Rheumatoid Arthritis in a case of Primary Biliary Cirrhosis - An unusual Association

Subrata Chakrabarti, Koushik Pan

1&2 Post graduate Trainees, Department of General Medicine, IPGMER& SSKM Hospital, Kolkata, India.

ABSTRACT
Primary biliary cirrhosis is an autoimmune disease that tends to progress to fibrosis and cirrhosis with hepatic failure. Primary biliary cirrhosis is often associated with other non-hepatic autoimmune diseases. A rare association with rheumatoid arthritis is found to coexist in 3-5% of patients with primary biliary cirrhosis. B cells seem to play a major role in the pathogenesis of both rheumatoid arthritis and primary biliary cirrhosis. We describe the case of a 46 year old man with severe erosive rheumatoid arthritis and primary biliary cirrhosis treated with rituximab. He was treated with rituximab.

KEYWORDS: Primary biliary cirrhosis, rheumatoid arthritis, rituximab.

INTRODUCTION
Primary biliary cirrhosis (PBC) is an autoimmune disease characterized by chronic destruction of bile ducts that can lead to liver cirrhosis. It can be accompanied or preceded by various autoimmune disorders [1] like Sjögren’s syndrome [2], autoimmune thyroid disease , and systemic sclerosis [3]. The association of PBC with rheumatoid arthritis (RA) is exceptional, and the true prevalence of PBC in RA is not well known [4]. In both diseases, B cells play a prominent role in pathogenesis [5]. We describe an unusual case of a patient with PBC and RA treated with rituximab.

CASE REPORT
A 46 year old male presented to the Out Patient Department (OPD) of SSKM hospital with an inflammatory, deforming polyarthritis of both his small and large joints. Morning stiffness was present. Physical examination revealed swollen, painful joints with restriction of mobility with accompanying synovitis in bilateral wrist, metacarpophalangeal , proximal inter-phalangeal and knee joints with accompanying synovitis in those joints. No axial involvement or nodule was present, however, bilateral ulnar deviation hand deformities, Z-thumb deformity; swan-neck and boutonniere deformities were noticed. Rest of the systemic examination was non-contributory. He was diagnosed with Primary biliary cirrhosis (PBC) 5 years back. The diagnosis was based on characteristic liver biopsy along with high levels of alkaline phosphatase (5 times the upper normal limit) and gamma-glutamyltransferase (4 times the upper normal limit); positive type 2 anti-mitochondrial antibodies (1:320). He was being treated with ursodeoxycholic acid (UDCA) at a dose of 12mg/kg (500mg/day).

Laboratory tests showed normocytic, normochromic anemia. Erythrocyte sedimentation rate was raised (66mm/first hour), and so was C-reactive protein level (17mg/L). Alkaline phosphatase, gamma-glutamyltransferase were still raised. Renal function tests were normal. Rheumatoid factor was positive at high titre (1013U/L), and also anti-citrullinated protein antibody level was significantly raised (662 UI/mL).

Radiographs showed erosions and peri-articular osteopenia in involved joints. Based on the clinical, biological and radiological evidence, a diagnosis of active and severe RA was made. He was treated with low dose methotrexate (7.5mg/week) along with rituximab (two doses of 1000mg separated by two weeks). He demonstrated good response in arthritis follow-up after 6 months but his abnormal liver function tests persisted.
Figure: 1 Showing boutonniere deformity in hand

Figure: 2 Showing swan neck deformity in hand

Figure: 3 Showing diffuse periarticular osteopenia and some erosions
DISCUSSION

The association of PBC with RA is rare and not clear, although studies have pointed to a possible association. However, the true prevalence of PBC in RA is not well known [6]. Sjögren’s syndrome, scleroderma, autoimmune thyroid disease were the most common connective tissue disease associated with PBC [3-6]. The etiologic and pathogenetic mechanisms of PBC are not yet fully understood and several factors have been implicated. Among them, it has been suggested that B cells may have different roles in the induction of PBC [6]. Both B-cell and T-cell responses to the E2 subunit of the inner mitochondrial membrane enzyme pyruvate dehydrogenase complex have been documented in PBC and implicated in its pathogenesis [1]. The serological hallmark of PBC is the presence of anti-mitochondrial autoantibodies, especially to the E2 subunit of pyruvate dehydrogenase complex, which are present in 90% to 95% of patients.

The therapeutic management must consider the two pathologies. Methotrexate (MTX) is tried as a treatment of PBC, especially when conventional Ursodeoxycholic acid (UDCA) monotherapy is ineffective [7]. MTX can help in RA as well. Rituximab can also be used in this combination of RA and PBC. The mechanism is probably related to the fact that both are B-cell mediated disorders [8]. The pro-inflammatory cytokine tumor necrosis factor alpha seems to play a major role in the pathogenesis of both RA and PBC. Response is noted with anti-TNF alpha agents especially etanercept [9-10].

CONCLUSION

The association of Rheumatoid arthritis (RA) and Primary biliary cirrhosis (PBC) is rarely reported in the literature. Further studies are needed to determine the actual prevalence of this association.

REFERENCES


*Corresponding author: Dr Subrata Chakrabarti E-Mail: subratchakrabarti2011@gmail.com