CASE REPORT

Can lenalidomide play a role in the management of scleritis?

Hassan A Al-Jafar,¹ Nadia Abul,² Niranjana Kumar,² Adel Al-Awadhi³¹Department of Haematology, Amiri Hospital, Kuwait, Kuwait²Department of Ophthalmology, Al Bahar Eye Center, Shuwaikh, Kuwait³Faculty of Medicine, Kuwait University, Jabriya, Kuwait**Correspondence to**

Dr Hassan A Al-Jafar, cbc9@hotmail.com

SUMMARY

Lenalidomide is an immunomodulatory agent that was approved for the treatment of a monoclonal bone marrow disorders, myelodysplastic syndrome del(5q) (MDS del(5q)), in 2005; the drug was subsequently also approved for the treatment of refractory multiple myeloma, a bone marrow malignancy of the B-lymphocyte lineage. The purpose of this study is to report a case of MDS del(5q) in a female patient, which was most likely secondary to the immunosuppressive drugs that the patient was taking for scleritis. After lenalidomide treatment, the patient's haematological symptoms rapidly resolved and she became transfusion independent, with normal haemoglobin levels. This medication also helped control her dependence on high doses of oral prednisolone. The patient continued to receive treatment with low-dose lenalidomide, and her scleritis has been in long-term remission for 3 years. A larger prospective study can further define the role of lenalidomide in the management of scleritis.

BACKGROUND

This case is important because chronic refractory scleritis responded very well to the lenalidomide immunomodulatory therapy. The patient also showed aggressive relapses when the lenalidomide doses were reduced.

Scleritis response on the low doses of lenalidomide did not show any side effects from lenalidomide while the patient suffered from other treatments' side effects.

This case written because it might lead to research trails in using lenalidomide in chronic refractory scleritis.

INTRODUCTION

Scleritis is a severe, painful, inflammatory condition of the eye that primarily affects the sclera and, sometimes, the adjacent structures. The condition may develop idiopathically or secondary to connective tissue disorders, including systemic lupus erythematosus, rheumatoid arthritis and ankylosing arthritis.^{1 2} Occasionally, scleritis may be secondary to bacterial, viral, fungal or parasitic infections. Typically, the afflicted patient presents with pain, redness, tearing, photophobia and decreased visual acuity. Scleritis may have sight-threatening complications, such as corneal opacification and melting, scleral thinning and perforation, staphyloma, uveitis, cataract formation and glaucoma.³

Treatment of the condition usually requires specific therapy for the underlying disease,⁴ but topical steroids or non-steroidal anti-inflammatory

drugs (NSAIDs) are normally added as an adjunctive treatment. Topical antibiotics are used if the scleritis is suspected to be infectious. Systemic treatment with NSAIDs, corticosteroids or immunosuppressive agents, such as methotrexate, azathioprine, mycophenolatemofetil, cyclophosphamide or cyclosporine, may be needed in severe cases. Tumour necrosis factor (TNF) inhibitors, such as infliximab or adalimumab, have also been used.⁵ Subconjunctival steroid injections are often helpful in certain situations or if systemic side effects of these drugs are of concern.

Lenalidomide, a derivative of thalidomide, was recently introduced for the treatment of certain types of myelodysplastic syndromes (MDS), such as MDS del(5q), and has been approved as a second line of treatment for refractory multiple myeloma.⁶ The drug has multiple mechanisms of action, including immunomodulatory activity.⁷ To the best of our knowledge, its role in the management of scleritis has not been previously reported.

This case showed coincidental improvement of refractory scleritis when lenalidomide was used to treat the haematological bone marrow disorder MDS del(5q). An unusual case of complete remission of MDS del(5q) after a 7-day treatment with lenalidomide was also previously reported.⁸

CASE PRESENTATION

In 2001, a 54-year-old woman presenting with pain, conjunctival congestion and tenderness was diagnosed with nodular scleritis in her right eye (figure 1). Her visual acuity was 20/30 (OD) and 20/20 (OS); the results of her anterior segment and fundus examination were within normal limits. The patient's rheumatologist had evaluated her to rule out systemic connective tissue disorders, and the results of all autoimmune profile tests, C reactive protein evaluation and rheumatoid factor assessments were negative. Her scleritis was treated with numerous medications, including topical corticosteroids and systemic prednisolone, methotrexate, azathioprine, mycophenolatemofetil and cyclosporine. However, she had recurrent attacks that later involved the left eye, despite the daily, oral administration of prednisolone (50 mg). She then began to receive subcutaneous administration of 40 mg of adalimumab every other week.

She was presented with weakness and pallor 9 months after beginning adalimumab treatment. At that time, she became weaker and anaemic. Her haemoglobin level dropped to 5 mg, and she required blood transfusions. She was referred to our haematology outpatient department in 2010 because of a

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low blood count and progressive anaemia. She had become transfusion-dependent, requiring two units of blood every 3–4 weeks. Haematological investigations revealed macrocytic anaemia with hypogranular granulocytes, Pseudo-Pelger-Huet anomaly, myelodysplastic features, and normal levels of platelets, serum vitamin B₁₂ and folate, and serum ferritin. Bone marrow aspiration results showed normocellular dysplastic red blood precursors, a high number of frequently hypobulbated megakaryocytes, the absence of ring sideroblasts and 4% blast cells. A cytogenetic karyotype study revealed MDS del(5q). As a result, the patient was prescribed a daily dose of lenalidomide (10 mg, orally). However, she developed pancytopenia and chest infection after 7 days of treatment. As a result, lenalidomide administration was stopped, and she was admitted to the hospital where she received blood transfusions, platelet transfusions and intravenous antibiotics.

Within 3 weeks of discontinuing lenalidomide treatment, the patient's blood count gradually improved, and she was discharged from the hospital 4 weeks after admission. By week 8, her blood count had returned to normal, and she started lenalidomide therapy on a maintenance dose of 5 mg daily. At week 12, she underwent a second bone marrow examination that revealed a normal cytogenetic karyotype. At that point, the lenalidomide maintenance dose was reduced to 5 mg twice per week, resulting in normalisation of her haemoglobin level and scleritis remission. At week 16, the lenalidomide dose was further reduced to 5 mg once per week; the aim was to administer the lowest possible dose of lenalidomide that would maintain her blood level within normal values. During the period of pancytopenia, the patient experienced complete remission of her scleritis, without any pain or redness, enabling her to discontinue taking prednisolone.

However, after the lenalidomide dose was decreased to 5 mg/week, the patient began to experience a gradual relapse of scleritis. As a result, the lenalidomide dose was increased to 5 mg daily and she began taking prednisolone (50 mg daily) again. This resulted in an improvement of her eye condition, allowing the lenalidomide to be tapered back to 5 mg twice per week again; her prednisolone dose was also gradually reduced to 5 mg daily. The episodes of relapsing scleritis occurred five times whenever the lenalidomide dose was decreased to 5 mg once per week. The patient's haemoglobin level remained within normal levels, but her mean corpuscular volume increased whenever the lenalidomide dose was reduced to 5 mg once per week.

At the last follow-up examination, the patient had a visual acuity of 20/80 (OD) and 20/30 (OS). Her intraocular pressure was 14 mm Hg OU, and she demonstrated superotemporal (OD) and superonasal (OS) scleral thinning with temporal corneal scarring (OU). The patient also demonstrated mild cataract (OU) and disc pallor (OD).

DISCUSSION

Scleritis is a severe, potentially blinding ocular inflammation often associated with systemic connective tissue or vasculitic diseases including some with high morbidity and mortality.⁹ Systemic corticosteroids and immunosuppressive drugs are the mainstays for the management of severe, recurrent or resistant scleritis.^{10–11} Some non-necrotising cases of scleritis respond to systemic NSAIDs. However, non-responders and patients with posterior or necrotising scleritis require systemic and/or local corticosteroid treatment. Systemic corticosteroids are given orally or intravenously with a starting dose of 1 mg/kg/day. The dose is slowly tapered down after a disease response has been

Figure 1 The patients' chronic refractory scleritis before lenalidomide treatment

noted; local corticosteroids are given in the form of posterior, sub-Tenon's injections. In the event of a poor response to corticosteroids or corticosteroid complications, immunosuppressive agents such as cyclosporine, mycophenolate, methotrexate or anti-TNF drugs are administered.

However, these medications all have serious systemic adverse effects, and many times may fail to control the inflammation associated with severe scleritis. The present patient had recurrent and severe scleritis despite receiving high doses of systemic corticosteroids and adalimumab. Additionally, she developed MDS with transfusion-dependent anaemia. Lenalidomide therapy controlled the MDS, but she experienced the known side effects of lenalidomide at the 10 mg dose; side effects were not observed at lower doses. The side effects (pancytopenia and chest infection) were successfully treated with blood transfusion products and intravenous antibiotic administration. Her scleritis was controlled with lower doses of both lenalidomide and prednisolone.

Lenalidomide is a hypomethylation agent with an immunomodulatory mode of action. The drug affects both cellular and humoral immunity,¹² and has also been shown to have antiangiogenic properties, which stops the formation of new blood vessels and subsequently, decreases the blood supply to cause tumour regression.¹³ A crucial component of many of the anti-inflammatory properties of lenalidomide is its ability to suppress expression of TNF- α by affecting TNF signal transduction.¹⁴ Lenalidomide's activity across a spectrum of neoplastic conditions highlights the possibility of multiple sites of action,¹⁵ even though the exact molecular targets of lenalidomide are not well known.

CONCLUSION

Lenalidomide plays a role in the management of severe scleritis case. However, there is a need for larger studies with longer follow-up periods, preferably a randomised controlled trial, to explore the complete potential of this drug.

Learning points

- ▶ Lenalidomide could be a new line in treating refractory scleritis.
- ▶ Refractory scleritis could be an autoimmune disease, but we might need new markers to detect it.
- ▶ More molecular study on B and T lymphocytes in low risk MDS could lead to more understanding to this disorder and its complications.

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REFERENCES

- Okhravi N, Odufuwa B, McCluskey P, *et al*. Major review. *Scleritis Surv Ophthalmol* 2005;50:351–63.
- Ahn SJ, Oh JY, Kim MK, *et al*. Clinical features, predisposing factors and treatment outcomes of scleritis in the Korean population. *Korean J Ophthalmol* 2010;24:331–5.
- Keino H, Watanabe T, Taki W, *et al*. Clinical features and visual outcomes of Japanese patients with scleritis. *Br J Ophthalmol* 2010;94:1459–63.
- Sainz de la Maza M, Molina N, Gonzalez-Gonzalez LA, *et al*. Scleritis therapy. *Ophthalmology* 2012;119:51–8.
- Bawazeer AM, Raffa LH. Adalimumab in the treatment of recurrent idiopathic bilateral nodular scleritis. *Oman J Ophthalmol* 2011;4:139–41.
- Mariz JM, Esteves GV. Review of therapy for relapsed/refractory multiple myeloma: focus on lenalidomide. *Curr Opin Oncol* 2012;24(Suppl 2):S3–12.
- Vallet S, Witzens-Harig M, Jaeger D, *et al*. Update on immunomodulatory drugs (IMiDs) in hematologic and solid malignancies. *Expert Opin Pharmacother* 2012;13:473–94.
- Al-Jafar HA, Al-Azmi S, Qassem JA, *et al*. Complete remission of del(5q) myelodysplastic syndrome after 7 days of lenalidomide therapy gives an alert!. *Case Rep Oncol* 2012;5:586–91.
- Sainz de la Maza M, Jabbur NS, Foster CS. Severity of scleritis and episcleritis. *Ophthalmology* 1994;101:389–96.
- Watson PG, Hayreh SS. Scleritis and episcleritis. *Br J Ophthalmol* 1976;60:163–91.
- Murphy CC, Ayliffe WH, Booth A, *et al*. Tumor necrosis factor alpha blockade with infliximab for refractory uveitis and scleritis. *Ophthalmology* 2004;111:352–6.
- Adès L, Fenaux P. Immunomodulating drugs in myelodysplastic syndromes. *Hematology (Am Soc Hematol Educ Program)* 2011;2011:556–60.
- Martiniani R, Di Loreto V, Di Sano C, *et al*. Biological activity of lenalidomide and its underlying therapeutic effects in multiple myeloma. *Adv Hematol* 2012;2012:842945.
- Wobus M, Benath G, Ferrer RA, *et al*. Impact of lenalidomide on the functional properties of human mesenchymal stromal cells. *Exp Hematol* 2012;40:867–76.
- McDaniel JM, Pinilla-Ibarz J, Epling-Burnette PK. Molecular action of lenalidomide in lymphocytes and hematologic malignancies. *Adv Hematol* 2012;2012:513702.

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