

Success Treatment of Severe and Active Graves' Orbitopathy with Tocilizumab After Thyroidectomy and Maximum Dose of Intravenous Methylprednisolone

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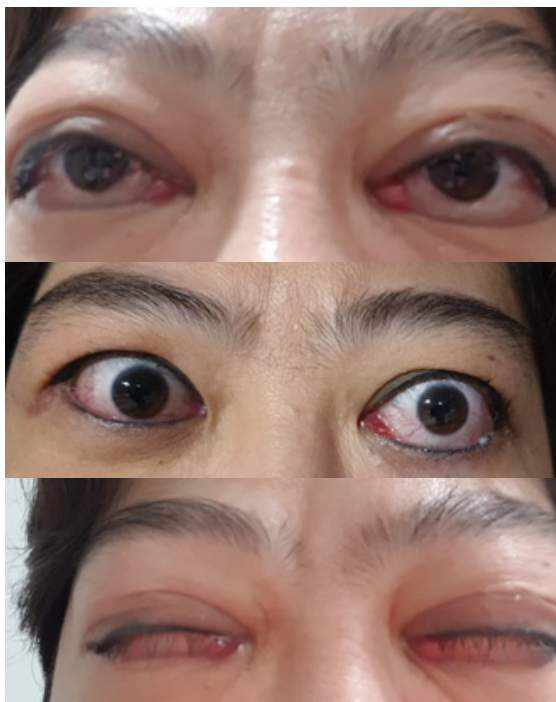


Figure 1. Patient's eye before tocilizumab infusion.



Figure 2. Patient's eye after first (upper) and second (lower) tocilizumab infusion

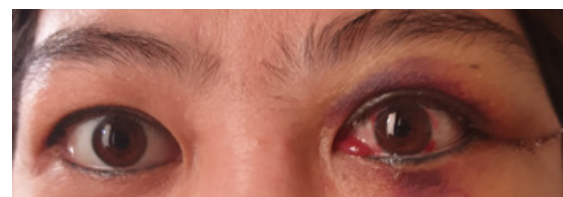


Figure 3. Patient's eye after third tocilizumab infusion and orbital decompression surgery (1 week).

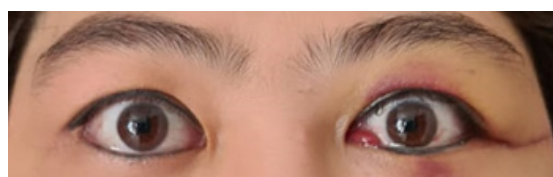


Figure 4. Patient's eye after third tocilizumab infusion and orbital decompression surgery (3 weeks).

Graves' orbitopathy or thyroid eye disease is the most prevalent and difficult-to-treat extrathyroidal comorbidities in patients with Graves' disease.¹ Moderate to severe and active Graves' orbitopathy treated with intravenous methylprednisolone 0.5 g weekly/ 6 weeks combine with mycophenolate sodium 0.72 g daily/ 6 weeks. If there is only partial response, guidelines recommend another 0.25 g weekly intravenous methylprednisolone for 6 weeks combine with mycophenolate sodium 0.72 g daily/ 18 weeks. If no response, we should move to second-line treatment.²

The latest, 2021 EuGOGO (European Group on Graves' Orbitopathy) Clinical Practice Guidelines mention several second-line treatment options after failure with maximum dose of intravenous methylprednisolone. These options are second course of intravenous methylprednisolone (total dose 7.5 g), oral prednisolone or prednisone with oral immunosuppressants such as cyclosporin or azathioprine, orbital radiotherapy with oral or intravenous glucocorticoids, teprotumumab, rituximab, or tocilizumab.² These second-line treatments rarely use in our patients since there are not many dedicated thyroid eye center or clinic in Indonesia.

The use of teprotumumab in severe and active Graves' orbitopathy patients never been done in Indonesia since teprotumumab not yet marketed in Indonesia. Whereas, teprotumumab has very good efficacy for treating difficult cases of Graves' orbitopathy.³ Likewise, the use of tocilizumab (anti-interleukin 6 or anti-IL6) also never been reported in Indonesia. Not many trial and case report published the outcome after treatment using tocilizumab in severe-active Graves' orbitopathy patients. The use of teprotumumab and tocilizumab itself has not been stated in the Indonesian practical guidelines management of Graves' ophthalmopathy published in 2019.⁴ This is the first case report in Indonesia evaluating the use of tocilizumab for treatment of difficult case of Graves' orbitopathy.

In this medical illustration, we report a woman, 45th year old with Graves' disease

treated with anti-thyroid drug (thiamazole). She came to our clinic with severe and active Graves' orbitopathy. We treated her with high dose intravenous methylprednisolone weekly (0.5 g weekly/ 6 weeks) and mycophenolate sodium 0.72 g daily/ 6 weeks. Because of her longterm consumption but not successful to achieve remission of anti-thyroid drugs and the size of her goiter, we decided to do total thyroidectomy. Only one week after thyroidectomy, her eye inflammation grade was reduced, but still bulging. We continue with the intravenous methylprednisolone weekly. Because of the partial response, we continue with another dose of methylprednisolone (0.25 g weekly for another 6 weeks).

After 12 weeks of intravenous methylprednisolone (maximum dose for 1st course 4.5 g), there is a partial response make it to moderate to severe grade but still active inflammation. Our team decided to give her second-line treatment and we give her intravenous tocilizumab monthly for 4 weeks. This scheme is based on the study of tocilizumab for treatment of steroid-resistant Graves' orbitopathy.⁵ At the time we decided to give tocilizumab, the thyroid function was normal with daily levothyroxine, FT4 1.46 ng/dL (normal 0.92-1.68 ng/dL), TSHs 3.92 uIU/mL (normal 0.27-4.2 uIU/mL). TSH Receptor Antibody (TRAb) was 5.46 IU/L (normal < 1.75 IU/L) and Interleukin 6 (IL-6) was very high 17.9 pg/mL (normal < 7 pg/mL).

After three tocilizumab infusion, the inflammation is reduced remarkably. Her overall appearance is getting better. But, because of her sight was not improved much as the inflammation reduced, we done orbital MRI and we decided to do another intravenous methylprednisolone 1 g for three days followed by orbital decompression surgery. Shortly after the orbital decompression, her sight was improved very well. She can now doing activities she can do previously. After recovery, we plan to give her the fourth (last) tocilizumab infusion. Overall, tocilizumab improves clinical outcome in patient with active corticosteroid-resistant moderate to severe Graves' orbitopathy.⁶ Patient's quality of life also improved.

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