

**Case report:**

**Naturally Occurring 'enzyme only' Anti-E antibody: A Rare Occurrence**

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**Abstract:**

Naturally occurring anti-E, present without obvious antigenic stimulation is a rare occurrence of red cell antibody of the Rh blood group system. It is mentioned that such naturally occurring anti-E react only with enzyme modified E-positive red cells. This case report describes a rare case of naturally occurring anti-E in a patient with autoimmune haemolytic anaemia (AIHA).

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**Introduction:**

Anti-E is one of the most common alloantibody formed following sensitization by blood transfusion or pregnancy. Occasionally, it has been reported as a naturally occurring antibody without any obvious antigenic stimulation<sup>1,2</sup>. However, this type of spontaneously occurring, non-immune anti-E antibodies may not be a true anti-red cell antibody, but most possibly caused by their cross reactivity with the other red blood cell-borne structure giving their apparent specificity<sup>2</sup>. The frequency of naturally occurring anti-E is 0.1% in E antigen negative individuals and it usually best detected by their reaction with enzyme treated E positive red cells at room temperature<sup>3</sup>. This case report describes the presence of naturally occurring anti-E in a patient with autoimmune haemolytic anaemia (AIHA).

**Case report:**

An 18 year-old-girl was admitted with severe anaemia. She has no history of blood or blood component transfusion or other sensitizing event like child birth or abortion. On admission, her haemoglobin was 5.4g/dl and required blood transfusion. The pre-transfusion investigation showed that she was grouped A Rh D negative with cde/cde (rr) phenotype. Her antibody screening was positive (3-cell panels,

BIO RAD ID-DiaCell I-II-III Asia). Direct Coomb's test (DCT) was positive with polyspecific anti human globulin (AHG) (ID-Card "LISS/Coombs") by gel technique (manual method). Further testing showed DCT was positive with monospecific anti-IgG and anti-C3d. Antibody identification (11 cell panel, BIO RAD ID Dia Panel, ID DiaPanel-P, gel technique) showed pan-agglutination and suggestive of presence of nonspecific auto IgG autoantibody. To exclude presence of underlying alloantibody, auto adsorption test was done in a LISS environment with polyethylene glycol (RAMPEG CSL). Testing of the autoadsorbed plasma confirmed presence of anti-E antibody with two different enzyme treated panel cells (BIO RAD and CSL). In view of the positive DCT, red cell elution was performed using ELU-KIT™ PLUS kit, IMMUCOR GAMMA red cell elution system and antibody identification with eluate showed only nonspecific auto-IgG antibody. As there was no history of previous sensitizing events, it was concluded that the anti-E identified is most likely naturally occurring. The patient was successfully transfused with ABO and Rh phenotyped specific blood (E antigen negative) without complication.

**Discussion:** In this case report, we presented a patient with AIHA whom developed non-specific

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autoantibody and a naturally occurring anti-E. In the literature, naturally occurring anti-E antibodies are formed spontaneously<sup>2</sup> and best react with enzyme treated E positive red cells at room temperature<sup>3</sup>. In view of this patient's history showed absence of antigenic stimulation for developing anti-E such as transfusion or pregnancy, and the antibody identification showed anti-E specificity which was only reactive with papain treated E-antigen positive red cells, we have concluded that the anti-E is naturally occurring. At this moment, only a few case reports have described such naturally occurring anti-E<sup>2,3,4</sup>.

Naturally occurring anti-E has not shown any evidence of haemolytic transfusion reaction<sup>3</sup> or haemolytic disease of foetus and newborn (HDFN)<sup>4</sup> and thus categorised as of non-clinical significance<sup>5</sup>. However, Michalewska et al (2005)<sup>6</sup> has reported a case of 'Enzyme-only' anti-E to be associated with acute haemolytic transfusion reaction, but it was not mentioned whether this anti-E is naturally occurring or not. In standard transfusion practice, any patient with clinically significant alloantibody irrespective whether it is of naturally occurring or following

sensitization, antigen negative red cell must be given for transfusion.

**Conclusion:** This case report highlights a very rare presentation of a naturally occurring 'enzyme only' anti-E in a patient with autoimmune haemolytic anaemia. Because of the lack of evidence of the non-clinical significance of such antibody, for transfusion safety, E-antigen negative blood remained the first priority for transfusion in such cases.

**Ethical clearance:** This case report was approved ethically from ethics committee of Universiti Kebangsaan Malaysia Medical Centre prior to submission.

**Conflict of interest:** The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

**Individual Contribution of the Authors:**

Conceptual work: Yousuf R, Leong CF

Data collection: Yousuf R, Thalith NFA, Loong TY, Leong CF

Manuscript writing: Leong CF

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