3- Cholestatic Jaundice

Occur when conjugated bilirubin is unable to enter to bile canaliculi and passes back to the blood, also because there’s failure of clearance of unconj.bilirubin arriving liver cell.

Aetilogy:1-failur of hepatocyt to initiate bile flow intrahepatic cause

2-obstruction in bile flow or portal tract (PBC,alcohol,drug,

viral and autoimmune

hepatitis)

3-obstruction of extrahepatic bile duct between extrahepatic cause

Portal hepatic and ampulla of vitra (choledocholithiasis,

Carcinoma,biliary strictures,

Parasitic infestation)

Clinical features:

Early features:1-jaundice -2-dark urin -3-pale stool -4-pruritus

Late features:1-xanthomas -2-malabsorption -3-weight loss -4-steatorrhoea -5-osteomalacia -6-bleeding tendency

These are:

1-due to cholestasis

2-due to secondary infection(cholongitis)

3-those of underlying liver disease

Investigation: decided by history and examination

Alkalin phosphat&GGT↑↑more than enzymes ALT,AST

U\Sto identify biliary dilation followed by MRCP or ERCP

Ascitis :accumlation of free fliud in peritoneal cavity commonly due to 3C:

1-cirrhosis -2-congestive heart failure -3-carcinoma -4- rare cause→malnutrision,nephrotic syndrom,hypoprotienemia,post dialysis, TB, bacterial peritonitis,Budd-charie syndrom

Clinically:→shifting dullness appear when

→thrill fliud >1 L

→distension

U\S detect300 cc fliud in right side pleural effusion(hepatic hydrothorax)

Pathogenesis in cirrhosis:

Porto-systemic shunt causes↑ nitric oxide lead to splanchnic vasodilation which factor for ascitis.this cause hypotension leading to secondary aldosternism &water retension.

Portal hypertention +splanchinic arterial vasodilation lead to alter intestinal capillary permeability that promot fliud accumulation.

Investigation:

1-U\S(the best)→confirm ascitis specially in obesity.

2-paracentesis→confirm the diagnosis &obtian fliud for analysis:

A-appearance→straw colour→cirrhosis

bloody→malignancy

cloudy→infection

bile staining→biliary communcation

milky→lymphatic obstruction

B-albumin&protien concetration→>30 g\L exudate

<30 g\L transudate

(serum-ascitis albumin gradient SAAG)because 30%of transudate reach 3gm\L

3-cytology→malignancy &AFB

4-WBC count→leucocytosis→infection

5-serum amylase→acute pancreatitis

6-microscopy&culture

Management

Succeful Rx relieves discomfort but not prolong the life. Vigorous aspiration lead to disorder in the fliud &electrolyte causing hepatic encephalopathy. Rate of Na&fliud loss measured by weighting the pt. regularly.

Note:it’s important to avoid removing more than 1 L of fliud daily ,so body weight shouldn’t fall by more than 1 kg daily to avoid fliud depletion in other tissue.

1-sodium&water restriction:100mmol\day→restiric diet salt

Avoid Na contain drug avoid also drug causes water&sodium retention(steroid& NSAID)

Restric water to 0.5-1L\day only when plasma Na fall bellow 125mmol\L

2-diuretic drug:Spironolactone(100-400mg\d) the drug of choise

S.E→gynecomastia+hyperkalemia

Some pt. need Furosemide(potent)although causes fliud,electrolyt&renal function disorder.

The action of diuretic ↑↑if the pt. in rest state(horizantal).

If pt.not respond to 400mg spironolacton+160mg furosemid→considered refractory ascitis which need other type of Rx

3-paracentesis:the first line Rx of refractory ascitis,can remove 3-5 L daily safe with infusion of albumine (6-8 gm\L of ascitis removed).paracentesis can be used as initial theraby(3-6L safe) or when other Rx fail

4-peritoneo-venous shunt(leveen):subcutenous tube between peritoneum &internal jugular vein in the neck. It allow fliud to pass directly to circulation. It’s useful for refractory ascitis. Complication:1-infection -2-SVC thrombosis -3-DIC -4-pulmonary edema -5-oesophageal varices bleeding

5-TIPSS(transjugular-intrahepatic-portosystemic-stent-shunt):for resistant ascitis but not prolong the life,used for pt. awiating transplantation &for pt.with reasonable LFT.(stent between portal&hepatic vein)

Prognosis:10-20% survive 5 year

Good prognostic factor→1-well maintained L. function -2-good response to theraby -3-treatable precipitating cause -4-diagnosis the cause of cirrhosis

Complication:

1. Renal failure:2type→1-pre-renal

→hepatorenal syndrom

1. Spontenous bacterial peritonitis
2. Infection:from→GIT endoscopy

→injection sclerotherapy

→spontenous

The invasive investigation had bad prognosis.

Hepatorenal syndrom (HRS): 10%of the pt.with advance cirrhosis &ascitis develop HRS. it’s due to sever renal vasoconstriction. 2 clinical types:

1. Type1 HRS(progressive oliguria,rapid ↑in S.creatinine)→poor prognosis. No protien urea&urin Na<10 mmol\d &urin/plasma osmslility ratio>1.5

Rx: I.V albumin +terlipressin.

1. Type2HRS: occur in pt.with refractory ascitis. Charactrized by moderate ↑ in S.creatinine→has better prognosis.

Spontaneous bacterial peritonitis (SBP)

Cirrhotic pt. are very susceptible for SBP. It present with sudden abdominal pain,rebound tenderness,abscent bowel sound+ fever.1/3 of pt.without abdominal signs present with 1-hepatic encephalopathy(HE)

2-fever

Paracentesis →cloudy fliud (WBC>250ₓ10⁶)

Ascitic and blood culture→isolate microorganism (E.coli is the most commone entericorganism).

It must diffrentiated from perforated viscus which by that showing multi organism.

Rx: cefotaxim ,if recurrance→quinolones(ciprofloxacin 250mg or norfloxacin 400 mg/d).

Hepatic (portosystemic) encephalopathy(HE)

Is a neuropsychiatric syndrom caused by liver disease which progresses from confusiob to coma. HE due to biochemical disturbance in brain function &it’s reversable (no pathological change).HE need→liver failure

→portosystemic shunt

Biochemical neurotoxins →nitrogenous substance from GIT ,ammonia , ɣaminobutric acid,octapamine aminoacid,mercaptans,fatty acid

Factors precipating HE:

1-drug(sedative,anti-depressant)

2-dehydration(diuretic,paracentesis)

3-↑protien diet ,GIT bleeding

4-hypokalemia

5-infection

6-protosystemic shunt

7-truma (surgry)

Clinical assesment:include change in intellegance,personality, emotions,conciousness with or without neurological signs. Early feature mild &easily overlooked but in serious cases apathy,confusion,slurred speech,disorentation,convulsions, flapping tremor,babinski +, hyper reflexia..but HE rarly cause focal signs. Fetor hepaticus(mostly due to protosystemic shunt).sweet odour to breath.rarly chronic HE give rise to cerebral dysfunction,parkinsonian synd.,spastic paraplegia &dementia

Clinical grading:I,II,III,IV

Investigation:1-clinical is essential -2-EEG:slow alpha wave,delta wave appear -3-↑↑arterial ammonia (not of diagnostic value)

Management:HE usully reversable

1-Remove precipitating causes

2-suppress neurotoxin production by bacteria

3-dietary protien restriction(rarly needed &not recommended)

4-Lactulose 15-30 ml 8 hr→reduce colon pH .the does ↑↑ untile bowels moves 2 times/day (lactitol ia an alternative)

5-neomycin 1-4 g 6hr.→reduce the bacterial content in the bowel

6- refractory HE is the main indication for liver transplantation.

Acute liver failure (ALF)

Sudden sever impiarment of hepatic function occuring within 8 wks.of onest of the precipitating illness,in the absence of evidence of pre-exist liver disease characterize by mentalchange(HE)

classification→hyperacute<7d→viral,paracetomol

→acute 8-28 d

→subacute 29 d-12 w

Aetiology

1-drugs:70-80%(paracetamol,halothen,anti-TB (INH), herbal medicine)

2-cryptogenic:5-10%

3-viral hepatitis:5%

4-miscelleneous:<5%

5-poisouse:<5%

Clinical assesment:

1. Hepatic encephalopathy is the cardinal menfistation→ reduce alertness,confusion,flapping tremor, behavioral change.
2. Jaundice develop rapidly and usully deep.
3. Cerebrall edema features→abnormally reacting pupils

→hypertension

→bradycardia

→sweating

4-liver &spleen usully normal size

5-presence of ascitis suggest Buddi-chiari synd.

Investigation :used to determine the cause and prognosis

1-screen in blood and urin

2-HBcore IgM Ab is the best screening test+HbsAg

3-PT prolong (done 2times daily).factor five IIV level can be used instead of PT.

4-S.bilirubin

5-careruloplasmin,S.copper,slit-lamp eye examination

6-P.albumin→remain normal unless in prolong cases

7-autoantibody&immunoglobin

8-liver biopsy→contraindicated dueto coagulopathy

9-U\S of liver with doppler of hepatic vein

Management :according to the cause

1-↑↑PT,HE→needed I.C.U

2-Rx of complication

3-conservative Rx N-acetylcysteine therapy

4-Liver transplantation

Complication:1-HE -2-hypoglycemia -3-metabolic acidosis -4-infection -5-renal fialure -6-multiorgan failure

Chronic liver fialure

Also called decompansated liver fialure,it occur when functional capacity of liver can not maintain normal physiological condition &is characterised by 1-HE -2-ascitis.

It’s due to:1-insidious hepatocyte destraction

2-acute on chronic injury (viral,alcohol)

3-↑↑metabolic demand(infection,GIT bleeding)

Clinical feature:

1-worsening hepatic function

2-↑↑PT&↓albumine

3-jaundice

4-portal hypertension,variceal bleeding

5-hepatoencephalopathy

6-ascitis→spontaneous bacterial peritonitis

→hepatic,renal failure

Liver injury occur in >6 month

Chronic liver disease:

-cirrhosis

It’s due to: 1-prolong or recurrent hepatocyte death

2-prolong biliary damage

3-persistent block of venous return

Any condition lead to persistent or recurrent hepatocyte death may lead to cirrhosis

Due to activation of stellate cells→collagen production

→cytokine synthesis

Causes:

1-alcohol -2-viral -3-NAFLD

4-immune (PSC,autoimmune liver disease)

5-genetic (haemochromatosis ,wilson’s disease) -6-cryptogenic

Pathology:progressive hepatocyte death&fibrosis→loss of liver architecture lead to distorsion of vascularity in liver lead to portal congestion&portosystemic shunt leading to formation of nodules(rather than lobules) due to proliferation of surviving hepatocyte. The evolution of cirrhosis is gradual &progressive unless aetiological factor removed(alcohol,hemochromatosis,willson’s disease)

Histological classification:

1-micronodular→small nodules(alcohol)

2-macronodular→larger nodules

Clinical feature:

May be entirely asymptomatic and discover incidently(at surgery).

Non-specific symptoms→GIT symptom ,weakness ,fatigue ,muscle cramps ,weight loss,epistaxis

Other symptoms→hepatomegaly ,jaundice ,ascitis

→palmar erythema,spider telangiectasia

→endocrine changes

→hemorrhge tendency

→portal hypertenion

→HE

→dupuytren’s contracture

Pulmonary-arteriovenous shunt→hypoxia&eventialy cyanosis

Management:

1-Rx the cause

2-maintain nutrition

3-Rx the complication

4-transplantation

Prognosis:poor→depend on:

1-LFT(albumin,bilirubin,PT)

2-causes(alcoholic,wilson’s disease, haemochromatosis, infection)

Laboratory tests give only a rough giude to prognosis.

Detoriated liver function lead to bad prognosis→HE,jaundice, ascitis,↑PT&bilirubin, ↓albumin<30g/L, hyponatriemia

-Portal hypertension(PH)

It’s prolong elevation of portal venous pressure(normal 2-5 mmHg) if the pressure>12mmHg,it’s present with clinical feature or complication

Aetiology &pathogenesis

P.V.H determined by the portal venous flow &portal vascular resistance lead to collateral circulation and proto-systemic shunt.

Classification of PH according to site of obstriction→1-extrahepatic -2-sinusoidal -3-intrahepatic

Causes of PH according to site of abnormality:

1-extrahepatic→post.sinusoidal

→pre.sinusoidal

2-sinusoidal→cirrhosis (90%)

3-intrahepatic→post.sinusoidal

→pre.sinusoidal

Extrahepatic portal vien obstruction is the usual cause of PH in childhood & adolescence while cirrhosis causes 90% of PH in adult in developed countries. Schistosomiasis is the main cause in endemic area.↑↑portal vein resistance lead to ↓↓flow to liver lead to development of collateral vessels allowing portal blood passing to systemic circulation directly ,to esophegus, stomach, rectum,anterior abd.wall, renal, lumber ,testicular vasculture

Clinical feature:they result from portal venous congestion& collateral vessel formation.

Spleenomegaly is the cardinal manfestation (not>5 cm size),hyperspleenism→↓RBC ,↓WBC ,↓platelet

Callateral vessel in the ant.abd.wall

Rectal varices→mistaken with hemorrhoid

Fetor hepaticus→result from portosysremic shunt (mercaptans)

Investigation:

1-radiological&endoscopic examination of upper GIT can show varices

2-U\S show portal hypertension features as collateral vessels, spleenomegaly

3-portal venography→determine the site&cause of portal venous obstruction

4-portal venous pressure masserment

FHVP-WHVP=HVPG

FHVP=free hepatic vien pressure

WHVP=wedge hepatic vein pressure

HVPG= HVP gradient

Complication of PH:

1-variceal bleeding(esophageal,gastric,others)

2-congestive gastropathy

3-hypersplenism

4-ascitis

5-renal failure

6-HE

-Variceal bleeding

Occur from esophageal-gastric junction(within 3-5 cm), or occur from gastric varices

Predisposing factors:

1-size of varices

2-red spot &red strips(by endoscopy)

3-high portal tension

4-liver failure

5-NSAID , aspirin

Mortality reach 50% in pt. with advance liver disease& in sever liver dysfunction

Management of acute variceal bleeding:

1-restore circulation with blood &plasma(priority) as shock↓ liver blood flow& lead to liver detoration

2-confirm source of bleeding by endoscopy to exclude other causes( 20% from gastric erosion)

3-general lines→include:

A-local measure:

1-endoscopic theraby (sclerotherapy or banding)

2-ballon tamponade(sengstaken-blakemore tube)

3-esophageal transection(by stapling gun)

B-reduction of portal venous pressure-2ways:

1-pharmacological Rx→terlipressin(relase vasoconstrictor vasopressin,it reduce portal pressure without systemic effect)

→octreotide(synthetic form of somastatin

2-TIPPS and shunt therapy:used for acute bleeding not response to sclerotherapy and or banding

4-antibiotic(ciprofloxacin)to eradicate sepsis

Prevention:

1-band ligation-more effective than sclerotherapy. PPI used for prophylactic acid suppression

2-sclerotherapy-(largely abandoned)

3-TIPPS-(stent placed between portal &hepatic vein)

4-portosystemic shunt

5-Beta blocker

Primary prophylaxis of initial variceal bleeding→ beta blocker(propanalol or nadalol) are effective as prophylactic band therapy

Congestive gastropathy

Due to long standing PH.

recognize by endoscopy as multipule area of punctate erythema. These area may eroded and bleed from multipule sites,usually minor bleeding repeatadly causes iron D.anaemia ,acute bleeding may occur

Rx:1-iron -2-blood transfusion -3-propanalol to↓↓ portal hypertension 4-TIPPS( if all above fail)

Pulmonary manfestation of chronic liver diseases

1. Hepatopulmonary syndrom:

Cirrhosis causes hypoxia due to pul.hypertension or pleural effusion or hepatopulmonary syndrom.

HPS characterize by resistant hypoxia & intrapulmonary vascular dilatation.

Hypoxia due to intrapulmonary shunt through art-venous comunication,belived result from N.oxide over production