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RESEARCH ARTICLE

ERASMUS SYNDROME: AN INTERFACE BETWEEN ENVIRONMENT AND AUTOIMMUNITY

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Abstract

Introduction: Erasmus Syndrome (ES) is a rare condition in which Systemic Sclerosis (SSc) is caused by exposure to silica. The term Erasmus Syndrome was coined after cases of SSc were found among gold miners in South Africa. In India, there is a paucity of such reported cases which might be more due to unawareness of the entity rather than low prevalence. Though the treatment remains the same, ES provides a template for the study of interactions between the environment and our immune system.

Case: We present the case of a male patient diagnosed with systemic sclerosis, who was referred to the Rheumatology Clinic of our institution, and which on further evaluation revealed the cause as occupational silica exposure thus changing the diagnosis to ES.

Conclusion: We conclude that ES represents an interaction of the environment and the human immune system, with the environment being the factor in the earlier and more severe progression of the disease. We also underline the importance of awareness of this entity among clinicians and of taking a proper history, especially the occupational history of any patient of SSc.

Introduction:-

Erasmus Syndrome (ES) is a rare condition in which Systemic Sclerosis (SSc) is caused by exposure to silica with or without the patient developing silicosis. Mostly reported in mine workers, it is found more in males, is mostly of the diffuse cutaneous type, and has a higher proportion of pulmonary fibrosis, and pulmonary artery hypertension (PAH). Though the treatment remains the same, ES provides a template for the study of interactions between the environment and our immune system. We present a case of ES which was referred to our institution as a case of SSc but detailed history revealed the cause as silica exposure due to the occupation of the patient thus changing the diagnosis to ES.

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Case Report

A 42-year-old male, resident of Bihar was referred to our institute as a case of SSc with complaints of breathlessness for one and a half years, initially on exertion but which progressed to being breathless at rest since the last 6 months, and cough with scanty expectoration, which had developed along with the shortness of breath. He had difficulty in opening his mouth for 6 months. He had polyarthritis and Raynaud's phenomenon. Examination revealed clubbing, sclerodactyly and digital ulcers with normal vitals. Systemic examination revealed chest expansion of 2 cm, basal crepitations and rhonchi, and a loud pulmonic component of the second heart sound.

Complete blood counts were normal, with normal liver and kidney function tests and negative viral markers. Erythrocyte Sedimentation Rate (ESR) was 33 mm in 1st hour, and C-Reactive Protein (CRP) was 7 mg/dl (normal < 1 mg/dl). Chest radiographs depicted diffuse nodular opacities with calcification (Figure 1). Anti Nuclear Antibodies (ANA) was positive with a speckled pattern, and anti-SCL antibodies were highly positive (>200 IU/ml, normal < 24 IU/ml). CT chest was suggestive of silicosis, with multiple randomly distributed nodules involving the basal lobes, progressive massive fibrosis, and multiple enlarged mediastinal lymph nodes (Figure 2). Sputum and bronchiolar lavage were negative for bacterial or fungal growth, malignant cells. Ziehl-Neelsen staining (ZN staining), and Catridge-based Nucleic Acid Amplification test (CBNAAT) were negative for tuberculosis. Bronchoscopy-guided bronchial biopsy was suggestive of fibrosis without granulomas or malignant cells. Nail fold capillaroscopy revealed distorted architecture, giant capillaries, and microhemorrhages, consistent with the active pattern of Raynaud's phenomenon. Lung spirometry showed a restrictive pattern with forced expiratory volume in one second (FEV1) of 42% and forced vital capacity (FVC) of 50% of the predicted values. Lung volumes revealed low functional residual capacity (FRC), residual volume (RV), and total lung capacity (TLC) suggestive of a severe restrictive process. The six-minute walk test was 370 meters, and echocardiography showed features of pulmonary hypertension and dilated right atrium and ventricle. The diagnosis in the case up to this stage was clear with the only question being the gender and the out-of-proportion PAH within a year and a half of the onset of symptoms. The history was again reviewed and it was found that though he was a resident of Bihar, he had worked in mines in Himachal Pradesh for over two decades as a stone cutter. After developing the symptoms, he went back to his home state. Thus, the final diagnosis of ES was kept.

He was treated with Cyclophosphamide 15 mg/kg body weight monthly injections and low dose prednisolone along with tadalafil for PAH. He is under follow up and has reported improvement in his symptoms.

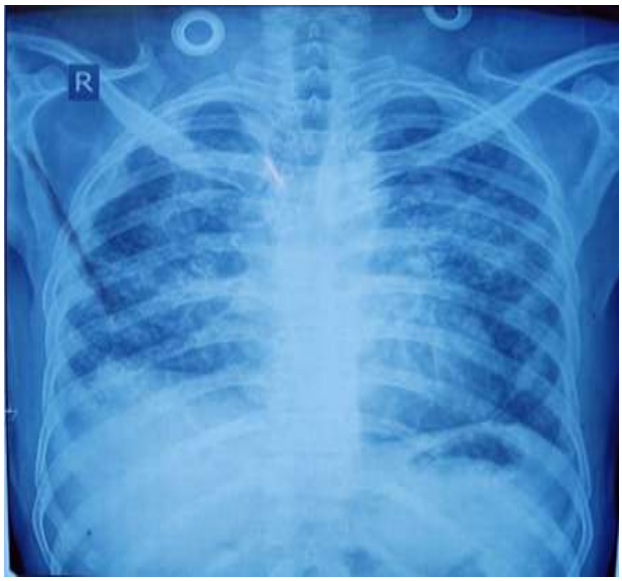

Figure 1:- Chest X-RAY depicting diffuse nodular opacities.

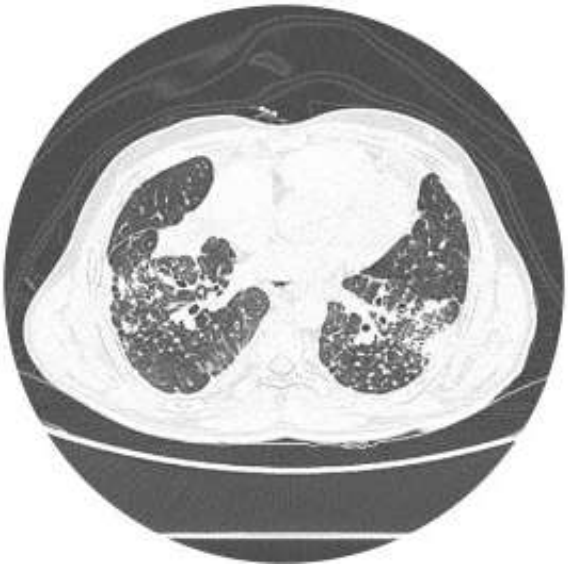

Figure 2:- CECT of the Chest showing multiple subcentrimetric nodules with fibrosis and ground glass opacities.

Discussion:-

Genetic predisposition, environmental factors, and immune regulation are thought to underlie the pathogenesis of autoimmunity. Epidemiological studies give increasing evidence of the role of the environment in autoimmunity(1). While genetic predisposition are thought to contribute to 30% of the cases, environmental factors contribute to 70%(2). Although there is a difference between environmental factors causing autoimmunity versus autoimmune diseases, it can be stated with confidence about some agents causing specific autoimmune diseases. While the role of smoking in Rheumatoid Arthritis (RA) is well known, attention is drawn to the role of silica in causing RA, Systemic Lupus Erythematosus (SLE), Systemic Sclerosis (SSc), and even ANCA associated vasculitis (AAV)(3). Of the ten patients of rheumatological diseases among denim sandblasters, six were found with SSc, three with RA, and one with SLE(4).

The lung is a common site where long term exposure to environmental agent causes toxicity, inflammation and subsequent fibrosis. Particulate matter hampers clearance and degradation and thus persistence of inflammation resulting in fibrosis (5). While this mechanism may have had an evolutionary principle in metazoa where silica dust caused increased pro-inflammatory cytokines especially Tumour Necrosis Factor α (TNFα), and increased collagen deposition resulting in stiffer body, the same mechanism preserved throughout evolution becomes a source of disease in mammals(6). Silica has also been found to increase DNA damage, and dysregulation of shelterin complex thus initiating pulmonary fibrosis (7). Regulation of the inflammatory process and progression of fibrosis may also be regulated by the autophagy signaling pathway(8).

Silica is ubiquitously found in the earth's crust in the form of quartz, quartz crystals, quartzite, silica sand, sand (others) and moulding sand. They are all coined together in one generic name 'silica minerals'. This is because all these commodities are essentially crystalline silicon dioxide (SiO2). Most of silica in India are found in Rajasthan, Himachal Pradesh, Haryana, Maharashtra, Telangana, Andhra Pradesh, Odisha, and Chhattisgarh(9).

The term Erasmus Syndrome (ES) was coined after cases of SSc were found among gold miners in South Africa. The cases are sporadically reported from parts of the globe where mining involves silica exposure. In India, there is a paucity of cases which might be more due to unawareness of the entity rather than due to low prevalence. There is a preponderance of ES among males, though it may be due to more males being involved in the mining profession as well as more of them being smokers. The prevalence of ES was found to be almost one sixth among cases of SSc in a series(10). However, clinical features hardly differ between ES and SSc except for more of the diffuse cutaneous type, more pulmonary fibrosis and pulmonary hypertension, and more male preponderance in the ES group(11). The treatment too remains the same.

Our case illustrates the rapid onset of and out of proportion PAH relative to the disease duration in ES. In contrast, PAH is known to occur with the limited cutaneous type (LcSSc) after almost ten years of the disease. Also, clubbing is not a well recognized feature in SSc. These features, namely early onset and more severe PAH, and presence of clubbing are indicative features of ES which should be helpful in making this diagnosis in the crowded out-patients offices. Of interest to note is also the fact that thoracic malignancies also occur with increased frequency in these cases and share common clinical features as well. Thus, it is necessary to investigate and rule out any underlying malignancy in these cases.

Thus, we conclude that ES represents interaction of the environment and autoimmunity, with the environment being the factor in earlier and more severe progression of the disease. We also underline the importance of awareness of this entity among clinicians and of taking a proper history especially the occupational history in any patient of SSc.

Disclosures:
None

Acknowledgement:
None

Conflict of interest:
None

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