uveitis with mild degree of ocular inflammation can be managed by topical noncorticosteroid or corticosteroid drug. The sub-Tenon's injection of corticosteroids is used when the patients have moderate inflammatory activities in the vitreous cavity. If the vitreous inflammatory activity and the retinal vasculitis are severe, oral corticosteroids are given, but a long-term administration of systemic corticosteroid should be avoided [13]. Recent report indicates that tacrolimus [36] and 5-azacitidine [37] are useful for the resolution of autoimmune manifestations in HTLV-1-related overlap syndrome (deratomyositis/ Sjögren's syndrome) and HTLV-1-related myelodysplastic syndrome, which might be potential alternative drugs to apply HTLV-1 uveitis complication in the future.

Despite advances of novel treatment agents, the prognosis for ATL remains poor. A variety of therapeutic approaches have been examined and effectiveness of them has been gradually improved. A combination of arsenic trioxide, zidovudine and IFN α achieved a significant remission rate with moderate toxicity [38]. Allogeneic hematopoietic stem cell transplantation (HSCT) is considered to be one of the best curative therapies [39–41], and a significant improvement of eye complications were observed in accordance with a decrease in the HTLV-1 proviral load after allogeneic HSCT. Recently, alternative treatments were reported, which showed that daclizumab (monoclonal antibody directed against the α chain of the IL-2R and denileukin diftitox (immunotoxin fusion protein that targets the IL-2R) improve ocular complications such as sclerotitis in patients with underlying ATL [42].

In cases of KCS, the first and most important mediation is lubricating for patients with mild and moderate severity. Lubricating drops are used to reduce tear film disorders and to prevent ocular complications such as superficial punctate keratitis and corneal ulcers [43].

#### RECENT BASIC RESEARCH

The recent basic researches have shown new insights of HTLV-1 infection and pathogenesis by pursuing molecular functions of HTLV-1 Tax HTLV-1 basic leucine zipper factor (HBZ) [44\*]. Transgenic mice expressing HTLV-1 Tax develop an inflammatory arthropathy [45], and transgenic rats expressing HTLV-1 env-pX develop Sjögren's syndrome, arthropathy, vasculitis and polymyositis [46]. Regulatory T cells in HBZ transgenic mice were functionally impaired [47]. This implies that HTLV-1-induced regulatory T-cell dysfunction may be one of the mechanisms that induce immune activation by HTLV-1-infected T cells. Taken together, HTLV-1

Tax and HBZ are thought to be responsible for immune dysregulation and are potential target molecules for targeted therapies.

## CONCLUSION

HTLV-1 infection causes sight-threatening problems not only in local endemic area but also metropolitan area. HTLV-1-related ocular manifestations are frequently associated with inflammation such as HTLV-1 uveitis. That is caused by the alternation of immune status the cytokine production from HTLV-1-infected nonmalignant cells. Therefore, corticosteroid is the first choice for treating these inflammatory diseases. Effectiveness of other drugs such as tacrolimus and 5-azacytidine on HTLV-1-related inflammatory disease has been reported, but careful attention should be paid.

ATL-related ocular manifestation is caused by HTLV-1-infected malignant cells, which infiltrate into ocular tissues and cause various ocular manifestations. The treatment is still difficult for these ATL patients. HSCT is considered to be the only curative therapy, but IL-2R treatment might be an alternative treatment in this ocular disorder.

Recent basic researches showed that HTLV-1 Tax and HBZ are responsible for immune disturbances so that they are one of the best candidates for future HTLV-1 therapy. Further endeavor is needed to investigate more detailed molecular mechanism to provide specific treatment of HTLV-1-related ocular diseases.

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### **Conflicts of interest**

There are no conflicts of interest.

# REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 569).

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