Clin. Lab. 2026;72:XXX-XXX

CASE REPORT

Rare Anti-f(ce) Detected During Cross-Matching

Jungjun Lee [1], Howon Lee [2], Dong Wook Jekarl [1, 3], Jayho Han [4]

[1] *Department of Laboratory Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea*
[2] *Department of Laboratory Medicine, Yeouido St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea*
[3] *Research & Development Institute of In Vitro Diagnostic Medical Device of Catholic University of Korea, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea*
[4] *Department of Laboratory Medicine, Uijeongbu St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Gyeonggi-do, Republic of Korea*

SUMMARY

Background: **The f(ce) antigen is a compound Rh antigen expressed with both c- and e-antigens coded in same haplotype. Detection of anti-f(ce) has rarely been reported due to both its rarity and difficulty to analyze. Here, we report anti-f(ce) detected during cross-matching, which was confirmed by two further tests.**
Methods: **A 66-year-old male who had never received a transfusion, was diagnosed with an abscess of the hip joint bursa in a previous institution. During therapy about 50 - 60 days ago, he received a total of 4 units of packed red blood cells (pRBC). Soon, he was transferred to our institution for an operation, and a post-operation pRBC transfusion was ordered. An initial antibody screening test (AST) using 2 cell-lines showed all negative results, but a subsequent cross-matching test showed incompatibility to 2 of 7 donor RBCs. Thus, an additional AST using 3 cell-lines and a further identification test revealed anti-f(ce) without any coexistent antibody. To reconfirm this antibody, "Rh CcEe subgroup profiling of incompatible donor RBCs" and "Re-AST using the patient's plasma after adsorption to incompatible pRBC" were planned.**
Results: **First, among all 18 cross-matched units of pRBCs, 16 units were compatible with the patient's serum, but 2 units were not. These incompatible units showed CcDe and cDEe phenotypes, respectively, suggesting that they might contain c- and e-antigen genes in cis. Second, Re-AST using the remnant plasma after adsorption to 1 (CcDe) of the above 2 incompatible units persistently showed anti-f(ce) in "3+". However, a modified test adding 1 more adsorption step that took 7 hours at 37℃ following the above typical method showed the same result but with a decreased strength "±".**
Conclusions: **All pRBCs showed suitable Rh phenotypes to their cross-matched results, supporting that f(ce) antigen exists only when c- and e-antigens are coded in same haplotype. Adsorption of anti-f(ce), which consists of mainly IgG, seems to require a longer incubation time compared to the typical method. Further studies for the affinity and avidity of anti-f(ce) and optimal conditions to maximize these features are needed.**
(Clin. Lab. 2026;72:xx-xx. DOI: 10.7754/Clin.Lab.2026.260225)

Correspondence:
Jayho Han, MD, PhD
Department of Laboratory Medicine
Uijeongbu St. Mary's Hospital
College of Medicine
The Catholic University of Korea
271, Cheonbo-ro, Uijeongbu-si, Gyeonggi-do
Uijeongbu, 11765
Republic of Korea
Phone: +82 031-820-3348
Email: jayhohan00@gmail.com

Case Report accepted February 24, 2026

KEYWORDS

anti-f(ce), anti-f

INTRODUCTION

Among Rh antigens, the f(ce) antigen is a compound antigen expressed when both c- and e-antigens are coded in the same haplotype [1-3]. The anti-f(ce) antibody, which binds to the above cis product, has rarely been detected for the following reasons. First, prevalence of

the f(ce) antigen is ranked "Common" [4] and the population that could be alloimmunized is inversely small. Second, this antibody usually coexists with either anti-c or -e, which could mask its presence [2,3]. Third, most antibody screening panels do not emphasize this unexpected antibody, and further antibody identification testing is needed. For these reasons, there have been only a few reports that mention anti-f(ce). Even those reports mostly did not mention purely identified anti-f(ce), as most cases accompany other alloantibodies. Detection of the anti-f(ce) antibody may be a significant challenge, as it seems to cause hemolytic disease and transfusion reaction [5-7]. With this potential harm, accumulation of strategies to anticipate and identify this rare antibody are needed. Recently, we experienced an anti-f(ce) result during a routine antibody screening test (AST) that incidentally was detected during the following cross-matching. Hence, we report a case to share both the situation that brought the anti-f(ce) to our attention and our approaches to reveal the anti-f(ce).

CASE PRESENTATION

About 60 days prior to presentation, a 66-year-old male who had never received a transfusion, was diagnosed with an abscess of the hip joint bursa in a regional hospital. During therapy, he received 2 units of packed red blood cells (pRBC) about 60 days prior and additional 2 units of pRBC about 50 days prior (total 4 units). More recently, he was transferred to our institution for an operation, and his initial hemoglobin concentration (Hb) was 16.4 g/dL.

However, after the operation, his Hb had decreased to 10.6 g/dL, and a pRBC transfusion was prescribed. His ABO & Rh (D) type was "AB(+)" and an antibody screening test (AST) using 0.8% Selectogen® (Ortho Clinical Diagnostics™) gave all negative results to 2 reagent red blood cells (RBC) (Table 1A). However, a subsequent cross-matching test showed incompatibility to 2 pRBCs (of 7 pRBCs). At first, with suspicion for anti-Di^a, which was not included in the AST panel, an additional AST using 2 Surgiscreen® (Ortho Clinical Diagnostics™) lots was performed. These lots presumed either anti-f(ce) or anti-K, rather than anti-Di^a (Table 1B, C). A sequential antibody identification test (ID) using 0.8% Resolve® panel C system (Ortho Clinical Diagnostics™) was performed. This ID identified pure anti-f(ce) in 3+, without any coexistent antibody (Table 1D). Moreover, an additional ID using ID-DiaPanel® (BIORAD) showed positive results only to reagent RBCs that expressed both c- and e-antigens, suggesting the presence of the compound antigen "f(ce)" (Table 1E). To reconfirm this antibody, we designed two methods. The first method was "Rh CcEe subgroup profiling of incompatible pRBCs". As the f(ce) antigen might be expressed only when both c- and e-antigens coexist, we anticipated that all pRBCs that showed positive results in the cross-match expressed both antigens. Mostly, the result from this patient was CDe, which might not express the f(ce) antigen and could produce an anti-f(ce) alloantibody. Among 18 cross-matched pRBC units, 16 were compatible and 2 (No. 6 and 7) were not. These 2 incompatible units showed CcDe and cDEe phenotypes, respectively, suggesting that these might contain c- and e-antigen genes in cis (Figure 1A). The second method was "Re-AST using the patient's plasma after adsorption to incompatible pRBC". As the patient's plasma after adsorption to incompatible pRBC might not have anti-f(ce), we anticipated that this plasma would show a negative result with any AST panel, contrary to the previous results. In the initial adsorption (to the incompatible unit, No. 6) attempt, composed of 3 cycles (each cycle for 30 minutes at 37°C), AST using Surgiscreen® (Ortho Clinical Diagnostics™) resulted in persistent anti-f(ce) in cell #3 (Figure 1B-a). However, an additional adsorption attempt (to the same unit) composed of 3 cycles (each cycle for 30 minutes at 37°C) followed by 1 cycle (for 7 hours at 37°C), AST using the same reagent cells showed a decreased trace result (Figure 1B-c). On the other hand, the plasma after adsorption to compatible pRBC (No. 18) as a positive-control showed persistent anti-f(ce) in both initial and additional attempts (Figure 1B-b and -d). We decided to transfuse pRBCs, which are compatible in the cross-match and lack the c-antigen. Within 3 days from the operation, the patient received a total of 7 pRBC units without any adverse reaction. His Hb increased and remained stable over the next several days. His final Hb was 10.2 g/dL, and he was discharged without need for a transfusion.

DISCUSSION

Since the amino acid residues that determine either C/c- or E/e-polymorphisms are close to each other, several compound antigens contributing to a single epitope could be developed. The f(ce) antigen is not only the first compound antigen, but also the sixth Rh antigen following D, C, E, c, e, in alphabetical order corresponding to their discovery. As mentioned in the introduction, the f(ce) antigen is believed to be expressed when both c- and e-antigens are coded in the same haplotype (in cis position). Although the f(ce) antigen has been found accompanied with only D and c antigens (cD-) [8-10], we could not find a detailed reference concerning this manifestation. From an alternate perspective, the anti-f(ce) antibody should be produced in individuals whose Rh haplotype contains neither cDe nor cde. Indeed, 3 previous case reports in South Korea included patients whose Rh phenotypes were CcDEe [10,11] and Cde [12]. In former cases of CcDEe, C and e would be rearranged in cis, and vice versa. Sometimes, contrary to expectation, this antibody may not react to RBC, which presumably have the f(ce) antigen. Jones [3] reported 3 negative reactions to RBCs of which probable genotypes were CDe/cde. Nah [11] re-

Figure 1A)

Packed RBC No.	Rh phenotype	Cross-match results		
		Step 1: LISS in RT	Step 2: 37°C	Step 3: AHG
1	CcDEe	0	0	0
2	CcDEe	0	0	0
3	CDe	0	0	0
4	CDe	0	0	0
5	CDe	0	0	0
6	CcDe	0	3+	3+
7	cDEe	0	3+	3+
8	cDE	0	0	0
9	CDe	0	0	0
10	CDe	0	0	0
11	CcDEe	0	0	0
12	CcDEe	0	0	0
13	CcDEe	0	0	0
14	CcDEe	0	0	0
15	CDe	0	0	0
16	CcDEe	0	0	0
17	CDe	0	0	0
18	CDe	0	0	0

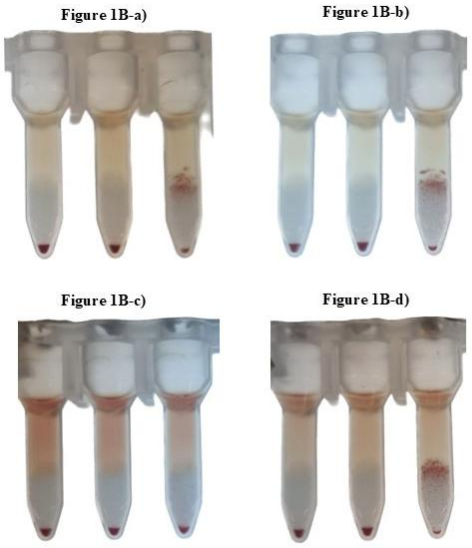

Figure 1. The results of cross-match and adsorption tests.

ported similar findings to the RBCs of which Rh phenotypes were CcDe and Ccde, respectively. These results are confusing and might be due to factors from either the f(ce) antigen on RBC used in the test or anti-f(ce) from patients. Jator [8] mentioned the f(ce) antigen to show reduced expression and qualitative differences of anti-f(ce) antibodies according to individual Rh genotype. Our case presents anti-f(ce) from a patient whose Rh phenotype is CDe. The reason for alloimmunization is uncertain, but previous pRBC transfusion is considered the cause. Interestingly, compared to other case reports that suggest further adsorption to remove coexistent antibodies (e.g., anti-c or -e) [3], our case revealed purely identified anti-f(ce) even without a positive autocontrol derived from previous transfused allo-RBCs. We might have missed this antibody if we had not chosen pRBCs that express the f(ce) antigen during cross-matching. In the initial AST using only 2 reagent RBCs lacking the f(ce) antigen, the result was negative such that sequential ID was not needed. But, the positive results during cross-matching inspired us to investigate further. Thus, additional ASTs using 3 reagent RBCs including the f(ce) antigen suggested a different result, and sequential IDs from 2 manufacturers finally revealed anti-f(ce). The detection of anti-f(ce) even without other coexistent alloantibodies has been extremely rare; thus, we attempted to reconfirm this result using 2 methods. First, as introduced in Nah's report [11], we performed cross-matching with a number of pRBCs consisting of various Rh phenotypes. There was no exception in their Rh phenotypes, as all pRBCs showed suitable Rh phenotypes to their cross-matching results. Moreover, during cross-matching, 2 incompatible pRBCs (No. 6 and 7) showed positive results in step #2 (37°C phase) and step #3 (anti-human globulin phase), suggesting that this anti-f(ce) might be IgG rather than IgM. Unfortunately, we could not perform a further titration test as conducted in Nakamura's report [13] due to the shortage of specimen. Second, as introduced in the Youk [12] and Nakamura [13] reports, we performed adsorption to pRBCs of which Rh phenotypes were already known. The residual plasma after initial adsorption to the incompatible unit (No. 6) needed a longer adsorption time to thoroughly eliminate anti-f(ce). We assumed that the amount of anti-f(ce) in plasma overwhelmed the number of epitopes on target RBCs, but the actual reason remains uncertain. Further studies for the affinity and avidity of anti-f(ce) and optimal conditions to maximize these features are needed.

CONCLUSION

In conclusion, there are many factors that should be considered in a positive cross-matching result. One of those is an unexpected antibody of which the target is not included in ordinary AST panels. Anti-f(ce) is no exception, as it is not only rare itself, but also usually coexists with other alloantibodies that can mask it. In a similar situation, broader AST panels should be considered to identify this antibody, which is potentially harmful. Additionally, further processes to reconfirm this antibody would be of help to blood banks worldwide.

Acknowledgment:
We thank all medical technologists in the blood bank for their contributions.

Declaration of Generative AI in Scientific Writing:
During the preparation of this work we used ChatGPT (OpenAI) to improve language clarity and check for grammatical errors. After using this tool, we reviewed and edited the content as needed and take full responsibility for the content of the publication.

Declaration of Interest:
This research was supported by the Ministry of Trade, Industry and Energy (Project No. RS-2024-00403563).

References:

1. Rosenfield RE, Vogel P, Sanger R, Race RR. A new Rh antibody, anti-f. Br Med J 1953;1(4817):975. (PMID: 13032583)

2. Sanger R, Race RR, Rosenfield RE, Vogel P, Gibbel N. Anti-f and the "New" Rh Antigen it Defines. Proc Natl Acad Sci USA 1953;39(8):824-34. (PMID: 16589338)

3. Jones AR, Steinberg AG, Allen FH, Diamond LK, Kriete B. Observations on the New Rh Agglutinin Anti-f. Blood 1954;9(2): 117-22. (PMID: 13126181)

4. Cohn CS, Delaney M, Johnson ST, Katz LM, Schwartz J. Technical Manual. 21 st. Bethesda, Maryland:American Association of Blood Banks;2023. https://www.scribd.com/document/725804903/AABB-Technical-Manual-21st-Ed

5. Levine P, White J, Stroup M, Zmijewski CM, Mohn JF. Hemolytic Disease of the Newborn probably due to Anti-f. Nature 1960;185:188-9. (PMID: 14416273)

6. Spielmann W, Seidl S, von Pawel J. Anti-ce (anti-f) in a CDe/cD-Mother, as a Cause of Haemolytic Disease of the Newborn. Vox Sang 1974;27(5):473-7. (PMID: 4213590)

7. O'Reilly RA, Lombard CM, Azzi RL. Delayed Hemolytic Transfusion Reaction Associated with Rh Antibody Anti-f: First Reported Case. Vox Sang 1985;49(5):336-9. (PMID: 4082530)

8. Jator EK, Pedde E. Anti-f in a 24-year-old male: a case study. Clin Lab Sci 2010;23(2): 68-71. (PMID: 20499529)

9. Reid ME, Lomas-Francis C, Olsson ML. The Blood Group Antigen FactsBook. Factsbook. Burlington, Elsevier Science, 2012. https://books.google.com/books/about/The_Blood_Group_Antigen_FactsBook.html?id=5YYwS-iVPDgC

10. Eun-Jung C, Hoi-Joo Y, Suk-Won S, Seog-Woon K. The First Case of Anti-f(ce) and Anti-Cs^{a} Antibodies in Korea. KJBT 2014; 25:160-4. https://www.kjbt.org/journal/view.html?spage=160&volume=25&number=2

11. Nah H, Shin S, Kim S, Lee E, Kim HO. A Case Report of Anti-f(ce) Identified in a Patient with Pancreatic Cancer. KJBT 2016; 27:174-82. https://www.kjbt.org/journal/view.html?doi=10.17945/kjbt.2016.27.2.174

12. Youk HJ, Kim JS, Hwang SH, Oh HB, Ko DH. Case Report of Anti-f(ce) Antibody Identified Simultaneously with Anti-M Antibody in a Patient with Liver Cirrhosis. KJBT 2022;33:32-8. https://www.kjbt.org/journal/view.html?doi=10.17945/kjbt.2022.33.1.32

13. Nakamura Y, Ohsawa T, Furuta Y, Tokida M, Ichikawa K, Ohsaka A. Successful Identification of Anti-f Alloantibody in a Non-transfused Male Patient Employing ID-Micro Typing System Gel Cards®. J Blood Disord Transfus 2015;6:6. https://www.walshmedicalmedia.com/abstract/successful-identification-of-antif-alloantibody-in-a-nontransfused-male-patient-employing-idmicro-typing-system-gel-card-29767.html