Case Series

Clinical Relevance of Anti-S and Anti-M Antibodies in Crossmatch Incompatibility: A Case Series

Dipshikhaa Ravi[1], Ashwin Anadan[1], R. Krishnamoorthy[1], Niranj Rathan[1,*], Sampat Kumar[1]

[1]Sri Ramachandra Medical College and Research Institute, Chennai, India

***Correspondence:** M1022001@sriher.edu.in

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Abstract

Background: Alloimmunization is a challenge in transfusion medicine, especially among patients with prior transfusions or pregnancies. Crossmatch incompatibility from unexpected red cell antibodies can delay transfusions, impact outcomes, and cause hemolysis.

Aim: To highlight the clinical significance of anti-S and anti-M antibodies of the MNS system in crossmatch incompatibility, by summarizing six cases managed in our department.

Methods: We present a retrospective case series of six patients exhibiting serologic incompatibility during pre-transfusion testing between May 2024 and May 2025 at a tertiary care center. Antibody screening and identification were conducted using column agglutination technology (CAT, Ortho vision) with 3-cell and 11-cell commercial panels. Quality control was ensured according to manufacturer protocols. Compatible and incompatible units were recorded using standardized grading and QC systems.

Results: Among 55,542 crossmatched patients, six (all females; mean age 36 years; range 11–53) showed crossmatch incompatibility owing to Anti-S (4/6) or Anti-M (2/6) antibodies. Most had prior transfusion or pregnancy history. Anti-M was reactive at 37°C/AHG phase in both cases. Compatible units were identified and transfused as indicated; overall, 51 units were crossmatched (29 incompatible, 22 compatible, see Table 1). Four patients were transfused uneventfully with compatible antigen-negative units.

Conclusion: Early identification of clinically significant red cell antibodies and provision of antigen-negative blood are crucial for safe transfusion. Anti-S and Anti-M antibodies, although uncommon, should be considered during incompatibility evaluation, particularly in settings with high transfusion exposure or pregnancy rates.

Keywords: alloimmunization; transfusion medicine; crossmatch incompatibility; red cell antibodies; anti-s; anti-m; mns blood group system

Introduction

Delivering safe blood to the appropriate patient at the appropriate time is a key role of transfusion services. Crossmatching is performed to ensure transfused blood is compatible, as part of pre-transfusion testing. Unresolved crossmatch incompatibility can delay crucial interventions and increase the risk of adverse outcomes. Here, we present a case series describing the detection and impact of Anti-S and Anti-M antibodies in six patients and highlight laboratory and clinical management strategies relevant to transfusion medicine practice.

Methods

Study design and setting

This is a retrospective case series conducted in the Department of Transfusion Medicine at a tertiary care center in India. The study period was May 2024 to May 2025. All cases with serological evidence of crossmatch incompatibility due to antibodies of the MNS system were reviewed after identifying the blood groups.

Laboratory workflow

Antibody Screening and Identification: Antibody screening was performed using 3-cell and 11-cell panels (Ortho vision Gel Cards) on a column agglutination technology (CAT) platform. Manufacturer: Quidel Ortho Corporation (P). Incubation was at 37°C for 10 minutes; results were graded according to standard agglutination scoring ("0" to "4+").

Crossmatching: Crossmatching was carried out by CAT (polyspecific anti-IgG+C3d), with grading as per manufacturer's scale. Grading was performed visually ("0" = negative; "1+" to "4+" = increasing agglutination). Units were randomly selected as per SOP and availability, informed by antigen prevalence statistics among donors.

Quality Control: Internal QC was performed daily on each lot of screening/identification panels and CAT cards by positive/negative controls per manufacturer and AABB (21st ed.) recommendations. Each test run included control wells.

Record-Keeping: For each patient, all units crossmatched (compatible and incompatible) were logged; results summarized in Table 1.

Case Descriptions

For each case, demographic details, clinical history (pregnancy, transfusion), serological findings, number of units crossmatched, and transfusion outcomes are summarized in standardized format.

Case 1: Anti-S

37-year-old female, primigravida with DCDA twins (16 weeks), no prior transfusion or abortion history. Admitted for cervical cerclage.

Immunohematology: B Rh(D) Positive; antibody screen positive. ABID: Anti-S(Figure 1). Crossmatched 4 units (1 as per request – incompatible) and additional 3 random units- 1 compatible. No transfusion required.

Outcome: Discharged uneventfully without any transfusions.

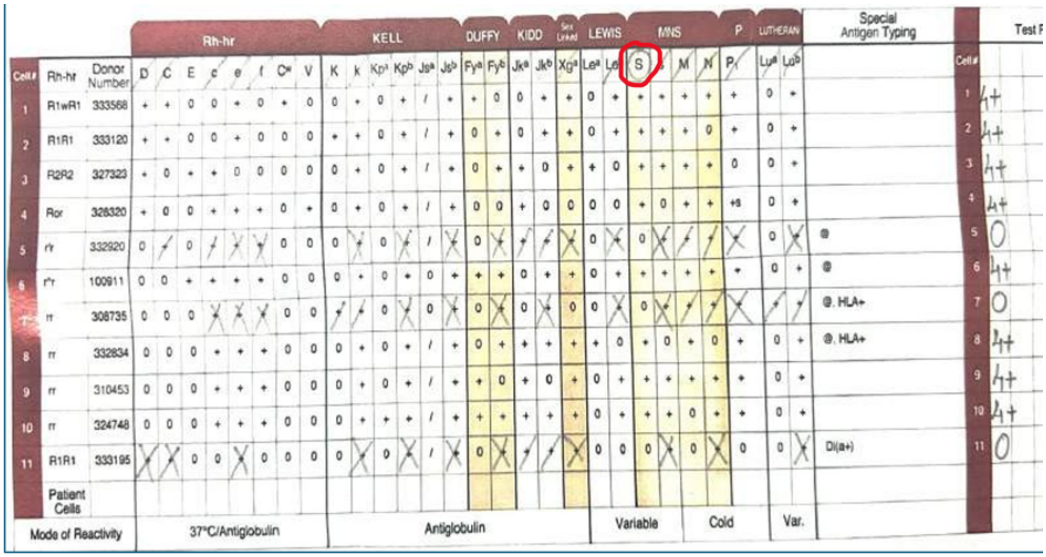

Figure 1: Antibody identified: Anti-S.

Case 2: Anti-S

27-year-old female, G4P1L1D1A1 at 35+6 weeks, GDM, previous LSCS. No prior transfusions. Reason for transfusion: For elective LSCS, hemoglobin 11.3 g/dL.

Immunohematology: A Rh(D) Positive; antibody screen positive, Anti-S identified (Figure 2). Crossmatched 7 units (1 requested- incompatible; 6 random units- 2 incompatible and 4 were compatible). One compatible unit transfused uneventfully.

Outcome: Good postoperative recovery.

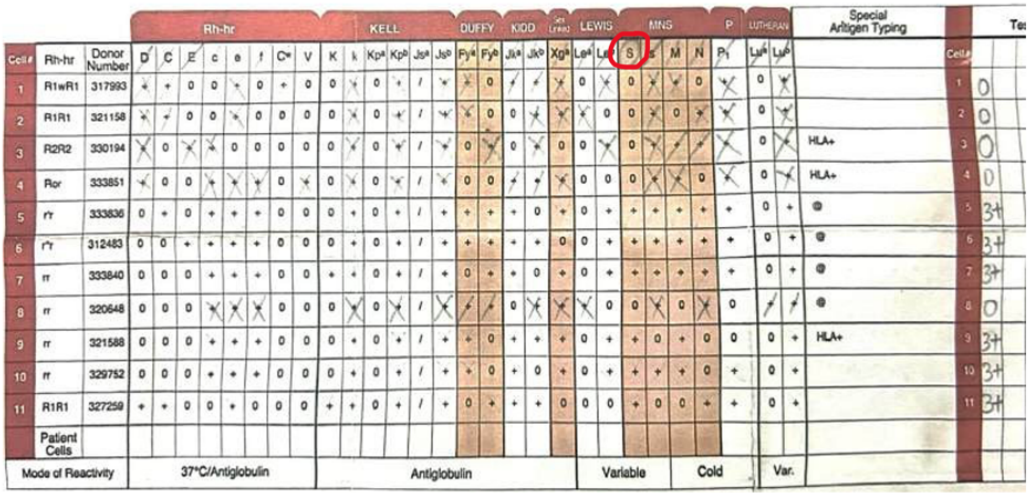

Figure 2: Antibody identified: Anti-S.

Case 3: Anti-S

53-year-old female, P1L1A1, with LRTI, MPGN, hypothyroidism, and AIHA (not transfusion dependent). Reason for transfusion: Hemoglobin drop (6.3 g/dL) during hospitalization.

Immunohematology: A Rh(D)Positive; antibody screen positive, probable Anti-S(Figure 3). Crossmatched 7 units (1 requested- incompatible and 6 units random- 2 were incompatible and 4 compatible). 3 compatible units transfused over hospital stay.

Outcome: No transfusion reactions.

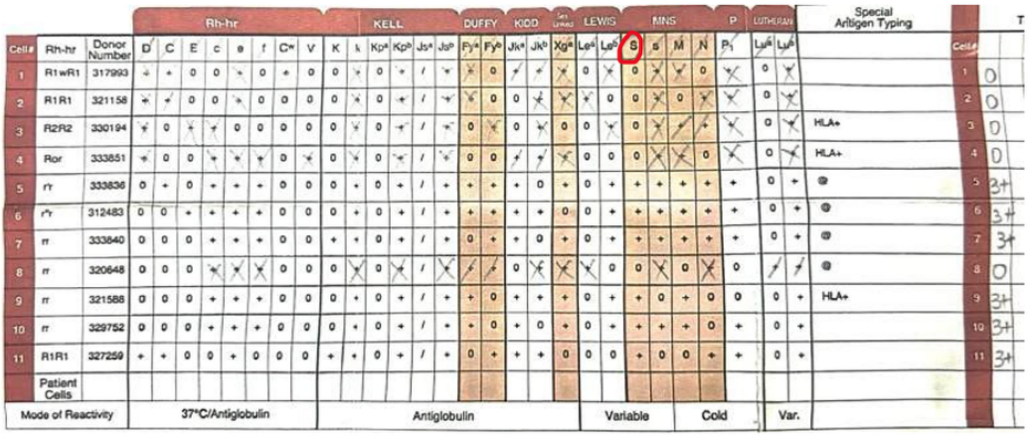

Figure 3: Antibody identified: Anti-S.

Case 4: Anti-S

49-year-old female, trauma (RTA), no previous transfusion or abortion, last childbirth 20 years earlier. Reason for transfusion: Anemia with hemoglobin 6.5 g/dL, preoperative for ORIF of humerus fracture.

Immunohematology: O Rh(D)Positive; antibody screen positive, Anti-S identified (Figure 4). Preoperatively crossmatched 7

units (1 requested- incompatible; 6 units crossmatched at random- 4 incompatible and 2 units compatible. One compatible unit transfused preoperatively; postoperatively, 6 units crossmatched, 4 compatible, but no further transfusions needed.

Outcome: Full recovery.

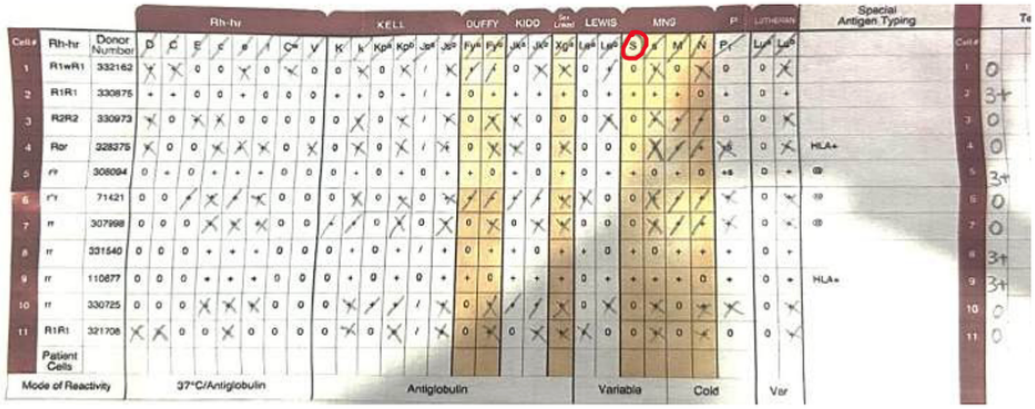

Figure 4: Antibody identified: Anti-S.

Case 5: Anti-M

11-year-old female, admitted for embolization of vertebral aneurysmal bone cyst. Reason for transfusion: Pre-procedure, hemoglobin 11.2 g/dL.

Immunohematology: O Rh(D) Positive; antibody screen positive, Anti-M identified (Figure 5). Crossmatched 12 units (1 requested- incompatible and additional 11 units were randomly crossmatched- 10 incompatible and 1 compatible. Anti-M reactive at 37°C/AHG. No transfusion administered.

Outcome: Successful procedure, no transfusion needed.

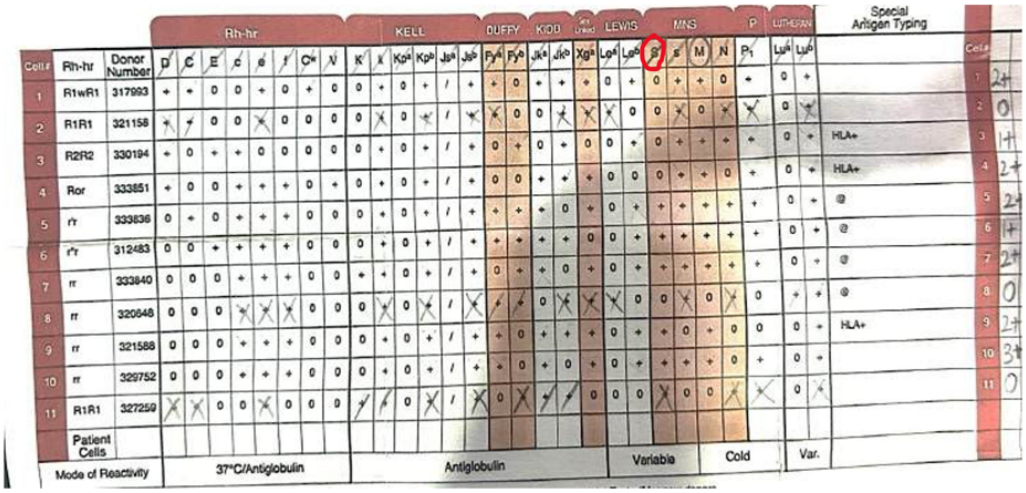

Figure 5: Antibody identified: Anti-M.

Case 6: Anti-M

41-year-old female, CA rectum post chemo, P2L2A1, prior transfusions (2), prior abortion. Reason for transfusion: Pre-ileostomy, hemoglobin 9.8 g/dL.

Immunohematology: O Rh(D) Positive; antibody screen positive, Anti-M identified (Figure 6), reactive at 37°C/AHG. Crossmatched 10 units (2 requested- incompatible, so 8 units randomly crossmatched- 7 incompatible and 1 compatible. One compatible unit transfused peri-operatively.

Outcome: Uneventful recovery.

The given table summarizes the cases with the antibody identified and the number of units crossmatched accordingly (Table 1).

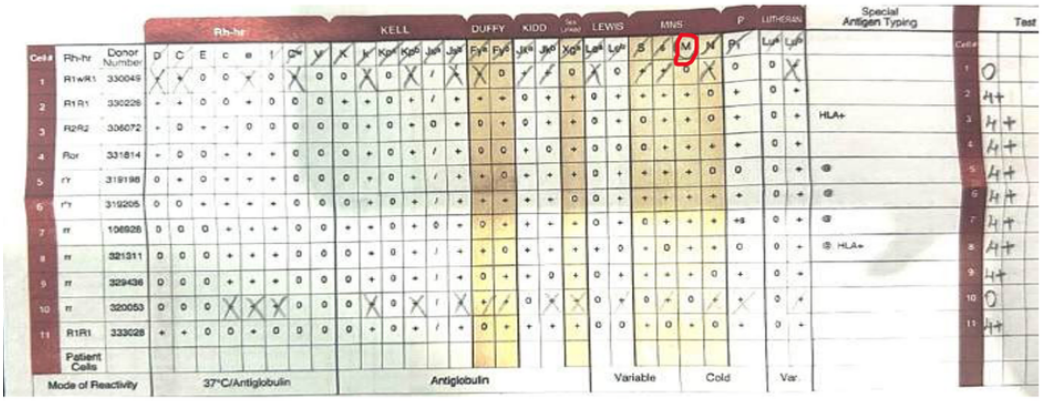

Figure 6: Antibody identified: Anti-M.

Table 1: Table 1 represents the summarized version of the cases.

Case	Antibody	No. units crossmatched	Compatible	Incompatible	Transfused	History
1	Anti-S	4	1	3	0	No transfusion/abortion
2	Anti-S	7	4	3	1	G4P1L1D1A1, no transfusion
3	Anti-S	7	4	3	3	P1L1A1, AIHA (not transfusion dependent)
4	Anti-S	13	6	7	1	Trauma, no previous transfusion/abortion
5	Anti-M	12	1	11	0	No transfusion/abortion
6	Anti-M	10	1	9	1	2 transfusions, abortion
Total	—	53	17	36	6	—

Discussion

Detection of unexpected red cell antibodies, especially those of the MNS system, is crucial for transfusion safety. Alloimmunization may result from transfusion or pregnancy. Clinically significant antibodies—those reacting at 37°C/AHG, especially IgG class—pose risk of hemolytic reactions and reduced RBC survival [1, 2]. Anti-S is a well-described clinically significant antibody and Anti-M, while often considered naturally occurring, can be significant if reactive at 37°C/AHG phase [3, 4, 5, 6]. In both Anti-M cases in our series, clinical relevance was established by positive reactions at 37°C/AHG.

We performed extensive crossmatching based on antigen prevalence (M antigen prevalence ∼87%, S ∼54% in Indian donors- Table 2) [7, 8], so multiple random units had to be screened to find compatible blood. This workflow aligns with institutional protocols and AABB guidelines. Record-keeping included detailed transfer histories and crossmatch logs, and all discrepancies (e.g., case histories, numbers of units transfused) were systematically reconciled.

Table 2: Prevalence of blood group antigens among blood donors.

Antigens	Prevalance of Antigen Positive	Prevalance of Antigen Negative
M	87.2	12.8
N	62.9	37.1
S	54.2	45.8
s	88.2	11.8

Our findings are consistent with other Indian and international studies documenting the rarity but major impact of MNS antibodies in transfusion settings [9, 10, 11]. Notably, four of six patients in our series received compatible antigen-negative transfusions uneventfully; two did not require transfusion. Routine inclusion of antibody screening and identification by CAT with proper QC improves outcomes.

Conclusion

This case series (6 patients) demonstrates that anti-S and anti-M antibodies, although uncommon, are clinically relevant causes of crossmatch incompatibility, with anti-M's significance confirmed at 37°C/AHG. Careful laboratory work-up, following standardized protocols and QC, and efficient identification and provision of antigen-negative compatible units is critical for transfusion safety. Pregnancy and prior transfusion are important risk factors; Obstetric and transfusion histories must be reconciled and standardized in reporting. Our experience underscores the value of robust screening and crossmatch protocols in the prevention of delayed or hemolytic transfusion reactions.

Key Abbreviations & Legends CAT: Column agglutination technology

ABID: Antibody identification
QC: Quality control
PRBC: Packed red blood cells
LSCS: Lower segment cesarean section
AIHA: Autoimmune hemolytic anemia
ORIF: Open reduction with internal fixation
RTA: Road traffic accident

Statement of Ethics: This study was conducted using the data retrieved from existing hospital records without any direct patient contact. The requirement for the individual informed consent has been waived off by the Institutional Ethical Committee.

Author Contributions: All authors made equal contributions, reviewed and revised the manuscript. All authors have read and approved the final manuscript

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Conflict of Interest: None declared.

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