

수혈로 인한 항-K 항체 동정 1예

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= Abstract =

A Rare Case of Transfusion-related Anti-K Alloantibodies

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저자들은 한국인 남자에서 우리나라에서는 극히 드문 항-K 항체를 동정하였기에 보고하는 바이다. 항-K는 심각한 신생아 용혈성질환이나 수혈부작용을 일으킬 수 있는 임상적으로 매우 의미 있는 동종 항체로서 주로 수혈이나 임신에 의해 생성된다. 국내에서는 2명의 환자에서 항-K항체가 동정된 보고는 있으나 이는 국내 비예기항체 검출빈도 조사 연구에 포함된 자료로 환자 개개인에 대한 자세한 정보는 확인할 수 없었다. 본 증례에서는 환자가 국내에서 수혈경력이 있으며, 세균감염에 의한 자연발생 항체 여부는 실험을 통해 배제할 수 있었다. 그러나 환자가 사망하였기에 타 기관에서 수혈된 혈액의 현혈자 정보는 찾지 못하였다. 한국인은 100% K-k+으로 알려졌지만, 최근 국내에 외국인도 많이 거주한다는 것을 고려하면 이 환자에서는 수혈이 항-K 항체 유발 원인이었을 것으로 충분히 추정된다. 따라서, 국내에서 항원 및 동종항체의 빈도가 변하고 있음을 고려할 때, 수혈 전 항체검사나 교차시험 시 한국인에서 극히 드문 항체라도 검출해 내는데 주의를 기울여야 할 것이다. (Korean J Blood Transfus 2008;19:250-254)

Key words: Kell blood group system, Red cell alloantibodies, Transfusion

Introduction

The Kell blood group system is complex, containing at least 21 antigens.¹⁾ Among them, the K antigen is strongly immunogenic and thus sometimes results in severe hemolytic diseases in newborns or major transfusion reactions. The anti-K antibody (anti-K) is known to develop by im-

munization during blood transfusion or pregnancy.²⁾ Given that 100% of the Korean race is known to have the K-k+ phenotype,³⁻⁵⁾ the source of K antigen is open to debate. On rare occasions, the naturally occurring anti-K was reported, possibly by bacterial infection.^{6,7)}

For the first time, we analyze the source of anti-K detected in the serum of a Korean men

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who had been previously transfused. To rule out bacterial infection as the K-like antigenic stimulus in our patient, hemagglutination inhibition (HAI) assays using bacterial culture preparations were performed.

Case Report

A 38-year-old man was admitted for hematemesis and melena that had begun 1 day previously. He had been diagnosed with hepatocellular carcinoma 10 years prior but had declined treatment. Metastases to the lung and spine had been detected 2 months before admission, and the patient had undergone chemotherapy at that time. On admission, potent anti-K was detected in his serum by the gel technique (DiaMed, Cressier sur Morat, Switzerland), and testing was repeated using a different constitution of K⁺ cells. His Kell phenotype was K-k⁺. The potency remained the same at 37°C and 20°C. The patient refused treatment and was discharged in 1 week. Although it was known that he had been transfused before in Korea, no further information regarding the transfusion was available. He had no history of injection of albumin or immune globulin.

Because there has been no proven case of anti-K development through transfusion in Korea, bacterial antigens were suspected as the K-antigen source. A random urine culture obtained 2 months prior to admission showed *Enterococcus faecalis*, but stool cultures were not performed. As the *Enterococcus faecalis* normally inhabit the bowel, the patient's stool was cultured in selenite broth for 2 day and the three types of bacteria were

Table 1. The effects of bacterial suspensions on anti-K antibody titer.

	Dilution				
	1 : 1	1 : 2	1 : 4	1 : 8	1 : 16
Serum+saline	3+	3+	3+	3+	1+
Serum+bacterial suspension*	3+	3+	3+	3+	1+

*Bacterial suspensions were made by sonication of four types of bacteria isolated from stool cultured in selenite broth for 2 days: *Escherichia coli*, *Enterococcus faecalis*, and *Klebsiella oxytoca*.

identified by subculture. To ascertain the organism responsible for the K-like antigen, the bacterial suspension in selenite broth and the subcultured bacteria (*Escherichia coli*, *Enterococcus faecalis*, and *Klebsiella oxytoca*) were dissolved in saline. The bacterial suspensions were each sonicated for 4 minutes at 4°C to expose K-like antigens inside the bacterial cell walls.⁷⁾ The suspension was incubated with patient serum at different dilutions at 37°C for 1 hour (Table 1). As a control, whole serum diluted with saline was tested in parallel. The incubated serum containing sonicated preparations was centrifuged at 3,500 rpm for 8 min, and the supernatant was used for anti-K detection using the gel column method. However, no anti-K inhibitory activities were observed (Table 1). The patient's antibody titer did not decrease during the 8 days before discharge.

Discussion

The incidence of K antigen varies widely among races. The allele responsible for the K

antigen is frequently present in 9% of Whites and 1~2% of Blacks.^{8,9)} In contrast, the frequency of the K antigen in Asians is very low;⁵⁾ for example, its frequency is 0.1% in Thai,¹⁰⁾ 0% in Taiwanese,¹¹⁾ 0.5% in other minor Chinese ethnic groups,¹²⁾ and 0% in Koreans.³⁻⁵⁾

Despite the transfusion history of this patient, we believed the probability was very low that transfusion had generated anti-K in his serum due to the absence of the K antigen in the Korean population. Blood donation by foreigners is actually limited in Korea and plasma donation has been recommended except for Rh negative donors to prevent alloimmunization by rare red cell antigens. However, certain national practices may affect the prevalence of K and anti-K in the near future, such as increasing international marriage and blood donation by people of different races. Since 2000 international marriage between Korean man and immigrated foreign women comprised 36% of marriage in the rural areas.

The first case of anti-K in Korea was reported in a blood donor without further information in 2003.¹³⁾ The second case of anti-K was detected in a patient with transfusion history¹⁴⁾ in 2006. But, no more information was available about the patient and the source of anti-K.

This is the first report of anti-K in Korean evaluating the patient's information and the source of anti-K suggesting transfusion-derived immunization. To rule out the possibility of naturally occurring anti-K due to the stimulus of bacterial infection, we determined whether the anti-K in his serum was inhibited by K-like antigens known to exist in the bacterial cell wall. The bacteria

reported to contain the K-like antigen is one subtype of *E. coli* 0125:B15,⁷⁾ *Shigella sonnei*,⁷⁾ and *Enterococcus faecalis*.¹⁵⁾ Although we found that anti-K was not inhibited, we could not exclude that possibility entirely; the patient's urinary tract had been infected by *Enterococcus faecalis* 2 months prior, which is a possible source of exposure to the K-like antigen. However, *Enterococcus faecalis* is the normal flora and becomes a pathogen according to the patient's condition, the two isolates from urine and stool would be the same type.

Among the many red blood cell antigens, the incidence of the Kell antigen varies considerably among races. We have documented the third Korean case of anti-K in a terminal cancer patient, presumably caused by transfusion. The globalization of Korea and resulting influx of foreign citizens may help explain this unusual finding, given the 100% frequency of the K-k+ phenotype in Koreans. Due to the fact that the K antigen is highly immunogenic, antibody detection testing should be processed with caution despite the extremely low incidence of the K antigen in Korean populations.

Summary

We report the extremely rare identification of anti-K antibodies in a Korean patient. Anti-K antibody is a very potent red cell alloantibody resulting in severe hemolytic diseases in newborns or major transfusion reactions, and has been shown to develop following immunization during blood transfusion or pregnancy. Anti-K antibodies

were recently reported in two Koreans, but without detailed clinical information. In the case reported herein, the patient with anti-K alloantibodies had a history of a blood transfusion in Korea, but the donor's Kell phenotype and race was not available. Although some reports in the literature describe cases in which anti-K antibodies develop naturally by bacterial infection, the suspected bacterial stimulus was excluded in our patient based on *in vitro* experiments. Given that 100% of the natural Korean population has the K-k⁺ phenotype, we believe his transfusion was the precipitating antigenic event, especially since the donation of blood products in Korea by other races has increased in recent years. For this reason, caution should be exercised in pre-transfusion testing, such as antibody detection and cross-matching to detect extremely rare antibodies, even in Koreans, due to the changing spectrum of antigen and alloantibody frequencies.

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