Autoimmune Hepatitis (AIH) is an autoimmune disease which constitutes 5% of all chronic liver diseases. It is seen mostly in females of 35 to 36 years of age which presents with arthritis, amenorrhea, hypergammaglobulinemia and extrahepatic manifestations[1].

It is of three types:-

**Type I:** AIH show presence of antinuclear antibody (ANA), antismooth muscle antibody, anti F-actin antibody. Immunosuppression is very good.

**Type II:** AIH is defined by presence of anti liver kidney microsomal antibody (anti LKM Ab). It is seen mostly in younger age group and response to immunosuppression therapy is poor and more likely to progress to cirrhosis[1].

**Type III:** AIH is characterized by presence of antibodies against soluble liver antigen (anti SLA Ab) and liver pancreas antigen. ANA and ASMA may also be present hence now not kept in type I AIH. Frequency of Anti SLA AIH varies from 9-16%[2]. Anti SLA have high specificity for AIH because 90% cases anti SLA positive patients have AIH & only 10% have primary biliary cirrhosis. Biochemical remission is achieved in 90% anti SLA positive AIH but relapse is seen in 53% patients after withdrawal of immunosuppressive drugs[2].

- Anti SLA antibody positive patient are mostly DRB1*03 positive and have anti SSA (R0-52) antibody, ANA and ASMA[3]. Prolactin is an immune stimulating hormone that stimulates immune complex mediated diseases and organ specific autoimmune diseases especially systemic lupus erythematosus (SLE). Prolactin is secreted by anterior pituitary. Microadenoma of pituitary, a rare benign tumor of the pituitary gland, can secrete excess prolactin and cause hyperprolactinemia. This condition is known as prolactinoma. The exact incidence of prolactinoma is not known, but it is estimated to be from 0.1% to 1.5% of the general population. Prolactinoma is more common in women, with a female-to-male ratio of about 10:1. The majority of prolactinomas are benign, but some cases may progress to invasive tumors.

The case presented here describes a 34-year-old woman who presented with jaundice, amenorrhea, arthritis, and lactation. Laboratory investigations revealed elevated aminotransferases, alkaline phosphatase, and all immunoglobulins. Her serum was positive for antinuclear antibody, anti SLA antibody, and antobody to F-actin. Other autoantibodies like anti ds DNA, anti SSA, anti SSB, anti ScI 70, anti Jo-1, anti-centromere, and anti-cardiolipin Ab were negative. There were no clinical features of any other autoimmune disease.

On MRI examination, microadenoma of pituitary gland was detected and her serum prolactin & T4 level were also high. She was finally diagnosed as a case of AIH with pituitary microadenoma and anti SLA Ab, which is an uncommon entity. She was kept on steroid and Bromocriptine, but follow up could not be done.

This case suggests that Autoimmune Hepatitis (AIH) with ANA, F-actin and anti SLAAb may present with Prolactinoma.
Hypothalamus secreting prolactin with AIH with anti SLA Ab is rare. Here we are reporting a case of AIH type II with pituitary microadenoma due to rarity.

Case Report

A 34 yrs old female came to SS Hospital, BHU with history of jaundice for last 6 months, amenorrhoea, weakness, lactation for last 6 months. She also developed low backache, pain in both lower legs, and gastritis for last 5 months. Patient was not pregnant and not having any manifestations to suggest SLE or any other autoimmune disease. Clinically she was suspected case of AIH.

Her viral profile of HbsAg, anti HAV IgM, antiHBV IgM and anti HCV IgG was negative. Liver function test revealed elevated SGPT 1311 U/L, SGPT 2222 U/L and alkaline phosphatase 3140 U/L. Her immunological test revealed that antibody to F-actin and soluble liver antigens (SLA) were positive. Anti nuclear antibody was also strongly positive but dsDNA antibody was negative. Anti thyroid peroxidase antibody was negative.

She had polycyonal hypergamma globulinemia [serum IgG 1997.90 mg/dl (normal 700 - 1600 mg/dl), serum IgM 413.34 mg/dl (normal 20 -230 mg/dl) and serum IgA 498.64 mg/dl (normal 70 - 400 mg/dl)].

In thyroid function test both T3 and T4 were on higher side of normal range. T3 was 2.30 (normal 0.92 to 2.33), T4 was 20.4 (normal 10 to 19.4) and TSH was 1.91 (normal 0.25 to 5.0).

Her CT Head showed ill defined subcennetric soft tissue density lesion s/o microadenoma of pituitary and her prolactin level was also high i.e. 60 mg/l (normal 10-25 mg/l).

Finally she was diagnosed as a case of AIH with microadenoma of pituitary and treatment was started.

Discussion

Prolactin is a hormone synthesized in lactotrope and pituitary tumor present in anterior pituitary. This maintains lactation, decreases folliculogenesis and granulosa cell aromatase enzyme hence produces amenorrhoea and decreases reproductive functions[6]. Prolactin also have immune regulatory effect[5]. Cells of the immune system synthesizes this hormone and also have receptors for cytokines secreted by immune cells like IL-1, IL-6, IFN gamma, TNF, platelet activation factor and substance P participate in the release of prolactin which act on lymphocyte.

Prolactin act as co-mitogen with concanavin A and induces IL-2 receptor on the surface of lymphocytes. It stimulates ornithine decarboxylase and activates protein kinase C which helps in differentiation, proliferation and function of lymphocyte.

Hyperprolactinemia is found in certain autoimmune diseases like SLE, Fibromyalgia, and Rheumatoid arthritis[8].

Prolactinoma (a prolactin secreting tumour) have been found associated with autoimmune diseases. A study from Turkey have found that patients of prolactinoma have nodules in thyroid gland and autoimmune thyroid diseases[9].

There are few reports to suggest that hyperprolactinemia occurs in SLE patients and these patients have high incidence of anemia and serositis[8,9].

A study from Mexico reported that 25% of SLE patients displayed hyperprolactinemia, there lymphocytes showed increased CD69 expression and produced prolactin when cultured invitro[10].

In our case patient had typical feature of autoimmune hepatitis because she had arthralgia, jaundice, hepatomegaly, amenorrhea and her anti SLA, F-actin and ANA was positive but there was no any other feature suggestive of SLE or any other autoimmune disease. Lactation without pregnancy could be explained by hyperprolactinemia. Associations of AIH with primary biliary cirrhosis and primary sclerosing cholangitis have been described[2]. Association of AIH with organ specific poly-glandular autoimmune disease have also been found due to defect in autoimmune regulatory gene (AIRE) but no association with microadenoma of pituitary and hyperprolactinemia have been described[1].

Probably we are the first who are reporting AIH with F-actin, ANA and anti-SLA Ab in 34 yrs old lady with prolactin secreting adenoma of pituitary gland.

Acknowledgement: We are thankful to UGC advanced Immunodiagnostic training and research centre, IMS, BHU for financial support.

References

1. Berg, P. A., Klein, R. Autoimmune hepatitis and overlap syndrome: diagnosis. (2002) Praxis 91(34): 1339-1346.
2. Efe, C., Ozaslan, E., Wahlin, S., et al. Antibodies to soluble liver antigen in patients with various liver diseases: a multicentre study. (2013) Liver Int 33(2): 190-196.
3. Vitozzi, S., Lapierre, P., Djilali-Saiah, I., et al. Anti-soluble liver antigen in patients with autoimmune liver disease. (1993) Pharmacoepidemiology 2(2): 101-108.
4. Melmed, S., Jameson, J.L. Disorders of the anterior pituitary and hypothalamus. In: Kasper DL, Braunwald E, Fauci AS, et al, editors. Harrison’s Principles of Internal Medicine.16th Ed. New York: McGraw-Hill.p. 2076–2097.
5. Compan, G.D., Martinez, A.N., Vargas, C.M., et al. Hyperprolactinemia and autoimmunity. (1996) Revista Alergia Mexico 1995 (Tecamachalco, Puebla, Mexico: 1993) 43(5):128-132.
6. Jara, L.J., Lavalle, C., Fraga, A., et al. Prolactin, immunoregulation, and autoimmune diseases. (1991) Semin Arthritis Rheum 20(5): 273-284.
7. Sayki Arslan, M., Sahin, M., Topaloglu, O., et al. Hyperprolactinaemia associated with increased thyroid volume and autoimmune thyroiditis in patients with prolactinoma. (2013) Clin Endocrinol 79(6): 882-886.
8. Orbach, H., Zandman-Goddard, G., Boaz, et al. Prolactin and Autoimmunity: Hyperprolactinemia Correlates with Serositis and Anemia in SLE Patients. (2012) Clin Rev Allergy Immunol 42(2):189-198.
9. Walker, S.E., Allen, S.H., McMurray, R.W. Prolactin and autoimmune disease. (1993)Trends Endocrinol Metab 4(5):147-151.
10. Chavez-Rueda, K., Legorreta-Haquet, M.V., Cervera-Castillo, H., et al. Prolactin effect on CD69 and CD154 expression by CD4+ cells from systemic lupus erythematosus patients. (2005) Clin Exp Rheumatol 23(6): 769-777.