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ASPERGILLOSIS RELATED-IRIS IN INVASIVE ASPERGILLOSIS INVOLVING LUNGS AND BRAIN.

Neurology

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ABSTRACT

Immune Reconstitution Inflammatory Syndrome (IRIS) is an entity defined as a development of new clinical symptoms or worsening of existing symptoms after reversal of the immune deficit status. It is commonly known to occur after initiating Antiretroviral therapy (ART) in HIV individuals.1 It can also occur in patients with other diseases like fungal infections, solid organ transplants and hematopoietic transplant once there is recovery of immune system resulting in exaggerated Immune response.[2] Here we present a case of a female with diabetes mellitus, diagnosed to have Invasive aspergillosis, involving lung and brain. She developed worsening of her neurological symptoms after initiating of antifungal treatment and had features suggestive of IRIS, and was successfully treated with steroids.

KEYWORDS

Case History-

A 57 years old lady, known to have Diabetes Mellitus, was evaluated elsewhere with history of chronic cough and dyspnea on exertion, and was diagnosed to have PulmonaryTuberculosis on the basis of her radiological imaging, and was started with antitubercular treatment empirically, which she discontinued after a few days. She also had history on seizure episode in past and was treated symptomatically. She presented to us with complaints of fever, cough and generalized tonic clonic seizures. MRI Brain showed multiple ring enhancing lesion in the brain with perilesional edema (left frontal, left temporal and left parietal). Radiological imaging was suggestive of infective etiology and keeping the chronic history in mind the differentials were considered to be chronic infective etiology like tuberculosis and hence ATT was not discontinued. Preliminary work up done in terms of Blood culture, Complete blood counts and Liver and kidney function were normal and the inflammatory markers were markedly raised. The x ray Chest done showed mediastinal widening, hence the malignancy was added to the list of differentials. A subsequent whole-body PET-CT scan showed avidly enhancing left upper lobe lung lesion with mediastinal lymphadenopathy. Biopsy of the lung lesion showed fungal hyphae with acute angle branching and septations, suggestive of Aspergillosis. She was started on with Voriconazole, and anticonvulsants, with which a slight improvement in symptoms was noted. On day 15 of her admission, she developed difficulty in speaking and her neurological evaluation revealed Wernicke's Aphasia with Subtle Right upper motor neuron facial weakness and no limb weakness. Antitubercular medications were stopped. Brain biopsy was planned but deferred as the patient improved symptomatically, considering probable same etiology and invasive nature of the investigation. It was decided to keep her under close follow up and re-do the imaging at a later date if the symptoms worsen or persisted. A follow up MRI Brain done after 2 months of medication showed a mild reduction in size of brain abscess and surrounding edema, hence voriconazole was continued at 4mg/kg body weight twice a day.

After another2 months, she presented with complaints of confusion and irrelevant speech. Imaging was repeated and MRI Brain scan showed increase in size and enhancement of the lesion along with marked increased in perilesional edema, but no clinical worsening. CT scan of the thorax showed marked reduction in size of left upper lobe lung lesion from 6.4 cm X 9.6 cm to 4.0 cm X 7.4 cm. She was started on steroids and voriconazole was continued.

Her clinical condition also improved significantly and speech difficulty significantly recovered. She was followed up closely to look for underlying cause that lead to development of Invasive Aspergillosis, and was later diagnosed to have Sjogren's syndrome with interstitial lung disease.

DISCUSSION –

IRIS is considered as exaggerated immune response that occurs after recovery of the immune system. It is described to be of two types, *Paradoxical* type or *Unmasking Type*. The former refers to worsening of pre- existing infection due to secondary inflammatory response wherein the pre-existing symptoms increases after the treatment for underlying disease is introduced. *Unmasking* IRIS wherein the new symptoms appear after the immune recovery[2]. Aspergillosis related IRIS is seen commonly in neutropenic patients and rapid neutrophil recovery.[3] It has also been described in post lung transplant patient, autologous stem cell transplants. [1,4] The Pulmonary worsening are commonest findings described in most of the Aspergillus related-IRIS described in available literature and unmasking type is probably the commonest one associated with neutropenic recovery.[3] The data emphasizes on utility of biomarkers like Serum galactomannan. If the serum galactomannan showed declining value and the clinical symptoms showed worsening with no other attributable cause then the likelihood of IRIS increases.[5]

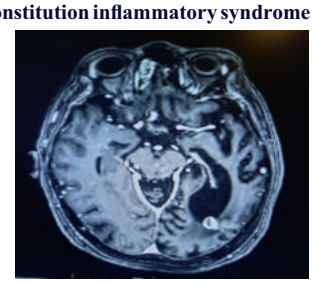
Our patient had history of respiratory and the neurological symptoms with histopathologically proven Invasive Aspergillosis in the lungs. Aspergillosis related-IRIS has not been commonly described with neurological invasive disease. Her pulmonary symptoms and imaging did improve with the voriconazole initiation, but the neuro-imaging showed worsening on the repeat scan. Patient was started on anti-inflammatory for the same. The dosage used was Prednisolone at 0.5mg/kg tapered over 4 weeks. She improved clinically and repeat MR- Brain also showed significant resolution. Her treatment was stopped and there was no delayed worsening, even at 6 months after cessation of antifungal treatment. As there is no diagnostic test to prove IRIS, the diagnosis is generally corroboration of clinical signs and symptoms along with radiological imaging. A caution should be taken to rule out all other possible causes as such patients are usually immunocompromised individuals and can have other concomitant infections mimicking the same.

Conclusion-

We conclude that, in a patient with Invasive Aspergillosis with CNS involvement, if we notice any worsening after the treatment initiation, Aspergillus related-IRIS should be considered as one of the differentials, along with other differentials.

Glossary-

Immune Reconstitution inflammatory syndrome (IRIS)



MRI post contrast T1 showing ring enhancing lesion with peri lesional oedema in left occipital region

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