

Acute Liver Failure

Mohammad Hossein Somi

Associate professor of gastroenterology

Liver and Gastrointestinal Disease Research Center

Tabriz University of Medical Sciences

آیین وفا کار طبیب است که باشد

او را غم یاران و کسی را غم او نیست

DEFINITION

- Acute liver failure refers to:

The rapid development of severe acute liver injury with impaired synthetic function and encephalopathy in a person who previously had a normal liver or had well-compensated liver disease.

The development of encephalopathy within eight weeks of the onset of symptoms in a patient with a previously healthy liver.

The appearance of encephalopathy within two weeks of developing jaundice, even in a patient with previous underlying liver dysfunction.

SubFulminant Hepatic Failure

Patients who have ~~Subfulminant Hepatic Failure~~ rapid deterioration of liver function with the development of encephalopathy within six months.

Acute and subacute liver failure differ in their clinical features and prognosis.

As an example, cerebral edema is common in fulminant disease and rare in subfulminant disease.

In contrast, renal failure and portal hypertension are more frequently observed in patients with subacute liver failure.

INCIDENCE

- some data are available
- Approximately 2000 deaths occur annually from acute viral hepatitis
- 3.5 deaths per million people.

ETIOLOGY

- Acute liver failure can result from a wide variety of causes (table 1)
- A prospective study involving 17 sites in the United States (the Acute Liver Failure Study Group) collected data regarding the etiology, clinical and laboratory features, and outcome of patients presenting with liver failure.
- During the period from 1998 to 2001, the most common causes of liver failure were :
 - Acetaminophen overdose (39 percent)
 - Indeterminate (17 percent)
 - Idiosyncratic drug reactions (13 percent),
 - Viral hepatitis A or B (12 percent)

Table 1

Mnemonic for causes of acute liver failure: The ABCs

A	Acetaminophen, hepatitis A, autoimmune hepatitis
B	Hepatitis B
C	Cryptogenic, hepatitis C
D	Hepatitis D, drugs
E	Esoteric causes - Wilson's disease, Budd-Chiari syndrome
F	Fatty Infiltration - acute fatty liver of pregnancy, Reye's syndrome

ETIOLOGY

- Amoxicillin-clavulanate was the most common drug implicated in a registry study that included 461 patients with drug-induced liver injury, accounting for almost 13 percent of cases.
- Among 1014 patients referred to King's College Hospital in the United Kingdom between 1973 and 1991, 57 percent were acetaminophen-induced while only 9 percent were attributable to hepatitis B or D.
- Among 502 patients referred to the Hospital Beaujon in France between 1972 and 1990, 45 percent were related to hepatitis B or D while only 2 percent were attributable to acetaminophen .

Hepatitis viruses

- Although hepatitis A is the most common form of acute viral hepatitis, it is rare for acute infection to progress to ALF
- Hepatitis B is probably the most common viral cause of ALF.
- Furthermore, the incidence of acute liver failure from hepatitis B may be underestimated. Precore or pre-S mutant hepatitis B viruses that are able to produce infection but do not produce HBsAg or HBeAg may be difficult to diagnose by routine serology.
- This was illustrated in a study in which evidence of hepatitis B infection was detected by PCR in 6 of 17 patients (35 percent) who underwent liver transplantation for what was initially thought to be non-A, non-B hepatitis.

- Hepatitis C virus does not appear to be a significant cause of ALF.
- Other viral etiologies of ALF include :
 - Hepatitis delta virus coinfection or superinfection,
 - Hepatitis E (especially in pregnant women in endemic areas),
 - Epstein-Barr virus,
 - Cytomegalovirus,
 - Herpes simplex virus,
 - Varicella zoster.

Toxins

- Acetaminophen is the most common toxin associated with ALF in most reports (table 2)

- Most cases occur after ingestion of large doses in an attempt to commit suicide.

However, can result from therapeutic doses in patients with underlying liver disease (particularly with ongoing alcohol use) and in patients who are taking medications known to induce the cytochrome P450 system such as anticonvulsants.

Drugs and toxins associated with acute liver failure

Acetaminophen
Alcohol
Amiodarone
Carbon tetrachloride
Dideoxyinosine
Gold
Halothane
Isoniazid
Ketoconazole
MAO inhibitors
Methyldopa
NSAIDs
Phenytoin
Poison mushrooms (<i>Amanita phalloides</i>)
Propylthiouracil
Rifampin
Sulfonamides
Tetracycline
Tricyclic antidepressants
Valproic acid

Vascular

- Vascular causes of ALF include:
 - Portal vein thrombosis
 - Budd-Chiari syndrome (hepatic vein thrombosis)
 - Veno-occlusive disease
 - Ischemic hepatitis

Metabolic

- A number of metabolically-related disorders have been associated with ALF including :
 - Wilson's disease
 - Acute fatty liver of pregnancy
 - Reye's syndrome

Miscellaneous

- ALF has also been reported in patients with
 - Malignant infiltration of the liver
 - Heat stroke
 - Sepsis, and autoimmune hepatitis
- Serologic markers alone do not establish the diagnosis of autoimmune hepatitis in patients with ALF.

- A cause for ALF can be established in approximately 60 to 80 percent of cases.
- Establishing the underlying disease may be important because it can influence treatment options, determine prognosis, and help to counsel families as illustrated by the following observations:

- ALF due to acetaminophen intoxication is treated with a specific therapy, N-acetylcysteine.
- The mortality in ALF appears to be higher for idiosyncratic drug reactions, Wilson's disease, and non-A and non-B hepatitis and lower for cases of ALF caused by hepatitis A, hepatitis B, and acetaminophen .
- Family members of patients with ALF secondary to Wilson's disease may need genetic counseling as well as screening for the disease

خانم ۳۵ ساله ای که از سه سال پیش داروی ضد بارداری خوراکی مصرف می کرده با شکایت ضعف، سستی، کاهش اشتها، و پررنگ شدن ادرار مراجعه کرده است. سابقه فامیلی و سابقه پزشکی دیگری ندارد. در معاینه ایکتر واضح دارد، کبد ۱۱ سانتی متر، طحال نرمال، و شکم حساس نمی باشد. در آزمایشات همراه:

AST = 710

ALT = 650

Alkp = 316

PT = 23

Bili (T = 11, D = 5)

بیمار در بخش بستری می شود.
چه اقدامات تشخیصی و درمانی را توصیه می کنید؟

HAV(IgM) منفی
مارکرهاى اتوایمیون منفی
HCVAb منفی
HBSAg مثبت
PT= 27 (INR=3.8)
Bili= 21
AST=800
ALT=715
ALkp=312
Plt=139000
سرولوپلاسمین در حداقل نرمال

در سومین روز بستری آزمایشات ذیل آماده شده است :

در سونوگرافی کبد اکو افزایش یافته با آسیت خفیف وطحال نرمال مشاهده می شود،
و در معاینه خواب آلود است.

چه اقدامات و آزمایشات تکمیلی را توصیه می نمائید ؟