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Medicine

CHALLENGE IN THE MANAGEMENT OF A CASE OF MUCOPOLYSACCHARIDOSIS TYPE-1

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ABSTRACT 3years old baby girl had fever since 1year of age. Based on clinical evaluation, serum enzyme assay and excess glycosaminoglycan level in urine, patient was diagnosed to have mucopolysaccharidosis type I. Glycosaminoglycan progressively accumulates within the cells and compromises organ function. After a few weeks course of enzyme replacement therapy, haematopoietic stem cell transplantation was done. But fever persisted. Clinical evaluation and investigation did not find out any infective focus. Initially fever was thought to be due to engraftment syndrome. But in spite of neutrophil recovery in Day+14 after transplant, fever spike continued to be same. Immunosuppressant therapy was increased and fever spike improved because of settled immunological reactions in the body. So, in case of fever after bone marrow transplant immune mechanism is to be kept in mind.

KEYWORDS : mucopolysaccharidosis, glycosaminoglycan, transplant, immune

INTRODUCTION-

Mucopolysaccharidosis are lysosomal storage diseases produced by an inherited deficiency of an enzyme involved in the degradation of acid mucopolysaccharides, also called glycosaminoglycans (GAGs)[1]. These diseases are autosomal recessive, except for mucopolysaccharidosis type II, which is X-linked[2]. Among all types, mucopolysaccharidosis type I (MPS I) is by far the most common type.

Glycosaminoglycan is a constituent of the extracellular matrix, connective tissue and joint fluid[3]. Its' progressive accumulation within the cells of various organs ultimately compromises their function. Mucopolysaccharidosis type I is caused by a deficiency of the lysosomal enzyme alpha-L-iduronidase[4]. As a result, glycosaminoglycans progressively accumulate in the lysosomes and causes dysfunction of cell, tissue and organ.

Case report-

3 years old baby girl from Pakistan had fever since 1year of age. Baby also had developmental delay, difficulty of vision and swelling in the back. Initially baby was managed symptomatically in Pakistan. In view of persistence of symptoms, she was brought to a tertiary care hospital in New delhi for further management. On evaluation, she was found to have umbilical hernia, kyphosis, median nerve neuropathy and corneal clouding. Based on serum enzyme assay and excess glycosaminoglycan level in urine, she was diagnosed as a case of mucopolysaccharidosis type I. She was managed with few weeks course of enzyme replacement therapy and symptoms were persisted. After 5 weeks of last enzyme replacement, she was admitted to bone marrow transplant unit. After finishing the conditioning chemotherapy, allogenic unrelated bone marrow transplant was done. Immune suppressant therapy in form of injection Cyclosporin was started from 2 days before transplant. But fever persisted. Antibiotics were upgraded. Blood culture, urine culture, procalcitonin, CRP, serum galactomannan, blood CMV RTPCR, urine EB virus-all were negative. Injection hydrocortisone was started from day+9 of transplant thinking the possibility of engraftment syndrome. But fever did not subside. CT chest and abdomen ruled out infective focus. Pulse steroid methyl prednisolone from day+24 to day+27 and intravenous immunoglobulin on day+33 were given. On day+34, hickman line was removed and new peripherally inserted central line was placed. But still no improvement was found. Cyclosporin which was started two days before transplant was stopped and replaced by tacrolimus on day+36. Mycophenolate mofetil which was started on day+1 was continued. Then her fever spike decreased on day+37. After being afebrile for 48 hours, she was discharged and asked for follow up.

DISCUSSION

Today, enzyme replacement therapy and haematopoietic stem cell transplantation are the standard options worldwide[5]. Haematopoietic stem cell transplantation can treat the brain in the course of the disease, as stem cells can engraft and differentiate in the CNS. In contrast, infused enzyme replacement therapy can not cross the blood brain barrier easily due to large size[6]. Following autologus transplant, patient may develop fever and skin rash. This may be due to engraftment syndrome. Release of proinflammatory cytokines, including interleukin-1 and tumor necrosis factor α are responsible for such happening[7]. Our patient had fever, skin rash, diarrhoea during neutrophil recovery period. But there was no such feature like pulmonary infiltrate, jaundice, weight gain, hypoalbuminaemia or neurological manifestation. Neutrophil recovered on Day+14 of post transplant. All the infective possible causes of fever were ruled out. Increased immunosuppressant therapy improved the symptom which was caused by non-infective immune reaction.

Conclusion-

Treatment of mucopolysaccharidosis type I disease is a challenge. Post stem cell transplantation, fever always may not be due to only infective cause. Immunological mechanism should be kept in mind. Increased immunosuppressant therapy will help to improve such group of patients.

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