Original Research Paper

Volume-8 | Issue-9 | September-2018 | PRINT ISSN No 2249-555X

Medicine

ADULT ONSET STILL'S DISEASE AND GRAVES' DISEASE CO-EXISTING IN A YOUNG PATIENT: A CASE REPORT AND REVIEW OF LITERATURE.

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ABSTRACT The association between Adult Onset still's disease (AOSD) and Graves' disease (GD), an autoimmune thyroid condition is well established and however in literature it is often under-reported. GD association with other autoimmune diseases are well known. Here we present an interesting case of a young female who was diagnosed with GD and later developed features of AOSD was managed with corticosteroids and was discharged home in normal health.

KEYWORDS : Adult onset Still's Disease, Graves' Disease

INTRODUCTION:

Hyperthyroidism is a condition in which thyroid gland produces excessive thyroid hormone. Clinical features of hyperthyroidism include heat intolerance, nervousness, palpitation, sleeplessness, increased bowel movements, tachycardia, tremors, weight loss, warm and moist skin and staring look. GD is an autoimmune condition due to circulating auto-antibodies and it is the most common cause of hyperthyroidism. AOSD is a rare autoimmune systemic inflammatory condition characterized by fever, arthralgia, salmon colored evanescent rash and multisystem involvement. AOSD is often a diagnostic challenge and diagnosis is made based on Yamaguchi criteria after excluding malignancy, infections and connective tissue disorders. Early diagnosis and timely treatment of this condition can prevent complications and result in favourable outcomes.

Case presentation:

A 44 year old female with no co-morbids was admitted in our hospital with fever, arthralgia, skin rash and extreme fatigability. She was initially admitted at an outside hospital one week back with palpitations, tremors and tachycardia and was diagnosed to have GD (low TSH, high free T3, free T4 and anti-thyrotropin receptor antibody positive). She was started on Carbimazole and later developed neutropenic sepsis requiring intravenous antibiotics and antifungals for her recovery. She was then referred to our hospital for further management. On examination she was febrile 101 F, pale, tachycardic 124/min, tachypnoea 35/min, hypotension 80/50 mm Hg, MAP 55mm Hg and was started on nor-adrenaline. Evanescent maculopapular skin rash was present in both forearm and elbows. Baseline investigations revealed WBC 5600x103/mm3. Serum ferritin was 22090 ng/ml (normal: 10-120) with AST 538 U/L (normal< 31), ALT 265 U/L (normal<43). Serum was negative for ANA and RF. Routine cultures of blood, urine, and stool were negative. Dengue serology and malarial antigen were negative. AOSD was diagnosed based on Yamaguchi's criteria and she was initially started on Injection Hydrocortisone 50 mg 6th hourly in the view of AOSD, GD and low blood pressure and later bridged with oral steroids (dexamethasone 6mg/day) and propranalol 40 mg/day. After the initiation of steroids, she improved dramatically in all aspects. Serum ferritin at the time of discharge was 800.4 ng/dl and later during outpatient follow-up it was 114 ng/dl. She was suggested radioactive iodine ablation for her GD and under regular outpatient follow-up with the department of nuclear medicine.

DISCUSSION:

The pathogenesis of AOSD and certain autoimmune disorders are inter-related. Immunopathogenesis in AOSD is due to a Th_1-mediated response with high concentrations of tumor necrosis factor-α, soluble tumour necrosis factor receptor-1, interleukin-18, and interleukin-6.[1] AOSD is precipitated by the predominance of Th_1 cytokine. Histopathologically, it is characterized by perivascular inflammation with deramal edema consisting of lymphocytes, histiocytes, and neutrophils of the papillary dermis[2]. Autoimmune thyroid disease is also a Th_1 predominant disease[3]. Other possible hypothesis for this coexistence is molecular mimicry.[4]

Our patient developed carbimazole induced agranulocytosis and subsequently went in for neutropenic sepsis requiring intravenous antibiotics and antifungals for recovery. Approximately 0.5–1% of patients treated with methimazole, carbimazole, or propylthiouracil (PTU) develop granulocytopenia. The mechanism of such drug hypersensitivity remains debatable. However, complement-mediated destruction had been implicated as one of the possible mechanisms.[5]

In this case, we initially started her on Inj Hyrdocortisone 50 mg every 6 hours in the view of her low blood pressure, AOSD and GD and later it was converted to oral steroids (Dexamethasone 6mg/day) and beta-blocker. Steroids inhibit the glandular secretion of thyroid hormone, the peripheral conversion of T4 to T3 and also suppress production of antithyroglobulin auto-antibodies.[6] β-blocker helps in the suppression of tachycardia, tachyarrythmias and hand tremor; also it inhibits conversion of T4 to T3. Thus, steroids and β-blocker combination has synergic effect in the control of hyperthyroidism symptoms. Her GD also improved after starting on steroids.

Diagnosing AOSD is often difficult due to its nonspecific symptoms and the absence of specific serological biomarkers. The Yamaguchi criterion is most widely cited criteria and is most sensitive 96.2% and specific 92.1%.[7]

Major criteria:

(i)Fever of at least 39°C for at least a week.(ii)Arthralgia or arthritis for at least 2 weeks. (iii)Non-pruritic salmon colour rash on trunk/extremities.(iv)Granulocytic leukocytosis (10,000/microL or greater).

Minor criteria:

(i)Sore throat. (ii)Lymphadenopathy. (iii)Hepatomegaly/ Splenomegaly. (iv)Abnormal liver function tests. (v)Negative tests for RF and ANA.

Diagnosis requires at least 5 features, with at least 2 being major diagnostic criteria. Our patient had 3 major criteria (except leucocytosis) and all minor criteria.

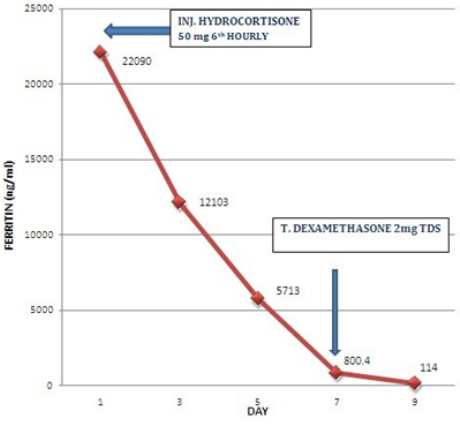

Figure 1: Line graph showing serum ferritin levels in response to steroid treatment.

Elevated ferritin level is a common nonspecific finding which is helpful in diagnosing AOSD and it is due to accelerated cytokine secretion by the reticuloendothelial system[8]. After the initiation of steroids, serum ferritin decreased significantly. These features support the fact that AOSD and Graves' disease may originate via similar autoimmune mechanisms.

CONCLUSION:

The concurrence of AOSD and GD is not uncommon but is often under-reported in our literature. However it is quite fascinating that how these autoimmune disorders have a similar pathophysiology. High index of suspicion is necessary when we deal with a clinical scenario of AOSD, as it is a diagnosis of exclusion. Association of AOSD with autoimmune thyroid disorders are gaining popularity and we need more case reports and case series to unravel the hidden mechanisms in such disorders

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