

From agammaglobulinemia to neutropenia: The TCF-3 has different clinical presentations

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Abstract:

Agammaglobulinemia is caused by genetic disorders affecting B cell development and is assumed to be autosomal recessive in up to 15%. Autosomal recessive agammaglobulinemia (ARA) is a condition that causes immunodeficiency, and it can lead to severe complications such as otitis, sinusitis, and pneumonia. Genetic mutations include μ heavy chain, $\lambda 5$, $Ig\alpha$, $Ig\beta$, BLNK, PIK3R1 and TCF3. There are several genes, including μ heavy chain, $\lambda 5$, $Ig\alpha$, $Ig\beta$, BLNK, PIK3R1, and TCF3, that have been associated with ARA. TCF-3 is responsible for the development of T and B cells. This report describes four cases, one of which was agammaglobulinemia, followed by two cases of Immunoglobulin (Ig) subgroup deficiency, one of neutropenia, and one of hypogammaglobulinemia (Table 1).

This report expands the spectrum of TCF3 deficiency types and highlights the crucial role of this transcription factor in B-lymphocyte differentiation.

Table1: The clinical and immunologic parameters of the patients.

| | Patient1 | Patient2 | Patient3 | Patient4 |
|--|---|---|---|--|
| Age/ gender | 8/M | 3/M | 5/M | 26/M |
| Clinical findings | Recurrent bronchiolitis Failure to thrive | Enterovirus encephalitis Facial dsymorfism | Recurrent upper respiratory tract infections, peritonsillar abscess | Recurrent otitis media and pneumonia, hearing loss |
| Diagnosis at admission | THI | Agammaglobulinemia | Neutropenia | Ig subgroup deficiency |
| Current diagnosis | Ig subgroup deficiency | Agammaglobulinemia | Hypogammaglobulinemia | Ig subgroup deficiency |
| Mutation | TCF-3 p.Pro177Leu (c.530C>T) heterozygous | TCF-3 p.Ala161Val (c.482C>T) heterozygous | TCF-3 C.1939C>A p.(pro647Thr) heterozygous | TCF-3 c.1813+8C>T (rs993094051) heterozygous |
| Immunologic parameters | | | | |
| ANS × 10 ⁹ cells/L | 3240 | 5660 | 62 | 3290 |
| ALS× 10 ⁹ cells/L | 3780 | 2010 | 2850 | 2730 |
| IgG(mg/dl) | 304 | 145< | 924 | 690 |
| IgA(mg/dl) | 81 | 6.7< | 33 | 110 |
| IgM(mg/dl) | 105 | 18< | 113 | 113 |
| Ig Subgroups (mg/dl) | IgG1:238 ↓ IgG2:255 IgG3:16.7 ↓ | N/A | N/A | IgG1 483 IgG2 166 ↓ IgG3 36.7 ↓ |
| CD3 × 10 ⁹ cells/L | 2683 | 1440 | 1995 | 1701 |
| CD4 × 10 ⁹ cells/L | 1738 | 274 | 769 | 1107 |
| CD8 × 10 ⁹ cells/L | 793 | 1080 | 1254 | 459 |
| CD19 × 10 ⁹ cells/L | 756 | 44 | 133 | 351 |
| CD3-CD16CD56+ NK cells × 10 ⁹ cells/L | 185 | 880 | 684 | 459 |
| Switched memory B CD19-IGgM-IgD+CD27 × 10 ⁹ cells/L | 18.9 | 0 | 28 | 21.6 |
| Vaccine response | positive | positive | positive | positive |

