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Case Report

Immunosuppressive Therapy in a Patient with Pulmonary Tuberculosis and Evans Syndrome with Established Graves Disease – Worth the Risk?

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ABSTRACT

A 55yr old Graves' disease female individual on irregular medication presented to our emergency department with complaints of increased generalized weakness and decreased appetite for around 30 days as well as a fever and breathlessness for six days and with many days history of gingival bleeding and petechiae on the abdomen, lower extremities which are recurrent. The initial evaluation led to the diagnosis of Pulmonary Tuberculosis [TB] in the background of graves. Further workup of the patient revealed the presence of Evans syndrome [ES]. Here, we report a case with TB and ES in an established Graves disease patient. Individuals with ES are generally managed with steroids. On the other hand, steroids can cause suppression of immunity, which raises the risk of TB and makes its management tougher. The co-occurrence of TB and ES in a Graves' disease individual is very rarely reported in the past. This patient was simultaneously effectively managed with prednisolone, carbimazole (in 3 divided doses), and antitubercular therapy [ATT].

Keywords: Immunosuppressive Therapy, Pulmonary Tuberculosis, Evans Syndrome, Graves Disease.

INTRODUCTION

Mycobacterium tuberculosis is the bacterium that causes TB, which is highly infectious and contagious. Although TB typically manifests as an infection of the respiratory system, it can also spread extra-pulmonary and affects multiple organs. Anemia and leukocytosis are manifestations in the blood of TB individuals, [1] which can also be seen in many other conditions. An increased risk of contracting TB exists in individuals who have compromised immune systems. [2] In addition to affecting the immune system, TB is also associated with autoimmune diseases. [3]

AIHA and immune thrombocytopenia (ITP) with associated neutropenia sometimes are two chronic blood disorders that combine to form ES [4] with positive DAT and antibodies to platelet [IgG]. [5] The 1st case of ES was described in 1951 by Evans et al., [6] many case reports of ES in association with autoimmune disorders have been reported since then.

Individuals with ES are usually managed with steroids. On the other hand, steroids can cause suppression of immunity, which raises the risk of TB and makes its management tough. The coexistence of TB and ES is very seldom reported previously. Here, we report a case with TB and ES in a known Graves disease individual. The co-occurrence of TB and ES in Graves' disease is hardly ever written about in the past.

CASE REPORT

A 55yr/F Graves' disease patient on irregular medication presented to the emergency department with complaints of increased general weakness, decreased appetite for around 30 days, and fever and breathlessness for six days. The patient also had many days' history of gingival bleeding and petechiae on the abdomen and lower extremities, which are recurrent.

Clinical examination

On physical examination, her temperature was 101°F; her blood pressure was 124/74 mmHg; her pulse rate was 98 bpm, and her respiratory rate was 24 /min. There were widely dispersed petechiae on the anterior trunk, abdomen, and extremities. There was no pallor, icterus, exophthalmos, or lymphadenopathy. The thyroid gland was palpable and non-tender; the right lobe measured 61 x 41 mm, and the left measured 59 x 39 mm. A few crackles were heard in the bilateral lung fields. The abdomen was soft and flat with no organomegaly.

Investigations

Her Chest X-Ray showed increased bilateral lung markings with diffuse patchy infiltration & computed tonography scan showed patchy infiltration and extensive miliary nodules in both lung fields [Fig-1].

The sputum smear acid-fast bacilli [AFB] report was positive [grade 3+]. Subsequent blood testing showed hemolytic

anemia, thrombocytopenia, elevated FT3, FT4; decreased TSH, a positive TSH receptor antibody, DAT; and the platelet IgG antibody. All significant investigative workups are depicted in Table 1.

Table 1: Significant investigative workup of the patient.

PARAMETER	VALUE
Hemoglobin	7.2 gm/dL
Total leukocyte count	3,380/µL
Red blood cell count	1,91,000/µL
Hematocrit	17.3%
Total platelet count	8,000/µL
LDH	378 U/L
AST	36 IU/L
ALT	28 IU/L
Total bilirubin	1.6 mg/dL
Indirect bilirubin	0.8 mg/dL
International normalized ratio [INR]	1.3
Partial thromboplastin time [PTT]	44 seconds
Ft_3	>18.0 pg/ml
Ft_4	7.54 ng/dL
TSH	0.02 µIU/ml
TSH receptor antibody	7.4 IU/L
Direct coombs test [DAT]	Strongly positive
Sputum smear AFB	positive [grade 3+]

The individual was finally diagnosed to be a case of Pulmonary TB and ES in the background of graves.

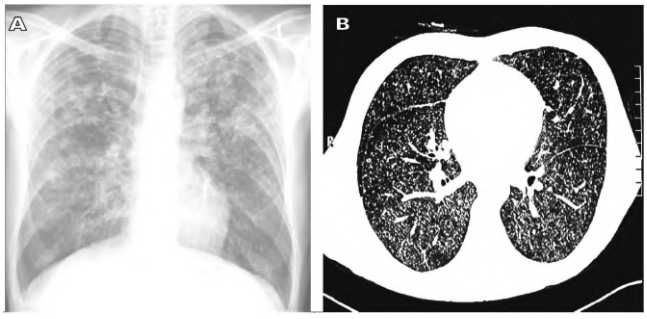

Fig.1 - Chest X ray (A) showing increased bilateral lung markings with diffuse patchy infiltration. CT Scan (B) showing bilateral patchy infiltration with extension miliary nodules in both the lung fields

Treatment & follow up

Once after reaching the diagnosis, therapy, including 1 mg/kg/day of prednisolone, 30 mg/day of carbimazole (in 3 divided doses), and ATT, were given simultaneously. Twenty-five days after the commencement of therapy, the platelet count and the hemoglobin level were increased. Coombs' test turned negative by day 60. Later, FT3 and FT4 came down to normal levels. After the improvement in anemia, platelet count, and thyroid functioning; steroid and anti-thyroid medication were reduced to maintenance levels and given continuously along with ATT after discharge.

DISCUSSION

ES is a rare immunity disorder that constitutes AIHA, ITP, and neutropenia. [5] Steroids are the mainstay of therapy for ES. Prednisolone at a dose of 1–2 mg/kg/day usually, and with a quantity of 4–6 mg/kg/day over 72 hrs in severe cases, can be administered to ES individuals. [7] Next line management constitutes IvIg [immunoglobulin's], Anti-CD20 [rituximab], Inosine monophosphate dehydrogenase inhibitors [mycophenolate mofetil], calcineurin inhibitors [cyclosporine], and alkylating agents [cyclophosphamide], which comprise an in general efficient remission rate of approximately 80%. [7] Relapses of ES have been seen in many individuals who have stopped their drugs.

When ES co-occurs with TB, management can be riskier because the immunosuppression required to manage ES might further increase the TB infection. Only a few case reports have previously been available on individuals with coexisting ES and TB [Table 2].

Table 2: Previous case reports on individuals with both ES and TB together.

S.No	Article	Age	Sex	Outcome
1.	Kim et al. [8]	52	Male	Recovered
2.	Morell et al. [9]	25	Female	Recovered
3.	Sharma et al. [10]	30	Female	Recovered
4.	Shi et al. [11]	26	Female	Recovered
5.	Gyawali et al. [12]	20	Male	Recovered

On the whole, all of these individuals are given ATT and immunosuppression together. Their TB and blood picture turned better after the combined therapy.

For a patient with coexisting TB and Evans syndrome, concurrent administration of antitubercular medication and immunosuppressive therapy can have a number of advantages. Antitubercular treatment assists in curing TB, slowing its spread, and avoiding consequences.

Immunosuppressive medication also aids in regulating Evans syndrome's autoimmune response by lessening the loss of platelets and red blood cells. It is feasible to regulate the autoimmune response while avoiding the reactivation or exacerbation of TB by successfully treating both illnesses at the same time. To ensure that the treatment regimens are precisely adjusted to each patient, maximizing the benefits and minimizing the hazards associated with the medicines, close monitoring and cooperation between the TB and autoimmune experts is important.

On the other hand, only a few case reports are available on individuals with coexisting ES and Graves's disease [Table 3]. Those articles suggested that both disorders occur from a common immune background, i.e., because of inadequate suppressor T-cell response. [13] However, the excessive stimulation of the reticuloendothelial phagocytic system by the thyroid hormone is the cause of the decreased platelet count, as reported by Lamberg et al. [14]. The disappearance of idiopathic thrombocytopenic purpura is seen with improved thyroid functioning, and steroid therapy might be mainly efficient because the two disorders might have the same etiological background. [15, 16]

In our present case, carbimazole and prednisolone were given simultaneously, and the therapeutic effect paralleled improved thyroid functioning, hemoglobin, and thrombocytopenia. Even though the etiological background of this individual remains unclear, our data tells us that genetics and immune background may play a crucial role in disease pathogenesis.

Table 3: Previous case reports on individuals with ES and Graves's disease together.

S.No	ArticleIto	Age	Sex	Outcome
1.	**Mey al.** [17]	36	Male	Recovered
2.	**Hiraoka Net al.** [18]	23	Male	Recovered
3.	**Sakai Y et al.** [19]	32	Female	Recovered
4.	**Sawada Y et al.** [20]	54	Female	Recovered

CONCLUSION

Whenever there is clinical data of AIHA and decreased platelet counts, proper workup, including the DAT and antibodies against platelets to be tested. Once after the establishment of coexisting TB and ES in an individual, the individual should be given both ATT and immunosuppressive therapy simultaneously. In these individuals, administering immunosuppressive and antitubercular treatments together has substantial advantages. It enables for successful TB therapy, slowing down the disease's course and avoiding complications, as well as controlling the autoimmune reaction in Evans syndrome. By ensuring a thorough and balanced approach to the care of both illnesses, this method maximizes treatment results and enhances the patient's general health and wellbeing. Their clinical courses should be observed keenly to ensure an adequate revival. Regular follow-ups and repeated routine workups should be done in these individuals.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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