LETTERS TO THE EDITOR

Statins as Potential Addition to Anti-Graves’ Ophthalmopathy Armamentarium

Sir,

Graves’ Ophthalmopathy (GO), the major extrathyroidal expression of Graves’ disease, has an autoimmune origin.1,2 GO causes significant cosmetic and/or functional ocular abnormalities.1 Current therapeutic options for GO include artificial tears, ointments and prisms for mild disease, glucocorticoids and orbital radiotherapy for moderate to severe disease, and decompressive or rehabilitative surgery.1

Herein, we explain the mechanisms by which statins, as safe and low-cost drugs, could be effective in the treatment of GO.

The pathogenesis of GO is not yet well-defined. The volume of both the extraocular muscles and retro-orbital connective and adipose tissue is increased in GO patients, mostly due to inflammation and accumulation of hydrophilic glycosaminoglycans that attract water.1,2 This increased orbital content mechanically explains most clinical manifestations of GO.1,2 Autoreactive T-cells, the major pathogenic factors in the pathobiology of GO,1 reach the orbit where they recognize the common antigen or antigens provided by Antigen-Presenting Cells (APC), such as dendritic cells, macrophages, and B-lymphocytes.1,2 This leads to a cascade of events, which results in secretion of proinflammatory cytokines such as TNF-α, IL-1, IL-6 and IFN-γ,1,2 which stimulate fibroblast proliferation, preadipocyte differentiation in adipocytes, and secretion of glycosaminoglycans from fibroblasts.1,2 Stimulation of proliferation of orbital fibroblasts by autoreactive T-cells is dependent on overexpression of class II Major Histocompatibility Complex (MHC) II antigens and costimulators such as CD40 on antigen-presenting cells.1,2 Antibodies against MHC II or CD40 have been shown to inhibit this process.1,2

Statins possess several anti-inflammatory and immunomodulatory effects.3 Most of these are due to inhibition of HMG-CoA reductase and decreased mevalonate production,3 which leads to inhibition of isoprenylation of small GTP-binding proteins Ras, Rac, and Rho having important roles in signalling pathways regulating cellular functions.3 Isoprenylation of these proteins is necessary for their optimal function.3 Therefore, by inhibition of isoprenylation of GTPases, statins modulate cellular functions of immune cells.3 Statins inhibit expression of MHC-II and costimulatory molecules CD40, CD80 and CD86 on endothelial cells, macrophages, B-cells, activated T-cells and maturing dendritic cells.3 Thus, via these effects, statins could inhibit APC induction of T-cell activation and proliferation.

Statins suppress the expression of cell-adhesion molecules such as LFA-1, CD11b, CD18 and CD49 on activated T-cells and ICAM-1, VCAM-1 and CD18 on activated endothelial cells.3 Therefore, these drugs could inhibit infiltration of T-cells into the orbital tissue and periocular muscles of GO patients.

Statins inhibit the production of proinflammatory cytokines such as IFN-γ, TNF-α, IL-1 and IL-6 by mononuclear cells.3 Cytokine signalling by APCs is required for antigen specific T-cell activation.3 Decreased production of these inflammatory cytokines will attenuate their stimulatory effects on fibroblasts, adipocytes, glycosaminoglycan production and T-cell activation. As an evidence, anti-TNF-α drugs such as etanercept have been shown to be effective in the treatment of GO patients.1

According to the above-mentioned mechanisms, it can be concluded that statins may be effective in the treatment of GO and that they could exert steroid sparing effect. Clinical trials on this subject are warranted.

REFERENCES

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Percutaneous Transvenous Mitral Commissurotomy in Mitral Restenosis and Situs Inversus

Sir,

I read with great interest the case report by Hussain and Ahmed on successful Percutaneous Transvenous Mitral Commissurotomy (PTMC) in a patient with mitral restenosis and situs inversus in JCPSP.1 Mirror-image
Dextrocardia has been estimated to have a population prevalence of 1:10,000. In areas endemic for rheumatic heart disease, the coincidence of rheumatic mitral stenosis and this cardiac malposition is purely coincidental. We agree with the authors’ speculation that the anticipation of technical complications could account for the rarity of PTMC performed in similar settings. Along with congratulating the authors for performing this technically demanding procedure, I would like to highlight a few specifics of the technique useful in PTMC in cardiac malpositions based on the experience in a similar case published earlier.²

The cardiac anatomy in mirror-image dextrocardia follows an exact left-right inversion pattern of normal situs. Today, many fluoroscopic systems are equipped with the option for left-right inversion of images on-line, helping the operator work on the more accustomed and conventional fluoroscopic views in these cases. Furthermore, the levophase of pulmonary angiogram helps in additional delineation of anatomical boundaries of left atrium, interatrial septum and mitral valve (Figure 1). Right atrial angiogram can also be used to detail the septal anatomy on the right side.³ Similarly, the practical utility of diligent probing of fossa ovalis for a probe patent foramen ovale can never be overemphasized to make the procedure further safer. Once an uncomplicated transseptal access is ensued, the left ventricular entry in these cases demand clockwise rotation of the balloon unlike the counterclockwise movement used in normal atrial situs. In addition, a reverse loop technique can serve as a good alternative to the standard technique for trans-mitral entry in cases with dilated left atrium.²

REFERENCES


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Due to an inadvertent mistake on the part of author and editorial office, a case report titled “Emergency Laparoscopic Cholecystectomy for Acute Empyema of the Gallbladder in Pregnancy” by Muthukumaran Rangarajan, Chinnusamy Palanivelu, Madhupalyam Velusamy Madankumar and Rangaswamy Senthikumar which was published in the JCPSP 2007, Vol. 17 (5): 275-276, got intermingled with another case report of the same author who mistakenly resubmitted the same as a revised of his second CR. The same titled case report has erroneously been republished in December issue of JCPSP 2008 Vol. 18 (12): 781-783.

The republished case report is, therefore, retracted from the December 2008 issue of JCPSP.

The oversight/mistake is regretted.

Editor