Case Snippets

Infectious mononucleosis presenting as acute hepatitis, with marked leukocytosis and renal involvement

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We report a 45-year-old lady with infectious mononucleosis due to Epstein-Barr virus. The unusual features of this case included a negative heterophile antibody test, marked leukocytosis, renal involvement and jaundice. [Indian J Gastroenterol 2003;22:62]

Key words: Drug reaction, Epstein-Barr virus, sulfasalazine

Infectious mononucleosis (IM) is classically caused by the Epstein-Barr virus (EBV) and is characterized by fever, pharyngitis, generalized lymphadenopathy, headache, myalgia, abdominal discomfort and exantheme rash. Heterophile antibody, a non-specific antibody, is found in 90% of patients with IM. Other causes of IM-like syndrome are cytomegalovirus infection, acute HIV infection, pseudolymphoma, subacute bacterial endocarditis and brucellosis, but in them pharyngitis or tonsillitis does not occur.

A 45-year-old woman presented with high-grade fever, diffuse pain in the abdomen, jaundice, arthralgia and generalized skin rash with severe itching of three days' duration. She had received sulfasalazine for low backache for three days prior to onset of the symptoms. A differential diagnosis of acute viral hepatitis and drug reaction was entertained. On examination, the patient was febrile (40°C) and had tachycardia. Skin examination revealed a morbilliform, maculopapular rash all over the body with relative sparing of the palms and soles. Per abdomen examination revealed hepatospleno-megaly.

Investigations: total leucocyte count 41,000/mL with lymphocytosis (48%) and atypical circulating lymphocytes. Her hemoglobin and platelet count were normal. Serum bilirubin was 3.0 mg/dL with ALT and AST levels of 282 and 231 U/L, respectively. The serum alkaline phosphatase was 1510 IU/L (normal 54-306). Urine examination revealed 8-10 RBCs/HPF and few granular casts; kidney function tests were normal. Ultrasonography showed increased cortical echogenicity of kidneys, maintained cortico-medullary differentiation, hepatomegaly with hypoechoic appearance, thickened edematous gall bladder wall (1.4 cm) and mild splenomegaly. Tests for IgM anti HAV, IgM anti HEV, HBsAg, anti-HCV, ANA, peripheral smear examination for malarial parasites and malarial antigen testing were negative. IgM anti-HBc done later was negative. Bone marrow aspiration was normal.

On the third day of hospital stay, the patient developed oedema and was found to have membranous nephropathy. She also developed cervical and axillary lymphadenopathy. The nodes were less than 1 cm in size, discrete and non-tender. Staphylococcus aureus was isolated on throat swab culture. A strong suspicion of IM-like syndrome was entertained. The heterophile antibody test (latex agglutination slide test, Omega Diagnostics; sensitivity 98%) was negative. IgM anti EBV (ELISA test for viral capsid antigen; IBL Immuno-Biological Laboratories, Hamburg, Germany; sensitivity 98%) was strongly positive for acute infection.

The patient was started on prednisolone 40 mg once a day, and after three days the oedema improved. The itching and skin rash also improved within a week. The leucocyte count and liver function tests normalized after two weeks. Urine examination at this time was normal. After three weeks of steroids she became afebrile.

This case had a few atypical features that need to be highlighted. First, the heterophile antibody test was negative. This test is positive in 90% of patients by the end of the third week; in our patient it was done in the second week. This patient had jaundice, which is seen in only 5% of patients with IM, and her serum alkaline phosphatase was markedly elevated, which led us to rule out acute viral hepatitis. Her total leucocyte count was >40,000/mL. Such a high count has not been reported in IM. Lastly, the patient had evidence of renal involvement, which is very rare in IM.

References

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Massive hepatomegaly: a presenting manifestation of multiple myeloma

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We report a 50-year-old woman presenting with isolated massive hepatomegaly. Liver histology showed dilated sinusoids within which some atypical cells, probably of hematopoetic origin, were identified. Bone marrow was densely packed with similar atypical cells with high nucleo-cytoplasmic ratio, which tested positive for plasma cell markers. Plasma protein electrophoresis

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showed a distinct M spike in the gamma globulin fraction and skeletal survey revealed multiple lytic lesions in the skull and pelvic bones. Thus, a final diagnosis of multiple myeloma was made. The patient has received six cycles of chemotherapy and is doing well. [Indian J Gastroenterol 2003;22:63-64]

**Key words:** Plasma cell

**Multiple myeloma** is a malignant proliferation disorder of plasma cells derived from a single clone. The clinical manifestations are generally due to bone-tissue invasion by the tumor cells and presence of monoclonal immunoglobulins. Bone pain is the most common symptom, affecting nearly 70% of the patients. Other common symptoms include weakness, fatigue, infections, manifestations of hypercalcemia, renal failure and occasionally hyperviscosity. The occurrence of hepatomegaly as a primary presenting feature of this disorder is very rare.

A 50-year-old non-smoking, non-alcoholic, non-diabetic woman presented with sensation of heaviness in the right upper abdomen since 7 months. There was no history suggestive of bowel irregularities or any hepatobiliary disease. There was no history of weight loss, significant anorexia or bone pains. The patient was multiparous and the obstetric history was normal.

On physical examination, she was overweight (body mass index 31 Kg/m²), vital signs were normal and there was mild pallor. Systemic examination was unremarkable except for the presence of massive hepatomegaly. The liver was palpable 12 cm below the costal margin in the mid-clavicular line, firm in consistency, with smooth surface and rounded edge. Splenomegaly, ascites or stigmata of chronic liver disease were absent. A possibility of benign infiltrative disorder was considered; non-alcoholic fatty liver disease was the first diagnosis.

Investigation showed mild anemia (hemoglobin 9.1 g/dL), raised ESR, normal leukocyte count and normal coagulation parameters, normal levels of bilirubin and aminotransferases, but significantly elevated serum alkaline phosphatase (35 KAU/L). Ultrasonography confirmed massive hepatomegaly with diffusely hypechoic pattern suggestive of fatty infiltration. Biliary radicals were normal in caliber and there was no evidence of portal hypertension or free fluid in the peritoneal cavity. Liver biopsy histology (Fig) showed diffuse fatty infiltration of the liver (both microvesicular and macrovesicular steatosis) with dilated sinusoids within which some atypical cells, probably of hematopoietic origin, were identified. Bone marrow aspiration biopsy showed densely packed similar atypical cells with high nucleo-cytoplasmic ratio, which tested positive for plasma cell markers.

Skeletal survey showed multiple lytic lesions in the skull and pelvic bones. Serum protein analysis showed total serum protein concentration of 11.5 g/dL with albumin 4.25 g/dL, α1 globulin 0.46 g/dL, α2 globulin 0.62 g/dL, β globulin 1.24 g/dL, and γ globulin 5.22 g/dL. A distinct M spike was present in the gamma globulin fraction. A final diagnosis of multiple myeloma was made and the patient was treated with chemotherapy cycles comprising melphalan 8 mg/m² and prednisolone 40 mg/m² administered for 5 days every 4 weeks. At present, the patient has undergone 6 such cycles and is doing well.

Unlike the general belief, hepatic involvement is common in multiple myeloma and it may manifest itself in the form of clinical signs (hepatomegaly or jaundice), or abnormal liver function tests or may occur as histological infiltration of liver with plasma cells. Hepatomegaly is the most common clinical manifestation of liver involvement in multiple myeloma; however, a majority have mild to moderate enlargement, which remains asymptomatic. In contrast, in our patient, despite extensive disease, the only presenting feature was due to massively enlarged liver. A review of the literature reveals only isolated cases where massive hepatomegaly has been reported as the primary presenting manifestation. The causes of hepatomegaly in multiple myeloma include myeloma cell infiltration, amyloidosis, myeloid metaplasia, extra-hepatic cholestasis and non-specific etiologies.

Jaundice is present in about 14% of patients. Portal hypertension is extremely rare. Hepatic encephalopathy, feter hepaticus, spider angioma, gynecomastia and other peripheral stigmata of cirrhosis are not seen. Ascites occurs in about 14% of patients and is generally attributed to peritoneal infiltration by plasma cells, co-existing tuberculosis or some indeterminate etiology. ALT and AST are elevated in approximately 60% of patients. The elevations are moderate in a majority. Alkaline phosphatase is abnormal in 40% of patients, being strikingly elevated in 13% of patients. It is the only biochemical marker that correlates with plasmacytic infiltrate of the liver.

Liver biopsy studies show evidence of plasma cell infiltration in about 40% of patients, while this figure increases to more than 50% in necropsy studies. Patients with hepatomegaly are more likely to show myeloma cell infiltration (up to 70%), although it can also be seen in patients without any clinical or bio-

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chemical signs of liver involvement. Histologically, two distinct patterns of hepatic infiltration have been described. In the tumor-forming variant, nodular lesions, about 1-2 cm in size, are distributed throughout the parenchyma. This variety can present as a space-occupying mass on ultrasonographic or tomographic evaluation. In contrast, the diffuse pattern shows flooding of the hepatic parenchyma with myeloma cells. In our patient plasma cell infiltration was of diffuse variety.

Our case report highlights that multiple myeloma can rarely present with isolated massive hepatomegaly.

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Capsule endoscopy diagnosis of ileal angiodysplasia

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A 59-year-old lady presented with iron-deficiency anemia secondary to occult gastrointestinal bleeding, which had needed multiple transfusions over five years. Standard investigations for gastrointestinal bleeding were normal. Capsule endoscopy, a new technique to visualize the small bowel, revealed angiodysplasia in the ileum. Bowel resection was performed. The patient continues to be well two months after the surgery without bleeding or drop in hemoglobin. [Indian J Gastroenterol 2003;22:64-65]

Key words: Gastrointestinal bleed, intra-operative enteroscopy

O bscure or occult gastrointestinal (GI) bleeding is an important cause of iron-deficiency anemia due to chronic blood loss. Despite multiple investigations, sometimes no obvious source of bleeding is found. There are preliminary reports of the use of capsule endoscopy in the diagnosis of obscure gastrointestinal bleeding.1

We report a lady presenting with iron-deficiency anemia due to occult GI blood loss where capsule endoscopy was used to diagnose angiodysplasia. We believe this is one of the first reports from India of the use of capsule endoscopy for diagnosing the source of occult GI bleed.

A 59-year-old housewife was hospitalized with symptoms of weakness, giddiness and palpitations since one month. On examination, she had severe pallor, but was hemodynamically stable. There was no other abnormality on clinical examination. Oral cavity did not reveal any telangiectasia. She had been diagnosed to have iron-deficiency anemia since five years and her hemoglobin had been maintained with blood transfusions at regular intervals. Iron studies had showed serum iron 26 μg/dL, total iron binding capacity 444 μg/dL, transferrin saturation 6.3%. Bone marrow aspiration was normocellular micronormoblastic with erythroid hyperplasia. All these were suggestive of iron-deficiency anemia.

Multiple stool examinations were positive for occult blood through she had no visible blood. Upper GI endoscopy had been negative on multiple occasions. Colonoscopy in another institution had shown suspicious telangiectatic lesions in the ascending colon and these had been injected with dilute adrenaline. However, she continued to drop hemoglobin and repeat colonoscopy did not reveal the same lesions. Small bowel barium study was normal, as was celiac and mesenteric angiogram.

Investigations on admission revealed hemoglobin 4 g/dL, MCV 70 fl, WBC count 11,600/κmm, platelet count 580,000/κmm. Prothrombin time was 14 seconds (control 12) and APTT 40 seconds (control 45). She was given 4 units of packed cells.

Capsule endoscopy (M2A: Given Diagnostic Imaging System, Yoeqam, Israel) was done with a view to assess the small bowel. This showed multiple, scattered, red, flat lesions measuring 3-5 mm, in the ileum (Fig). The ileum was identified by the lack of folds. The total transit time up to the ileo-cecal valve was two and a half hours.

Fig: Capsule view of angiodysplasia in ileum seen in left lower corner

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