

Ochrobactrum anthropi infection following corneal transplantation -A Case Report and Review of Literature

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Case Report

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Abstract

Background

Ochrobactrum anthropi is widely distributed and primarily infects patients with compromised immune functions. Although historically considered to possess low toxicity and pathogenicity, *Ochrobactrum anthropi* can lead to severe purulent infection. Here, we present a case of *Ochrobactrum anthropi* infection following corneal transplantation surgery, examining the occurrence and outcome of such infections post-transplantation.

Case presentation:

A retrospective analysis of cases involved examinations, genetic testing for diagnosis, and subsequent treatment. Patients with fungal corneal ulcer perforation, undergoing partial penetrating keratoplasty, exhibited anterior chamber exudation and purulence post-surgery. Despite unsuccessful antifungal treatment, genetic testing of anterior chamber fluid and purulent material confirmed *Ochrobactrum anthropi* infection. Antimicrobial treatment specifically targeting *Ochrobactrum anthropi* proved efficacious.

Conclusion

Inflammatory reactions following corneal transplantation should be vigilant for multiple infections. Genetic testing of aqueous humor holds significant guiding implications for clinical diagnosis and treatment.

Introduction

Ochrobactrum anthropi, a conditional pathogenic bacterium, is a Gram-negative rod that exhibits oxidase and catalase production and lacks fermentation capability. It is widely distributed and primarily infects patients with compromised immune functions [1][2]. Reports also indicate infections in hosts without prior illnesses and with normal immune functions [3][4]. The clinical manifestations of *Ochrobactrum anthropi* infections lack specificity, and it demonstrates robust drug resistance, posing challenges in clinical diagnosis and treatment [5].

Although historically considered to possess low toxicity and pathogenicity, *Ochrobactrum anthropi* can lead to severe purulent infections [6]. Reports exist of post-organ transplantation bacteremia [7], and in ophthalmology, occurrences of intraocular inflammation following cataract surgery [8][9]. However, cases of *Ochrobactrum anthropi* infection after corneal transplantation have not been documented. Here, we present a case of *Ochrobactrum anthropi* infection following corneal transplantation surgery.

Case report

A 51-year-old male patient presented with a 19-day history of redness and pain in the eye. The diagnosis was fungal keratitis (Fig. 1). Treatment included frequent instillation of natamycin eye drops (50mg/ml, North China Pharmaceutical, China) and intermittent application of intracorneal voriconazole injection (1mg/ml, Pfizer Limited, US). After one month of treatment, the examination revealed localized corneal ulceration with stable conditions but the development of corneal perforation (Fig. 2). B-ultrasound examination showed no abnormalities in the vitreous and retina. Subsequently, a partial penetrating keratoplasty was performed, and the surgery proceeded smoothly. Intraoperatively, aqueous humor and the affected cornea were collected for bacterial and fungal culture and identification. Voriconazole injection was used throughout the procedure for corneal margin and anterior chamber irrigation. The donor cornea, sourced from our eye bank, and residual donor cornea, along with corneal preservation solution (Corneal Chamber, Alchimial, Italy), were sent for bacterial and fungal culture postoperatively. Standard postoperative care included local application of natamycin and tacrolimus eye drops (0.1%, Senju Pharmaceutical Co, Japan), as well as levofloxacin eye drops (0.5%, Senju Pharmaceutical Co, Japan). Itraconazole capsules (200mg daily, Xi'an Yangsen Pharmaceutical Co., Ltd., China) were administered orally.

Following corneal transplantation, the corneal graft remained transparent. However, the aqueous humor gradually became turbid, and on the fourth postoperative day, anterior chamber pus accumulation was observed, raising suspicion of recurrent fungal infection. Consequently, anterior chamber pus was aspirated, and voriconazole injection was administered for anterior chamber irrigation and medication. Intraoperatively, the anterior chamber pus was found to be thin and watery, unlike the thicker purulent fluid seen in fungal infections. Anterior chamber pus smear examination revealed no fungal hyphae (Fig. 3D). Postoperatively, there was no significant improvement in anterior chamber reaction, and the cornea showed mild edema.

Microbiological examination of the recipient corneal ulcer, aqueous humor, donor cornea, and preservation solution yielded negative results for bacteria and fungi, likely due to preoperative antifungal and antibacterial treatment. However, considering the possibility of other infections postoperatively, aqueous humor and anterior chamber pus from the operated eye were collected again for genetic testing. During this period, the aforementioned eye drops were continued, and anterior chamber pus leakage gradually increased, leading to cloudiness of the corneal graft (Fig. 3A). Genetic testing results indicated the presence of *Ochrobactrum anthropi*. B-ultrasound examination revealed vitreous opacities (Fig. 3E). Ceftazidime injection (25mg/ml), amikacin injection (4mg/ml), and vancomycin injection (10mg/ml) were administered to the anterior chamber and vitreous, each three times. Oral antifungal medication was discontinued, and intracameral cefuroxime (1.0g three times daily) was given. To prevent fungal recurrence, natamycin eye drops were continued four times a day, along with tobramycin eye drops (0.3%, Tobramycin Eye Drops, Alcon-Couvreur n.v., Belgium), and levofloxacin eye drops (0.5%, Senju Pharmaceutical Co, Japan) every hour. After three days of treatment, anterior chamber pus showed a reduction (Fig. 3B), and after 10 days, complete absorption of anterior chamber pus was achieved. However, cloudiness of the corneal graft persisted (Fig. 3C), with B-ultrasound indicating a reduction in vitreous opacities (Fig. 3F). The patient's condition remained stable, with effective infection control.

"After six months of corneal transplantation in the patient, corneal opacities and pseudo-ptygium were formed in the operated eye (Fig. 4A). B-ultrasound examination showed no abnormalities. To improve visual function, a second partial penetrating keratoplasty was performed in combination with cataract removal surgery. Postoperatively, routine use of Tobramycin eye drops was applied to prevent infection, along with Tacrolimus and Prednisolone Acetate Ophthalmic Suspension (1%, Allergan Pharmaceuticals Ireland) to prevent rejection. One month after surgery, the corneal transplant was transparent (Fig. 4B), and corrected visual acuity was 0.1."

Discussion

Fungal keratitis stands out as the predominant cause of blindness in patients with infectious corneal diseases in China [10][11]. Therapeutic keratoplasty plays a pivotal role in the management of progressive fungal keratitis when conventional pharmacological interventions prove ineffective. However, a significant contributor to the failure of corneal transplantation is the recurrence of postoperative fungal infections, with reported recurrence rates ranging from 5–14% [12][13][14]. Risk factors for infection recurrence encompass the size of corneal ulcer infiltration, graft dimensions, and the type of fungus involved [15][16]. Furthermore, comprehensive antifungal treatment prior to corneal transplantation constitutes a critical determinant for surgical success. In the presented case, the patient received standardized antifungal treatment post-diagnosis, resulting in favorable therapeutic outcomes. Undertaking corneal transplantation at this juncture successfully averted postoperative recurrence of fungal infections. Hence, judiciously selecting the timing for corneal transplantation emerges as a pivotal strategy in controlling the recurrence of fungal corneal ulcers.

Anterior chamber pus appeared on the 4th day after surgery. Based on past experience, we preliminarily suspected a recurrence of fungal infection and performed voriconazole anterior chamber lavage in the operative eye. However, the observed nature of the intraoperative pus appeared thin and lacked the characteristic viscosity seen in fungal infections [17][18]. Subsequent exacerbation of the patient's condition after antifungal treatment raised suspicions of potential infection by other pathogens. To rule out the possibility of corneal contamination from the donor, another patient who received a corneal transplant from the same donor tissue at the same time was continuously monitored and no signs of infection were found.

Due to the fact that microbial cultures and smear examinations of the affected cornea failed to detect any pathogens, we conducted next-generation sequencing (NGS) on the anterior chamber pus to identify the infectious agent. NGS is a diagnostic technique widely used in microbiological research but infrequently employed in routine clinical microbiological diagnostics. It offers a rapid and accurate advantage in determining the nature and type of infection in clinical diagnosis [19], particularly demonstrating excellent diagnostic value for infections on the ocular surface and within the eye [20]. When traditional microbiological tests in ophthalmology prove ineffective, it serves as an efficient auxiliary diagnostic tool, significantly improving the detection rate of microorganisms that are challenging to culture in clinical samples [21].

Ochrobactrum anthropi is widely present in the environment, soil, and water sources (physiological saline, preservative solutions, dialysis fluid) [5][22][23][24]. Additionally, *Ochrobactrum anthropi* has been isolated from human bodily fluids [25]. As a rare conditional pathogen, most reported cases involve hospital-acquired infections, with infected patients using various indwelling and invasive medical devices such as central venous catheters, artificial heart valves, and drainage tubes [6][26]-[27]. Existing clinical case reports have found that *Ochrobactrum anthropi*-induced endophthalmitis is more common after cataract intraocular lens implantation [8, 9][28], [29], [30], and there is also a reported case of infection after artificial corneal implantation [31]. Infections related to implants may be associated with the propensity of *Ochrobactrum anthropi* to adhere to the surfaces of synthetic materials [32]. Some studies also suggest a correlation between post-cataract surgery endophthalmitis and contamination of intraocular irrigation fluids [29]. Another report found that after thorough cleaning of the cannula kit of an ultrasonic emulsification machine, the hospital's outbreak of *Ochrobactrum anthropi* infection promptly disappeared [33]. This report further confirms this hypothesis.

Ochrobactrum anthropi, being an opportunistic pathogen, manifests infection significantly in individuals with compromised immune function and a history of both local and systemic antibiotic usage [8][34], [35], [36], [37]. However, in this particular case, the patient did not employ any indwelling or invasive medical devices, and comprehensive examinations, both physical and systemic, failed to reveal any symptoms. Based on the patient's medical history, the human *Ochrobactrum anthropi* infection in this case can be attributed to local immune function decline after corneal transplantation. In addition, the patient had a history of topical antibiotic use for 1 month prior to surgery, which increased the risk of human *Ochrobactrum anthropi* infection due to dysbiosis and antibiotic resistance.

Despite the generally perceived low virulence of *Ochrobactrum anthropi*, its infection rates have gradually increased in recent years due to its inherent multidrug resistance to antibiotics [38]. *Ochrobactrum anthropi* exhibits resistance to β -lactam drugs, particularly cephalosporins and penicillins, while being sensitive to quinolone drugs and aminoglycoside drugs, especially amikacin and gentamicin [39][40]. Our patient received prompt and adequate antibiotic treatment upon confirmation of the infection, effectively controlling the infection rapidly. However, it is noteworthy that, after 14 days of treatment, although the infection was well controlled, the corneal graft still exhibited cloudiness. Currently, while there have been numerous reports on endophthalmitis caused by *Ochrobactrum anthropi*, there is limited documentation on the toxicity of this bacterium to the cornea itself and the resulting pathological changes. Nandini et al. reported a case of corneal inflammation caused by *Ochrobactrum anthropi* infection, presenting as anterior chamber purulence in a patient with a history of viral keratitis. This case was ultimately diagnosed as *Ochrobactrum anthropi* infection, with corneal histopathological findings showing detachment of the posterior elastic layer [37]. Generally, bacterial infections can lead to pathological changes such as corneal opacification, edema, ulcer formation, and endothelial damage [41]. However, when infecting corneal tissues, *Ochrobactrum anthropi*, generally considered a Gram-negative bacterium with low virulence, may induce more severe pathological changes. The cloudiness of the corneal graft after *Ochrobactrum anthropi* infection in this case may also be related to the local eye drops and anterior

chamber injections during the infection treatment, causing damage to the corneal endothelium [42][43][44].

Conclusion

This case constitutes the inaugural report of *Ochrobactrum anthropi*-induced keratitis following corneal transplantation. In the realm of this rare pathogen, the clinical manifestations post-infection lack specificity. Ophthalmologists must judiciously select the appropriate diagnostic approach to identify the pathogen and guide therapeutic interventions. For patients with conditions predisposing to local immune dysfunction, the possibility of *Ochrobactrum anthropi* infection should be considered promptly upon the onset of infection. The corneal pathology induced by this pathogen warrants attention and merits further investigation.

Declarations

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Contributions

Contributors: Hui Jia were involved in the conception, logistics/planning (obtained informed consent, image acquisition with medical images) and revising the article, Xiaoru Shi were involved in the image acquisition and revising the article . Lei Liu drafting the article and critically for important intellectual content and finished writing the final draft . Chunmei Wang participated in the patient's treatment,

involved in the logistics of the article. Hui Xu, Lulu Hou and Rong Huang participated interpretation of images. All authors approved the final manuscript.

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Ethics declarations

Ethics approval and consent to participate

The experimental protocol was established, according to the ethical guidelines of the Helsinki Declaration and was approved by the Human Ethics Committee of The First Hospital of Jilin University. Written informed consent was obtained from individual or guardian participants.

Consent for publication

Patients provided written consent for the use of their images. Written informed consent was obtained from patient for publication of this case report

Competing interests

The authors declare no competing interests.

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Figures

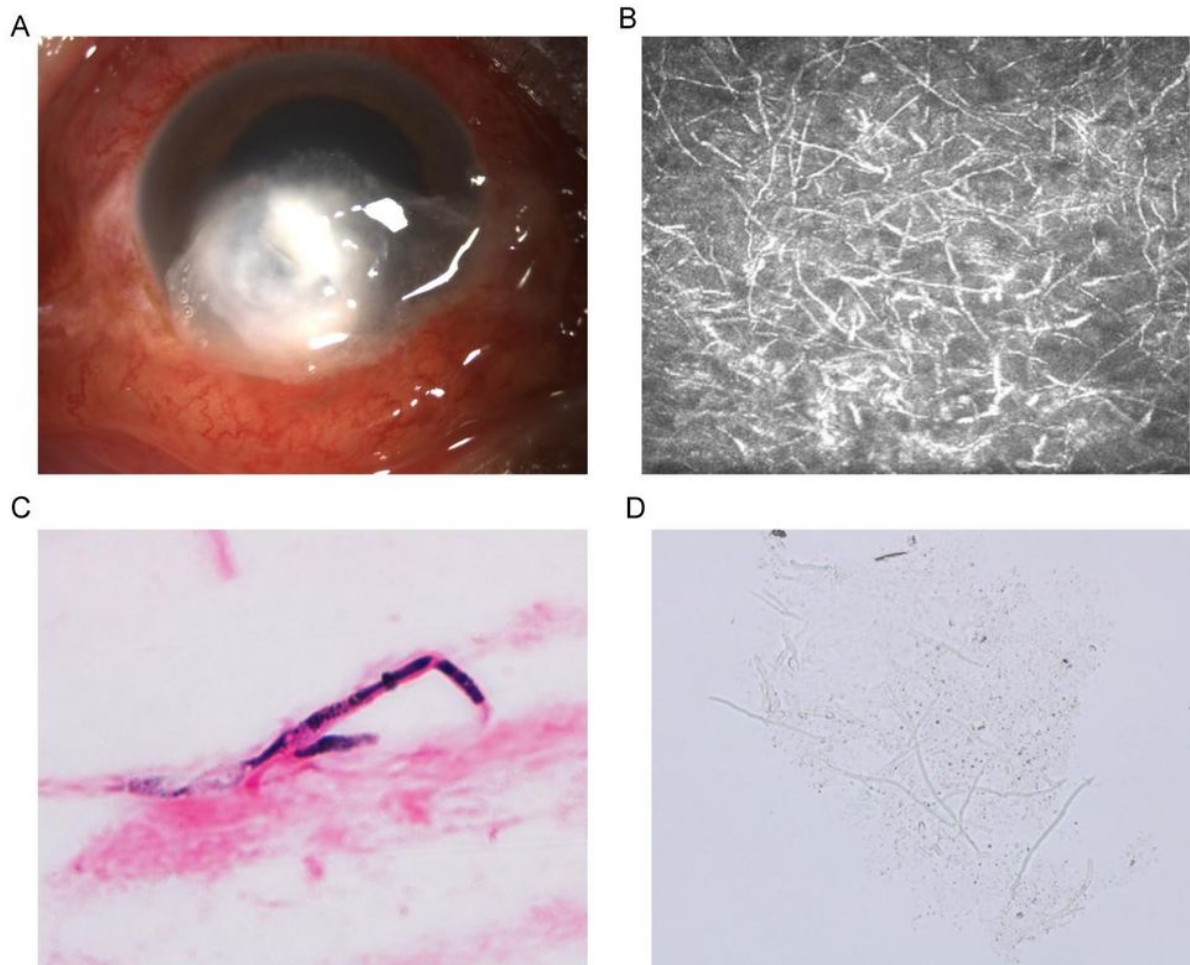


Fig 1

Figure 1

A Peripheral central corneal opacity and infiltration, showing typical elevated lesions, dry surface, and feathery infiltrating margins. B: Fungal hyphae are visible under confocal microscopy. C: Fungal hyphae are observed in corneal scrapings with Gram staining. D: Corneal scrapings with KOH wet mount reveal fungal hyphae.

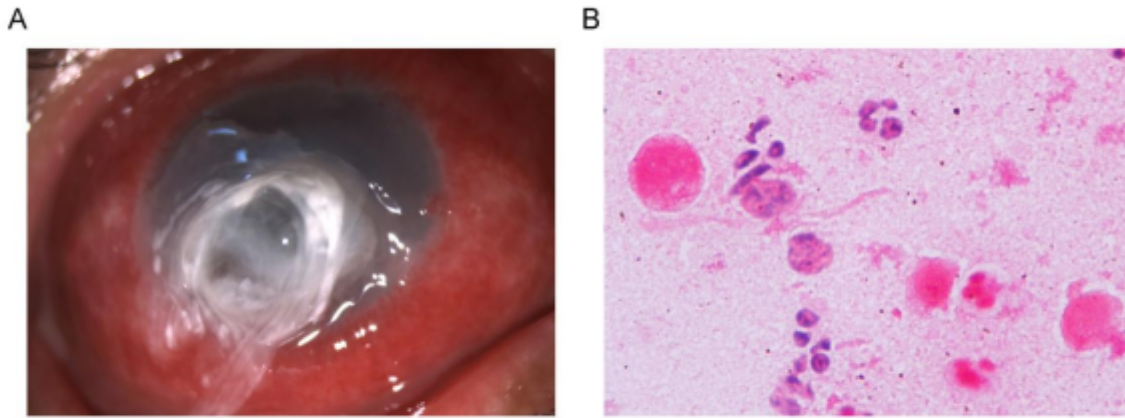


Fig 2

Figure 2

A After treatment, the corneal ulcer has healed, with localized margins and corneal perforation. B: No fungal hyphae are observed in corneal scrapings with Gram staining, but inflammatory cells are present.

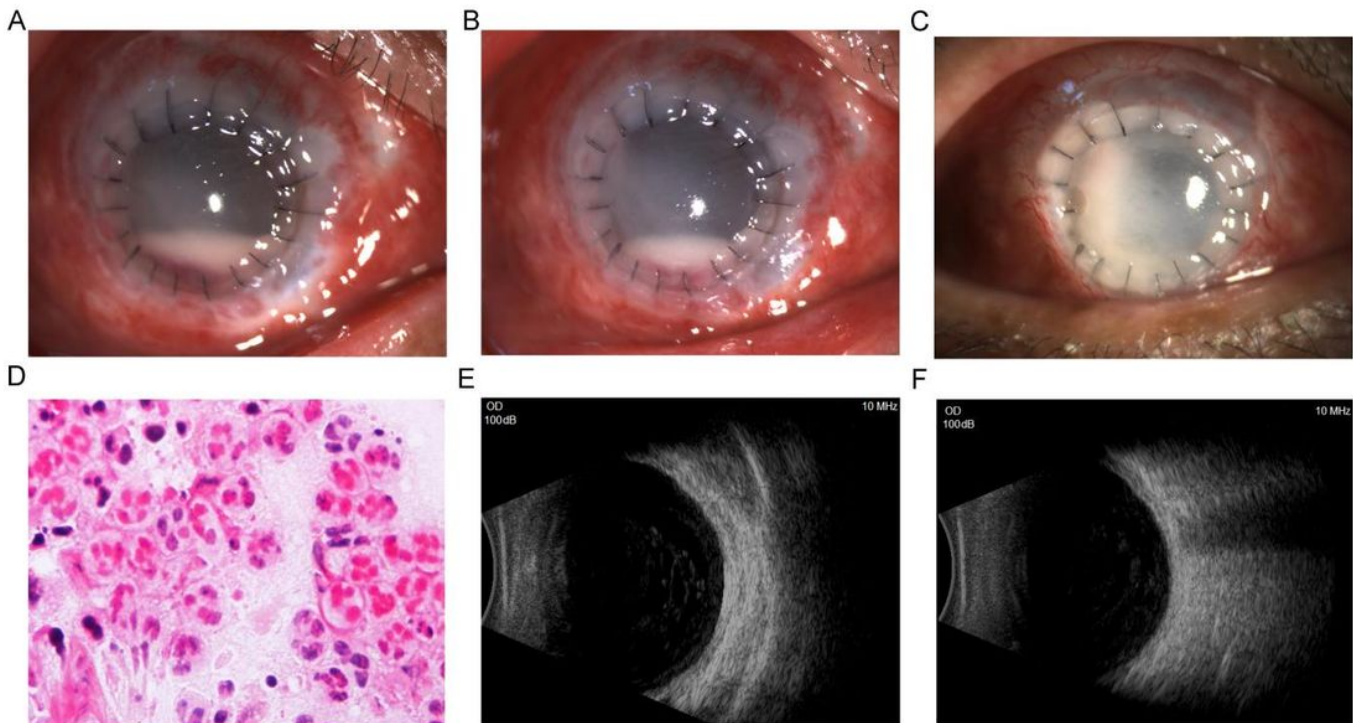


Fig 3

Figure 3

A: After corneal transplantation, there was anterior chamber pus accumulation, and the pus had a thin and watery consistency. B: Following treatment, there was some reduction in anterior chamber pus. C:

The corneal graft appeared grayish-white and opaque, and the anterior chamber pus disappeared. D: Gram staining of corneal scrapings revealed no fungal hyphae but showed a significant number of inflammatory cells. E: Turbidity resembling sediment was observed in the vitreous cavity. F: The vitreous opacities noticeably decreased compared to before treatment.

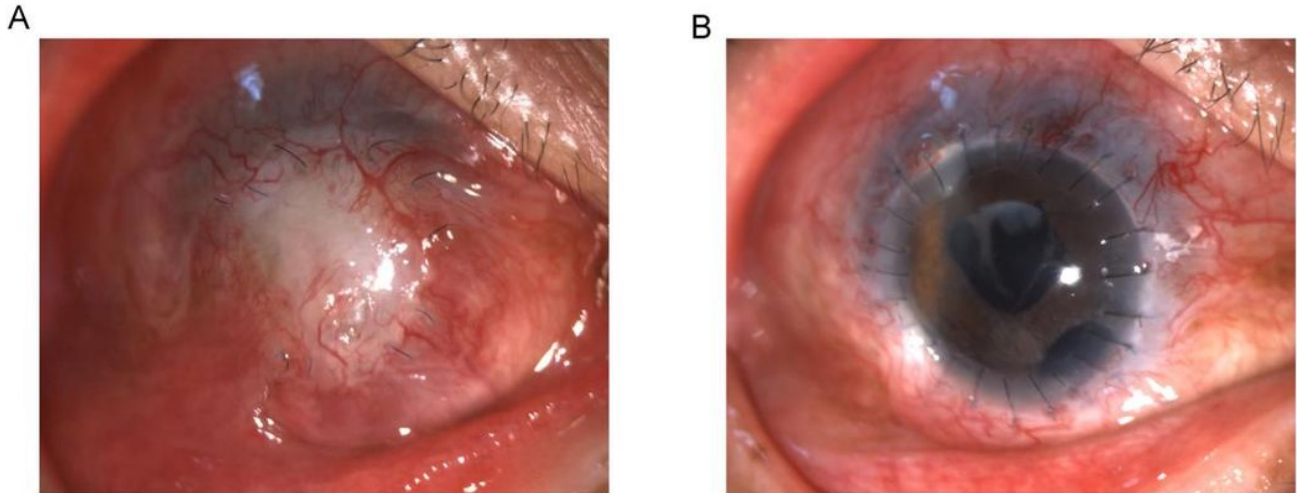


Fig 4

Figure 4

A: Pseudo-terygium and corneal opacities developed six months after corneal transplantation. B: After the second corneal transplantation, the corneal graft became transparent.