites –Fragmentation of the gallbladder wall –Sonographic Murphy sign (pressure over gallbladder (noted by ultrasonography) transducer produces pain)
Computed tomography criteria	The same as those for ultrasonography

expiratory pressure (PEEP), treatment with opiates, dehydration, massive blood transfusions, abdominal abscesses, acute or chronic renal insufficiency, and AIDS.^{8,16–18} The consensus is that its incidence is increasing.^{7,11}

The pathogenesis is not clear but there appear to be several factors involved in its development: (A) Bile stasis provoked by (1) prolonged fasting causing intestinal hypomotility or ileus, (2) narcotics (opiates) that induce Oddi's sphincter spasticity, (3) dehydration and hypoalbuminemia and, (4) an increase in bile production from massive blood transfusions. All of these factors are instrumental for changes in the concentration and in the chemical composition of the bile, and give rise to substances harmful to the gallbladder endothelium, such as lysophosphatidilcholine. (B) The increased internal pressure in the already atonic gallbladder from the use of opiates and/or mechanical ventilation with PEEP, and (C) gallbladder wall perfusion compromise, as well as the consequence of hypotension (shock), or else by the effect of endotoxins produced by gram negative bacteria with the subsequent activation of Factor XII and injury of the smaller vessels of the serous and muscular layers of the gallbladder wall.^{12,16} There is suggestive data that the autonomic denervation (similar to the denervation that occurs in those with

a spinal cord lesion above T5) can play an important role in the progression of the inflammatory process induced by an ischemic episode.¹⁹

The role played in the origin of AAC by total parenteral nutrition has been enhanced, since 4% of patients treated with total parenteral nutrition (TPN) for ileus develop AAC.⁸ Nevertheless a significant number of cases have occurred after reinitiation of normal oral feeding and even in patients not requiring TPN during the course of the illness.¹² It has been confirmed that the presence of biliary sludge is highly correlated with the duration of TPN, and that in 100% of patients it is present in the gallbladder after a 6 week period on TPN.¹² Nevertheless the sonographic confirmation of biliary sludge has a poor predictive value in the ultimate development of cholecystitis, and a low incidence of AAC (between 7–14%) has been found in patients with biliary sludge who are asymptomatic and whose laboratory tests are normal.^{20–22}

In our series, five patients (71.4%) were on TPN, and three were taking narcotics (two with TPN and one with enteral nutrition). A significant drop in blood pressure directly due to the spinal cord lesion prior to the onset of AAC was not documented in any patient. There was one instance of septic shock diagnosed simultaneously with the diagnosis of AAC. None of

Table 2 Laboratory reports

Patient	1	2	3	4	5	6	7
GOT (ASAT) (5–40)	62	9	77	60	69	117	29
GPT (ALAT) (5–35)	59	35	170	113	56	222	137
Total bilirubin (0.2–1.2)	1'1	0'7	3'9	4'2	17'5	8'6	0'8
Direct bilirubin (0–0.4)	0'9	0'4	3'1	3'2	13	6'5	0'6
Alkaline phosphatase (45–125)	500	129	286	249	265	154	377
GGTP (7–50)	204	64	188	241	638	432	276
Leucocytes	22 000	18 200	19 000	14 800	7200	11 000	21 700
Polymorphonucl. in %	57	67	76	84	44	79	62
Bands in %	4	9	10	5	28	15	8
Quick in %	63	65'3	63	64	47	64	64
Serum Amylase (20–105)	31	26	25	34	32	29	29

In the first column are showed normal values among parenthesis

Table 3 Ecographic findings

Patient	1	2	3	4	5	6	7
Biliary sludge	yes	yes	yes	yes	yes	yes	yes
Thickened wall	yes	yes	yes	yes	yes	no	yes
Double wall	no	no	yes	no	no	no	no
Hydrops vesicular	no	yes	yes	yes	yes	no	yes
Perivesicular fluid	yes	no	no	yes	no	no	yes

the other patients required pressor amines nor had received them a week prior to the onset of AAC. Four patients required mechanical ventilation with 5 cm H₂O pressure PEEP and three out of these four patients were on opiates.² Thus, we failed to find a single etiological mechanism to explain the development of AAC. We believe that each patient represents the conjunction of two or more of the previously described pathogenic mechanisms.

The signs and symptoms of patients with AAC do not differ from patients observed with cholelithiasis. In general AAC appear at some time between the second and fourth weeks after the SCI.^{8,14} Contrary to the occurrence of cholecystitis secondary to lithiasis it is predominant in males.^{8,10,15} These two facts were observed in this series, although one episode occurred later in the 12th week. Right upper quadrant abdominal pain was observed in only one patient, the one with a T12 lesion. All of the other patients presented with anesthesia at this site. A palpable mass in the right upper abdominal quadrant was found in all of the patients. Six (85.7%) presented a high fever. All had tachycardia of 103 beats per minute. Tachycardia is unusual in the acute stage of patients with spinal cord lesions above T5 and this finding should alert about a possible complication.^{11,12,22}

Laboratory reports were in accord with what has been previously described,^{11,14} and were compatible with a pattern of cholestasis. The transaminases were either minimally elevated or were not elevated. There was a clear increase of alkaline phosphatase, the gamma-glutamyl transpeptidase and the total bilirubin at the expense of its direct fraction.

The symptomatology and the biochemistry of AAC are not specific in patients critically ill, including those patients with spinal cord lesions in the acute stage.^{20,23} Two other adverse factors increase the diagnostic difficulty: the anesthesia below the level of a complete spinal cord lesion and the consequent lack of the cardinal symptoms: right upper quadrant abdominal pain. We feel that the diagnosis of AAC should be ruled out in all the patients with SCI in its acute stage who deteriorate after an initially favourable clinical course, or who present: a persistent respiratory failure, unexplained multisystemic failure, paralytic ileus abnormally prolonged, or sepsis of undetermined cause.^{8,15,16,23}

AAC can lead to serious complications and there can be a significant mortality^{14,23} (although the mortality due to cholecystitis by itself is very low^{8,11}). It can necessitate a very prolonged stay both in the intensive care unit and in the general ward resulting in highly increased expense. We must be cognisant of all of these facts and be constantly on the look out for them.⁷

The diagnosis can be confirmed by abdominal sonography or by abdominal CT scanning compatible with acalculous cholecystitis: distended parietic gallbladder, increased wall thickness (over 3.5 mm),

presence of biliary sludge, double wall image (sonolucent intramural layer) (Figure 1) and the presence of perivesicular fluid in the absence of ascites. The conjunction of three of these signs weigh more in favour of the diagnosis than if present singly.^{10,15,23} CT scanning has a similar diagnostic value as does sonography, and demonstrate a diffuse or nodular thickening of the gallbladder wall, a poor limit of demarcation between the liver and the vesicle, a distended vesicle with subserous edema, and fluid collection in the perivesicular space.¹¹ In our series echographic diagnostic signs were positive in six patients. Case 6 was diagnosed by a CT scan. Likewise echography can be valuable in the diagnosis of severe complications present in 40–100% of patients: emphysematous cholecystitis, gangrene, abscess and gallbladder perforation.

In our series ultrasound studies have been carried out in only 59 patients (30.9%) therefore we cannot know the real prevalence of AAC in patients with polytrauma and SCI in the acute phase, and prospective studies are required to know more about the epidemiology.

The noninvasive imidodiacetic acid hepatobiliary scan is another useful diagnostic test. It has a high sensitivity and specificity but we could not use it in our patients.

In patients critically ill from polytrauma a clear correlation has not been found either between the severity of the trauma, the clinical conditions and the incidence of AAC. In our series the ISS scale was used to calibrate the degree of severity of the trauma and the APACHE II scale to judge the patient's clinical status. The ISS was 34.4, similar to the whole of the patients with spinal cord lesions admitted to our

Figure 1 Abdominal sonogram

intensive care unit during a 4 year period (34.9 ± 1.4 with $P < 0.05$). These results coincide with those found by other authors.^{22,24}

In some patients asymptomatic with minimal laboratory abnormalities and ultrasonography or CT scan criteria of AAC, conservative treatment with antibiotics, total parenteral nutrition, gastric decompression by continuous nasogastric tube aspiration and hemodynamic stabilization, was effective in the remission of the clinical process.^{10,22} Isolation of bacteria in the bile is infrequent but reports of bile cultures were sometimes positive for *Enterococcus*, *Klebsiella*, *Pseudomonas*, *E coli*, *Candida*, *Staphylococcus* and *Bacteroides fragilis*. Based on these reports antibiotic treatment should be started with third generation Cephalosporins plus Metronidazole. If monotherapy is decided Imipenem/Cilastatin, Ticarcillin/Clavulanic or Piperacilin/Tazobactam should be used.^{26,27,28}

The general use of radiological intervention techniques has been of great benefit in the diagnosis and management of AAC. Gallbladder decompression by percutaneous cholecystostomy controlled by echography or by a CT scan can solve the situation with few complications, making cholecystectomy unnecessary.^{11,25,29} These techniques are very useful in the diagnosis of undefined clinical situations which are resolved with the abatement of symptoms in 24–48 h.²⁵ Cholecystectomy was the treatment of choice up to a few years ago¹³ and has now been left to deal with complications such as emphysema, gangrene, abscess or perforation of the gallbladder.^{16,29} We believe that the determination of using conservative or aggressive treatment must be individualized and depends on the degree of systemic affectation effects on the patient, on the available resources and on the skill and experience of the surgeon.

In summary our study attempts to call attention to clinicians who are in charge of the care of patients with posttraumatic SCI in the acute stage who can develop AAC. The estimated prevalence (0.4 to 4%^{8,14}) is increasing.³⁰ When routine sonographic studies are performed in critically injured patients this condition can be found in 14–18% of them.^{10,22} There should be prospective epidemiological studies to determine the real prevalence in the acute phase of SCI in patients with polytrauma. AAC should be diagnosed as early as possible¹⁵ because of its complications and mortality. Physicians should consider the possibility of acute acalculous cholecystitis in view of the above cited warning signs.

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