associated with an increased risk of medullary thyroid cancer. This cannot be considered as a risk for humans, as the experimental drug exposure level in rodents were many times higher than used in humans. The FDA expects to learn more about the drug’s safety from the post approval studies and clinical trials.

While the exact mechanism by which the GLP-1 mimetic therapy causes pancreatitis is still unclear, plausible hypotheses have been put forth by several studies. These are reviewed by Butler et al. A potential mechanism of ductal replication rates as found in obesity and type 2 diabetes is proposed. Pancreatitis may be initiated at the level of acinar cells or ductal cells. Aberrations in acinar-ductal systems can lead to local inflammation and acinar cell death and the consequent release of cytokines may trigger signals for chronic pancreatitis. GLP-1 therapy is reported to activate regenerative efforts in the pancreatic ducts with increase in duct cells positive for the transcription factor Pancreatic and duodenal Homeobox-1 (PDX-1). GLP-1 based therapy may also induce pancreatitis by its actions of altering enzyme secretions.

Animal experiments have demonstrated that GLP-1 receptor activation increases pancreatic mass and modulates the expression of genes associated with pancreatitis. Further studies are warranted to know whether GLP-1R activation modifies gene expression, enzyme secretion or inflammation in human pancreas.

The temporal relationship between the initiation of Liraglutide and the onset of symptoms of pancreatitis, and the resolution of symptoms and normalisation of laboratory parameters upon its discontinuation clearly indicates a causative role for the drug. Clinicians should use incretin – based therapy cautiously in patients with history of pancreatitis.

References


Disseminated Cryptococcosis with Caverno-Oesophageal Fistula in a Case of Idiopathic CD4+ T-Lymphocytopenia


Abstract

Idiopathic CD4+ T-Lymphocytopenia is a rare immunodeficiency disorder characterised by significantly low absolute CD4 lymphocytes in absence of any viral infections. We present a case of Disseminated Cryptococcosis with Caverno-
Oesophageal Fistula in a case of Idiopathic CD4+ T-Lymphocytopenia. 29 year old lady was referred to Institute in view of lung mass not responding to anti-TB treatment. Subsequently patient had developed headache. Radiological evaluation showed presence of ring enhancing lesion in the occipital region. On evaluation with Fibre-optic bronchoscopy, there was no evidence of malignancy or tuberculosis. Sputum showed presence and growth of Cryptococcus neoformans. Patient’s investigations were negative for virus infection. with normal immunoglobulin levels. Her CD4 counts were 129 cells/mm³. Patient was treated with injectable antifungals. Patient developed a Caverno-oesophageal fistula which was confirmed on endoscopy and radiology. Patient was managed with percutaneous jejunal feeding (PEJ). Patient improved symptomatically with CD4 count of 475 cells/mm³.

Background

Idiopathic CD4 lymphocytopenia (ICL) was defined by the United States Centers for Disease Control and Prevention (CDC) as a clinical condition in patients with depressed number of circulating CD4 T lymphocytes (< 300 cells/μl or < 20% of total T cells) at a minimum of two separate time points at least 6 weeks apart, with no laboratory evidence of infection with human HIV-1 or HIV-2, and the absence of any defined immunodeficiency or therapy associated with depressed levels of CD4 T cells. ICL is rare disorder characterised by opportunistic infections similar to that seen in HIV patients. Reduced immunoglobulins favour diagnosis of CVID. The disease should be suspected in presence of opportunistic infections in a non-HIV individual. Unlike congenital immunodeficiency disorders, this disease presents with onset from the third decade onwards. Remarkably, the patients have developed well without any previous illnesses in childhood.

Clinical Details

29 year old lady presented to the Chest OPD in this Institute for right upper lobe mass not responding to anti-TB treatment. She presented with chief complaints of right sided chest pain and cough. Patient was evaluated in the local hospital with radiology suggestive of right upper lobe mass (Figure 1). Fibre-optic Bronchoscopy revealed granulomatous infection. She was started on Anti-TB treatment (conventional 4 drug therapy) following which patient had deranged liver enzymes. She was started on hepatosafe anti-TB drugs.
However, in view of clinico-radiological deterioration, patient underwent CT guided biopsy which was suspicious of malignancy and hence she was referred to tertiary care institute for diagnosis.

At presentation, patient was afebrile with normal vital parameters. Her respiratory system examination revealed few rales on the right infra clavicular region. Rest of the systemic examination was normal. On admission to our institute, her hepatosafe anti-TB treatment was continued. A fibre-optic bronchoscopy was repeated that revealed unhealthy mucosa in the right upper lobe. Washings from the right upper lobe revealed presence of fungal hyphae. There was no evidence of tuberculosis or malignancy. Patient was given a course of anti-fungals (Fluconazole) for a period of 1 month along with hepatosafe anti-TB treatment. Patient improved in terms of symptoms and weight gain. Patient subsequently followed up after a month with pain in the neck, headache and increased cough. There was radiologic increase in the size of the lesion. Sputum was curdy white and increased in quantity. Sputum examination revealed Cryptococcus in India ink preparation. Her CT scan of the neck and brain revealed direct local invasion of the right upper lobe lesion into the adjacent cervical vertebra. There was another ring enhancing lesion in the occipital region about 2 cm in diameter (Figure 2). Patient was evaluated with various investigations for evaluation of immunosuppression. Her HIV tests were negative (ELISA and Western Blot). Epstein Barr antibodies and HTLV reports were negative. She was evaluated with CD4 counts which were 129 cells/mm$^3$. (Normal: 486 to 1250 cell/mm$^3$). Her immunoglobulin levels were normal. Thus, a diagnosis of Idiopathic CD4+ T-Cell Lymphocytopenia (ICL) was made.

Patient was started on Liposomal Amphotericin B (3 mg/kg/day) through a central line for a period of 42 days. Serial electrolytes and creatinine was monitored. Patient improved symptomatically followed by 6 months course of oral fluconazole (prophylaxis). During the subsequent follow-up visits, patient complained of cough while eating food with episodes of food particles in the sputum. Patient was evaluated with CT scan Chest and Abdomen (Figure 3) and barium swallow (Figure 4) suggestive of oesophageal-cavernous fistula. This was also confirmed on upper gastro-oesophageal endoscopy and fibre-optic bronchoscopy showing upper lobe bronchus opening showing salivary secretions. Patient subsequently underwent PEJ (percutaneous endoscopic feeding jejunostomy) as she was unable to take orally. Presently patient has improved symptomatically. She has gained 2 kg of weight and her CD4 count has improved to 475 cell/mm$^3$.

**Discussion**

Disseminated Cryptococcosis is a common manifestation in HIV infected individuals – especially those who have progressed to AIDS stage (CD4 cells - 75-125/mm$^3$). However, when a patient gets infected with Cryptococcosis with serum non-reactive to HIV – a strong possibility of Isolated CD4 T-Cell Lymphocytopenia (ICL) must be kept in mind. The other differential is common variable immunodeficiency (CVID). These two diseases can be differentiated by serum immunoglobulin levels. This must be differentiated from common variable immunodeficiency (CVID) wherein along with the CD4 counts even the serum immunoglobulin levels are significantly reduced.

ICL is a rare disorder characterised by low absolute CD4 lymphocyte counts in the absence of obvious causes of immunosuppression. Remarkably, ICL patients are apparently alright till the 2nd to 3rd decade of their life without symptoms. They are usually diagnosed after they are admitted for opportunistic infections. The above patient presented to us at the age of 29 years. She was asymptomatic till this age requiring no medical consultation. Although pulmonary cryptococcosis is less common than meningitis in AIDS patients, respiratory route is likely portal of entry. It is likely that cryptococcal pneumonia is under diagnosed and not recognised until dissemination. Patients with pulmonary cryptococcosis may present with cough, fever, malaise, shortness of breath, and pleuritic pain. Physical examination may reveal lymphadenopathy, tachypnoea, or rales. Chest radiographs typically reveal focal or diffuse infiltrates. Our patient presented with mass like appearance on radiology which was mistaken for tuberculosis or neoplastic aetiology. It is even more difficult when results of HIV are non-reactive.
Teenager Male with Burning Pain in Extremities – Suspect Fabry Disease, 2 Case Reports

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Abstract

Introduction: We present 2 cases of teenager males presented with burning pain in extremities and turned out to be cases of Fabry disease. The purpose of presenting this case is to highlight the fact that suspicion of Fabry disease in patients presenting with these symptoms will lead to early diagnosis and treatment of this condition before occurrences of complications.

Case Report 1: A 14-year-old male presented with severe burning pain in both hands and feet since last 4 yrs which persisted despite consumption of painkillers and becoming more disabling and without having any family history for such condition. On general examination patient had small reddish coloured lesions around the umbilicus, appearing like angiokeratomas. Skin biopsy confirmed the lesion. On enzyme assay his alpha galactosidase activity found to be ‘0’ nmol/hr/mg of protein, confirming his diagnosis. Patient’s creatinine and 2 D ECHO were normal and urine had 1+ proteinuria. Patient started on carbamazepine tablets for pain and referred to higher centre for genetic diagnosis and enzyme replacement therapy.

Case Report 2: An 18-year-old male referred to our hospital by general practitioner for fatigue and pedal oedema with deranged renal function tests. On history taking patient gave history of severe burning pain in both hands and feet since age of 9 yrs. Patient’s general examination revealed hypertension with pallor, pedal oedema along with angiokeratomas in bathing suit distribution. Patient’s ultrasonography of kidney revealed bilaterally normal sized kidneys with altered echotexture and urine examination showed fine granular foamy cells with sub nephrotic range proteinuria. 2 D ECHO revealed concentric left ventricular hypertrophy. Skin biopsy report supported the diagnosis of Fabry disease. Patient advised to undergo renal biopsy to confirm Fabry nephropathy but patient denied any further diagnostic workup for nephropathy or Fabry disease. Patient started on conservative treatment and carbamazepine in renal dose given for acroparaesthesias. On discharge patient has been advised to visit higher centre for further diagnostic work up and enzyme replacement therapy.

Conclusion: Suspicion of Fabry disease in teenager males presenting with symptoms of burning pain in extremities may lead to early diagnosis and treatment of this condition before occurrences of complications.

Introduction

Fabry disease is X linked lysosomal storage disease. It results from deficiency of enzyme alpha galactosidase and causes lysosomal deposition of globotriaosylceramide in cells throughout the body. It has its onset in childhood with severe pain in extremities (acroparaesthesias). It is associated with vascular cutaneous lesions (angiokeratomas), hypohidrosis, characteristic corneal opacities (cornea verticillata) and proteinuria which in untreated patients progress to end stage kidney disease. Cardiovascular and...