Nodular Regenerative Hyperplasia of Liver-A Rare Cause of Portal Hypertension in Patients of Rheumatoid Arthritis


Abstract
Nodular regenerative hyperplasia of liver (NRHL) is a rare entity and is infrequently associated with collagen vascular disease. Clinically patients present with recurrent abdominal pain, non-specific symptoms of underlying systemic disease and signs of portal hypertension. This entity is usually diagnosed by MRI and liver biopsy. Prognosis is usually good.

Introduction
Nodular regenerative hyperplasia is a rare entity and generally is encountered in association with collagen, hematologic, metabolic and endocrine diseases. Clinical presentation includes recurrent abdominal pain, nonspecific systemic symptoms and signs of portal hypertension such as ascites, bleeding esophageal varices or splenomegaly.

Diagnosed by MRI and liver biopsy. As with other forms of noncirrhotic hypertention, the prognosis is usually better than that of patients with portal hypertension due to cirrhosis. Portal diversion is useful in relieving symptomatic portal hypertension.

Case Report
A 35 year old female, a known case of rheumatoid arthritis, presented with progressive fullness of abdomen since the last one year, fever with chills and rigor and severe toothache for the last 10 days. Presently there was no history of joint pain, swelling, skin rash, jaundice, vomiting, abdominal pain or any other systemic complaint. Clinical examination showed patient was febrile with the temperature of 101°F with tachycardia. Patient was severely pale, with a swan neck deformity in both the hands and a dental abscess. Abdominal examination showed splenomegaly, 14 cm from costal margin, without hepatomegaly and free fluid. Investigation showed Hb 7.8 gm%, Total WBC count 1200/cumm, Total platelet count 85,000/ cumm. Peripherial smear examination showed neutrophil 57%, lymphocyte 36%, eosinophil, 7%. There were no abnormal cells and the platelets were reduced on smear. Bone marrow biopsy showed reactive hyperplasia of all three cell lines, otherwise normal study. Anti-CCP(Cyclic citrullinated peptide) antibody was positive. Rheumatoid factor and anti cardiolipin antibody were negative. Liver function tests showed, total protein 6 gm%, serum Albumin 3% gm, total bilirubin 0.6 mg%, direct 0.1 mg%, AST 38 IU, ALT 24 IU, ALP 255 IU and prothrombin time13 sec with an INR of 1.3. Doppler ultrasound showed, liver was 11 cm with altered echotexture, spleen 25 cm with dilated portal vein and absent phasicity. Upper G I endoscopy upto second part of duodenum was normal. Viral and auto-immune markers were negative with serum ceruloplasmin of 36.

MRI of Abdomen
Findings in MRI of abdomen were as shown in Figs. 1 and 2.

Liver Biopsy (Fig. 3)
Nodular Regenerative Hyperplasia (NRH), Regenerating nodules but absence of fibrous septa HE stain 100x.

With all this clinical information and investigation a final diagnosis of rheumatoid arthritis with nodular regenerative hyperplasia of liver with portal hypertension and splenomegaly with hypersplenism and dental abscess was made and the patient was treated with tooth extraction and antibiotics. She was alright after 10 days of therapy. She is on regular follow up and she has no recurrent infection. She has been told that she may require elective splenectomy for hypersplenism.

Discussion
Nodular regenerative hyperplasia is a rare entity and generally is encountered in association with other diseases like collagen diseases (rheumatoid arthritis, Felty syndrome, progressive systemic sclerosis, systemic lupus erythematous, polymyalgia rheumatica, polyarteritis nodosa), hematologic diseases (myeloproliferative disorders, lymphoproliferative disorders, idiopathic thrombocytopenic purpura), glomerulonephritis, metabolic diseases, endocrine disorders (lymphocytic duodenitis, diabetes mellitus) and lymphomas.34 It has an equal predilection in both sexes and can occur in all age groups and races. The disease can be described as hepatocellular nodule formation.
It may mimic hepatic cirrhosis and benign or malignant neoplasms of the liver. The possible complications of the disease include hepatic failure, rupture of the liver and malignant transformation.

Clinical presentation includes recurrent abdominal pain, nonspecific systemic symptoms of underlying systemic disease, signs of hypersplenism (splenomegaly or hematologic abnormalities) and signs of portal hypertension such as ascites, bleeding esophageal varices or splenomegaly. Wanless et al in a study of 64 cases, suggested that NHRL is a secondary and nonspecific tissue adaptation to heterogeneous distribution of blood flow and does not represent a specific entity. According to Cesar et al., patients with NRHL can be divided into three groups: (a) those presenting with hepatomegaly or splenomegaly; (b) those with a history of drug therapy and (c) those in whom NRHL appears to have no clear cause. Dachman et al. stated that NRHL, also known as nodular transformation, is characterized histologically by diffuse involvement of the liver with hyperplastic nodules, composed of cells resembling normal hepatocytes. The nodules range in size from smaller than a hepatic acinus to conglomerate nodules forming large masses. Portal areas may be trapped within the nodules. No significant fibrosis is found either in or around the nodules, which is an important feature distinguishing NHRL from cirrhosis and from focal nodular hyperplasia of the liver. Large nodules, viewed out of context of the diffuse nodularity, can mimic hepatocellular adenoma histologically. Thus, limited sampling by needle biopsy may yield a false diagnosis of hepatocellular adenoma or normal liver. The radiologic features of NRHL reflect its composition of cells resembling normal hepatocytes and Kupffer cells (presenting within or between the nodules), the tendency for large nodules to bleed and the presence of portal hypertension. Patients with NRHL may be asymptomatic or may present with idiopathic portal hypertension with varices, splenomegaly, or ascites which is evident radiologically. As with other forms of noncirrhotic hypertension, the prognosis is usually better than that of patients with portal hypertension due to cirrhosis.

Portal diversion is useful in relieving symptomatic portal hypertension. In conclusion, the diagnosis of NRHL can be made during physical examination, radiologically, or while investigating other diseases. Early treatment is important in the prevention of the development of complications. In cases with compatible findings, multiple needle biopsies, a laparoscopically guided needle biopsy or preferably an open wedge biopsy should be taken in order to arrive at an accurate diagnosis. References

Tongue Histoplasmosis Mimicking Malignancy

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Abstract
A 42 year old male presented with progressive difficulty in swallowing for the past 6 months. Oral examination revealed ulcer on right dorsum of tongue, which was mistaken for malignancy. Histopathology of incision biopsy specimen diagnosed it as histoplasmosis. The patient was put on oral itraconazole therapy and responded well to the treatment.

Introduction
Histoplasmosis, a chronic granulomatous fungal infection, also known as Darling’s disease, named after Darling who first described this clinical entity well in details.1 Histoplasmosis is endemic in central states of United States principally Ohio and Mississippi river valleys. In Indian literature first case of histoplasmosis was reported by Panja and Sen in 1954.2 In Indian subcontinent eastern states like west Bengal are considered endemic. Few cases have also been reported from southern India.3

Mucosal lesions of upper aerodigestive tract by histoplasmosis are not a common phenomenon. Moreover these lesions also mimic carcinoma, so a high index of suspicion must be kept in non endemic areas to reach at diagnosis of histoplasmosis. An immunocompetant individual with suspected tongue base malignancy that eventually diagnosed as histoplasmosis is reported here.

Case Report
A 42 years old male presented with complaints of progressive difficulty in swallowing for the past 6 months. There was no history of fever, prostration, cough, weight loss or bleeding from the mouth. He was chronic smoker for the last 20 years using approximately 2 packs per day. On examination a tender 2 X 2 cm ulcer with heaped up edges was noticed on the right dorsum of tongue (Fig. 1). Indirect laryngoscopy and lymph node examination was unremarkable. As patient had history of chronic smoking, ulcer seemed to be a malignant one. Incisional biopsy taken and submitted for histopathology revealed stratified squamous epithelium covered soft tissue. Subepithelial tissue showed large number of foamy macrophages filled with yeasts of fungii (Fig. 2). Gomori’s methenamine silver stain was positive. Diagnosis of histoplasmosis was kept most favourable. After which patient was investigated for any factor in his body compromising his immunity, but all investigations was with in normal limits. X ray chest didn’t reveal any sign of histoplasmosis in lungs and mediastinum. Oral itraconazole therapy was started and followed up. On 3 month follow up ulcer had disappeared completely (Fig. 3) and patient was relieved of symptoms.

Discussion
Histoplasmosis is caused by histoplasma capsulatum, a dimorphic fungus which exists in soil in the mycelial form but converts in yeast when exposed to the higher temperatures of the human body. Soil from chicken houses or from areas contaminated by bat or bird faeces is especially rich in histoplasma capsulatum organism.4

Human and animal infection is caused by inhalation of fungus in dust. Size of inoculum and immune status of the individual determine degree of infection and clinical presentation. Histoplasmosis infections have been classified in two categories pulmonary histoplasmosis and disseminated histoplasmosis. Pulmonary histoplasmosis occurs in patient with normal cellular immune mechanism while disseminated form manifests in patients whose cellular immune mechanism is compromised either by intercurrent malignancy, long term corticosteroids therapy, immunosuppressant drugs, or AIDS infection, thus incapable of killing the fungus.5

Head and neck manifestation of histoplasmosis occur primarily in patients with disseminated diseases and can be the only presenting symptom. Chronic disseminated disease has minimal systemic involvement and a tendency to develop more destructive and focal lesions and is characterised by mucosal lesions of upper aerodigestive tract. Oral involvement is seen in 30% to 50% cases; tongue, palate, and buccal mucosa being the frequently involved sites. Very rarely local oropharyngeal and laryngeal lesions are the primary and the only presenting sign as documented in our case.6 Clinically mucosal histoplasmotic lesions are seen as firm, painful ulcers with heaped-up edges suggesting malignancy. Proliferating lesions with a verrucous or plaque like appearance may be seen in the early stages: however, central ulceration occurs in untreated lesions. Laryngeal involvement has characteristic anterior located lesions in comparison to tuberculosis where posterior larynx is commonly involved. Sore throat, painful mastication, hoarseness, gingoial irritation and dysphagia are common presenting complaints of oropharyngeal histoplasmosis.7 Constitutional symptoms like fever, night sweats, and fatigue are relatively uncommon. The histoplasmotic lesions in the oral cavity, pharynx and