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SCIENTIFIC LETTER

# Interferon-α/β–Receptor-2 Deficiency Leading to Multiple Infections, Hemophagocytic Lymphohistiocytosis, and Fatal Encephalopathy after MMR Vaccination

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*To the Editor*: Interferons (IFNs) are cytokines responsible for mediating an innate immune response to viral infections through IFN receptors. Here is a rare case of interferon-α/β– receptor-2 (IFNAR2) defect. A 14-mo-old girl, born of third-degree consanguineous marriage, presented with high grade fever, rash resembling measles, loose motions, and swelling of the injection site following MMR vaccination. She had a history of four admissions for lower respiratory infections. Her immunoglobulins and lymphocyte subset analysis were normal. HIV was negative. Presently, she had anemia, leucocytosis, cryptosporidium in stools, positive EBV IgM, galactomannan assay, and measles IgM antibody. Her fever continued unabated. On day 8, she developed hemophagocytic lymphohistiocytosis (HLH), which responded to steroids and was discharged on day 21. She was readmitted with status epilepticus, encephalopathy, and cardiac arrest, to which she succumbed. The targeted sequencing detected a pathogenic homozygous nonsense variation in exon 4 of the *IFNAR2* gene (chr21: g.34617294C>T; Depth 104x) that results in a stop codon and premature truncation of the protein at codon 46 (p. Arg46Ter; ENST00000342136.4), resulting in immunodeficiency, OMIM 45 [1].

Type 1 IFNs are produced rapidly during viral infection and hinder its replication by binding to the IFNAR, which stimulates the downstream signalling pathway [2]. Human deficiency of IFNAR2 was first described by Duncan et al. [3] and later by Passarelli et al. [4] in infants, both presenting with encephalitis and HLH following MMR vaccination. These patients have natural killer cell dysregulation and a lack of inhibition of IFN-γ production leading to HLH [4]. IFNAR2 deficiency has an autosomal recessive inheritance and our patient is only the fourth case reported.

This primary immune deficiency helps us in understanding the role of IFN-α/β and its signalling cascade in antiviral defence. Any pathological dissemination of live attenuated viral vaccines or episodes of HLH must be investigated for subtle defects in immunity by genetic testing.

## Declarations

**Conflict of Interest** None.

## References

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