A 11-year-old boy presented with high-grade fever with chills and cough for 15 days. Cough was productive with yellowish sputum and streaked with blood. There was no history of vomiting, loose stools, abdominal distension, jaundice or hematemesis. He was a full-term normal-delivery baby with normal milestones.

In January 2004, he was found to be jaundiced and was diagnosed to have autoimmune hepatitis (AIH). At that time he had negative HBsAg, anti-HCV, anti-nuclear antibody (ANA) and liver-kidney microsome (LKM) antibodies; anti-smooth muscle antibody (SMA) was positive (++), serum ceruloplasmin was 44.7 mg/dL, Kayser-Fleischer ring was negative. Liver biopsy showed diffuse lobular disarray, interface hepatitis, porto-portal bridging fibrosis, and moderate activity. Hepatocytes showed features of regeneration with prominent pseudo-rosette formation. Gastroscopy revealed grade II esophageal varices. He was put on prednisolone and azathioprine.

In May 2005, he presented with esophageal variceal bleed. He was treated with endosclerotherapy. On investigation, he was found to have pancytopenia; azathioprine was stopped and prednisolone restarted.

In November 2005, he presented with ascites. Bilirubin was 1 mg/dL, AST 39 IU/L, ALT 127 IU/L, alkaline phosphatase 139 U/L, albumin 2.6 g/dL. The dose of prednisolone was increased to 60 mg/day, and frusemide and spironolactone were started.

On examination, his height was 148 cm and weight 43 Kg. He had cushingoid facies. Pulse was 120 per minute, body temperature was raised and he was pale. He was mildly icteric, with no cyanosis or clubbing. He had a palpable liver just beneath the right costal margin, firm. Spleen was palpable 5 cm below the left costal margin; clinical signs of ascites were doubtful. Cardiovascular system examination was normal. He had reduced breath sounds on the right inter- and infra-scapular regions with bronchial breathing and crepitations.

**Investigations (Table)**

ESR was normal, reticulocytes 4.9%, and malarial parasites were absent on peripheral smear examination. Serum bilirubin and alkaline phosphatase were normal. Sputum culture on two occasions was sterile; sputum smear for acid-fast bacilli was negative. Blood culture, including fungal, was sterile. Urine routine examination was normal. Arterial blood gases showed pH 7.55, pO₂ 64, PCO₂ 31, HCO₃⁻ 26, SPO₂ 89% (January 26) and pH 7.57, PO₂ 57, PCO₂ 33, HCO₃⁻ 29.8, SPO₂ 93% (February 6).

Ultrasoundography showed liver span of 13 cm with enlarged caudate lobe, coarse echotexture, irregular surface; portal vein measured 12 mm in diameter at the porta. Gall bladder and common bile duct were normal. Splenic vein was of normal caliber. Spleen was enlarged, measuring 15 cm. Both kidneys and pancreas were normal. Chest X-ray January 18 showed thin-walled large cyst in the left lower lobe with adjacent consolidation (Fig 1). Five days later, it showed increasing size of the cyst and opacity in the left lung, with multiple small nodular consolidations in the right lung. A week later X-ray showed increasing size of cavity as well as surrounding consolidation, with extensive nodular consolidation of the right middle and lower lobes (Fig 1). CT scan showed bilateral consolidation (nodular infiltrates) with cavitations. Radiological impression: infective condition or vasculitis. The infective causes would include bacterial, nocardial, fungal and tuberculosis, as the child was immune-compromised.

**Management and course in hospital**

Prednisolone (60 mg) and frusemide-spiroloactone (40-

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**Table: Laboratory investigations**

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<th>January 25</th>
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<td>110/3.4</td>
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**Clinico-pathologic conference**

**Macronodular cirrhosis and fever in a boy**

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100 mg) were continued. He was also started on anti-tubercular therapy on 3rd day, comprising ciprofloxacin, ethambutol and streptomycin. Steroid was tapered on the 5th day to 10 mg per day. High-grade fever persisted, with increasing lung shadows on X-ray. Ciprofloxacin was replaced by levofloxacin on the 7th day. Cefotaxime and amphotericin-B were added on the 16th day. He continued to have high fever and developed renal failure. Streptomycin was stopped and amphotericin-B was adjusted to renal doses. He succumbed to his illness after an episode of seizure followed by cardiac arrest.

Unit’s final diagnosis
Autoimmune hepatitis, decompensated cirrhosis of liver, portal hypertension, renal failure, ?intracranial bleed, pneumonia (?tubercular, ?fungal)

Discussion
Clinical protocol (Dhiman)
The underlying etiology for the liver disease could be viral (hepatitis B and/or C), autoimmune hepatitis (AIH), cholestatic liver diseases like primary sclerosing cholangitis (PSC) or primary biliary cirrhosis, overlap syndromes, metabolic disorders like Wilson’s disease, hemochromatosis or alpha-1 antitrypsin deficiency. Inborn errors of metabolism like defective carbohydrate, protein or lipid metabolism could also lead to chronic liver disease in a child. The most likely causes are AIH type 1,2 PSC and overlap syndromes.

Overlap of AIH and PSC is seen frequently in children, but histological features of sclerosing cholangitis were not present in the biopsy. Besides, features of cholestasis and inflammatory bowel disease were absent, and there was poor response to immunosuppressive therapy.

The other major problem was the pulmonary disease. Conditions that could produce cavitatory lesion include infection by anaerobic or gram-negative bacteria, Staphylococcus aureus, Pseudomonas aeruginosa, mycobacterium tuberculosis, nocardia, fungi, or thromboembolus from infective endocarditis; and non-infective conditions like Wegeners’ granulomatosis, bronchiolitis obliterans, neoplasms or pulmonary infarct.

The most likely conditions would be rapidly developing pulmonary tuberculosis with nocardiosis. Impaired cell-mediated immunity has been observed in patients receiving low doses of prednisolone; higher incidence of tuberculosis has been documented with increasing doses. In our experience in 143 patients on steroid, 7 (4.9%) developed tuberculosis (pulmonary 6, meningitis 1).3 Nocardia is known to infect the lungs, brain and skin. According to one report, corticosteroid administration was the commonest risk factor in 74% of patients infected with nocardia.4 Cancer patients receiving steroid had significantly higher incidence of nocardial infection than those receiving chemotherapeutic agents.5 Newer immunomodulating drugs have led to a reduction in corticosteroid use, thereby reducing the frequency of nocardial infection. Long-term steroid use would also be an ideal setting for fungal infection of the lungs. Clinical as well as the radiological features would suggest either aspergillosis or mucormycosis.

My final diagnosis would be decompensated cirrhosis of liver (etiology AIH type 1) with pneumonia with cavity formation (aspergillus, nocardia spp., M. tuberculosis or mucormycosis).

Nathkarni: The child did not improve on anti-tubercular therapy, amphotericin B and antibiotics.
Dutta: A possibility of cytomegalovirus infection of the lung needs to be considered, but the presence of cavitation and nodular consolidations would be unusual features.
Chakrabarti: We could also consider histoplasmosis leading to abscess formation in the lung parenchyma.
Singh: AIH is unlikely to be associated with hyaline sclerosis of the biliary tree.
Aggarwal: I had considered a possibility of bacterial pneumonia with abscess formation.
Thapa: We do not know about his compliance with treatment. He was an orphan who was living with his grandmother and also working as part-time household helper.
Pathology protocol

The initial liver biopsy specimen showed distortion of the lobular architecture as indicated by portoportal and porto-central bridging fibrosis. The portal tracts are enlarged and irregular with moderate mixed inflammation consisting of lymphocytes, plasma cells and few eosinophils. The inflammatory cells were spilling into the adjoining hepatic parenchyma, causing interphase hepatitis (Fig 2). Multiple foci of lobular inflammation were present. Hepatocytes show evidence of regeneration in the form of pseudo-acinar formation (activity grade 3, fibrosis stage 3). Immunostains for hepatitis B surface and core antibodies were negative. Because the serum tested positive for smooth muscle actin antibody, the features were reported as consistent with AIH.

At autopsy, excess of yellow colored fluid was present in the peritoneal cavity (>500 mL). Both pleural and pericardial cavities were normal.

Lungs were grossly overweight, weighing 890 g. Pleura showed patches of thickened areas of fibrin tags. The lung parenchyma looked variegated. Both lungs were firm and had large areas of consolidation and multiple pale nodular areas ranging in size from 1 to 5 cm. These nodules were merged to each other, forming larger geographic areas of pale necrotic foci. A few nodules were projecting above the cut surface. The left upper and middle lobes towards the hilar region showed a large cavity measuring 7 cm x 6 cm x 5 cm. This cavity had irregular margin and contained pale necrotic material with no definite fibrous wall. The tracheobronchial tree showed patches of congested mucosa (Fig 3). The hilar and carinal lymph nodes were grossly enlarged, measuring 1 to 2 cm. Cut sections of the lymph nodes looked pale and homogenous. Histology of the lung sections showed confluent acute necrotizing abscesses in the background of bronchopneumonia. The wall of the abscess showed dense acute inflammatory cell infiltration with degenerated cells, nuclear debris and necrotic material.

H&E-stained sections did not reveal any organisms. Special stains for gram-positive organisms, PAS for fungi and Ziehl-Nielsen for acid-fast bacilli failed to reveal any organism. Crushed smear from the necrotic material stained with silver methanamine Grocott’s stain showed long filamentous structures with branching organisms with beaded appearance (Fig 4). The morphology of these organisms was consistent with that of nocardia.

Liver weighed 840 g. It looked pale and nodular. The liver parenchyma was replaced by nodules ranging in size from 0.5 cm to 5 cm, separated by thick fibrous septa. The caudate lobe appeared enlarged and was also completely replaced by nodules. In some of the nodules, the central areas were hemorrhagic. The portal vein was dilated. Inferior vena cava, main hepatic veins and biliary tree were normal. Microscopy confirmed the presence of regen-
erative nodules separated by fibro-vascular septa. The extent and degree of inflammation in the autopsy liver was much less compared to the biopsy done two years before. Moderate amount of lympho-mononuclear cells present were restricted to the portal tract and fibrous septa (Fig 5). There was no inter-phase hepatitis or significant lobular inflammation. The fibrous septa showed dense collagenization. Portal tracts also showed mild to moderate bile ductular proliferation. Immunostains using antibodies against hepatitis B surface and core antigens and alpha-1 antitrypsin were negative. Special stains for demonstration of iron pigment and copper-binding proteins were negative. Copper estimation in the autopsy liver showed level of 16 mcg/g of wet liver tissue (normal 15-20). There was no Mallory’s hyaline or PAS-positive globule. Biliary tree looked well preserved. Fresh hepatocyte necrosis was seen in the areas corresponding to the central congested areas of the regenerating nodules, with sinusoidal dilatation, which is a well-known pre-terminal change in shock.

Western blot analysis and indirect immuno-fluorescence examination on the serum sample (1:80 dilution) from the first hospital admission had revealed bright hairy fluorescence for F-actin using Hep-2 cell line (Fig 6). Anti-F-actin is an autoantibody to the actin microfilaments of cell cytoskeleton, and has a sensitivity of 80% and specificity of approximately 100% in AIH.

Spleen weighed 320 g and had firm consistency. The capsule was thickened. Microscopy revealed capillarization of the sinusoids with depletion of white pulp. Stomach and esophagus appeared grossly normal and did not reveal any varix on gross examination. Microscopy revealed congested dilated veins in the submucosa of the esophagus and stomach. Bone marrow section showed hypocellular marrow with paucity of megakaryocytes. The erythroid and myeloid series were adequately represented. Rest of the organs examined were essentially normal.

Final autopsy diagnosis

A treated case of AIH with decompensation with
· Macronodular cirrhosis with portal hypertension
· Bilateral extensive necrotizing nocardial abscesses with confluent bronchopneumonia
· Hypocellular bone marrow – drug-induced

Discussion

Thapa: The sputum culture report received following the child’s demise showed nocardia.
Ray: In routine sputum culture nocardia may be present as commensals. The difficulty in demonstration of nocardia in paraffin sections could be related to fixation.
Gupta: If the terminal events were related to bacterial infection, and the child was in hospital for more than three weeks, there would have been organization and walling off of the abscess cavities. Could we try to age the pulmonary abscess?
Saikia: It was fascinating to see a beautifully bright stain on indirect immunofluorescence for the F-actin. Usually bright positivity is seen with fresh serum sample, and not with old sample.
Vaiphei: There is nothing specific or diagnostic on histology for AIH; similar features could also be seen in many other causes of hepatitis. Positive serological studies are an essential parameter for the diagnosis of AIH.
Dhiman: The child was in a terminal state of illness. He was receiving various broad-spectrum antibiotics including anti-tubercular therapy. He was malnourished and had decompensated chronic liver disease. He had been receiving steroid and was immunocompromised. Hence, his response to various treatment modalities would not be similar to that of a child who is in better state of health.
A 37-year-old woman presented with a scalp swelling for one month. She also had headache, vomiting and weakness. On examination, there was a huge globular swelling involving the entire forehead, non mobile, with smooth surface with prominent vessels, ulcerated in some parts, non tender, non pulsatile and associated with proptosis and chemosis of the right eye (Fig A). She had marked pallor and hepatomegaly. Rest of the examination was normal.

Investigations: hemoglobin 6 g/dL, bilirubin 1.3 mg/dL, alfa-fetoprotein 242,585 ng/mL, HBsAg negative. CT brain showed a large destructive lesion involving the right side of head predominantly, with extra- and intracranial extension (Fig B). CT scan of abdomen showed hepatomegaly with multiple hypodense lesions and ascites. FNAC from the scalp swelling showed metastatic carcinoma cells and liver biopsy was suggestive of hepatocellular carcinoma. Patient was started on supportive care but succumbed to the disease three days later.

Hepatocellular carcinoma (HCC) presenting as metastases is relatively uncommon. Metastasis of HCC mostly involves the lungs (34%-70%), lymph nodes (16%-45%), bone (6%), and adrenal gland.1 Swelling on the forehead as a presenting feature is very rare.

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Reference