Intra-articular spine injections of steroid as a contributing factor to glaucoma

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Propriety Interest: None

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Steroid-induced elevated intraocular pressure (IOP) leading to glaucoma is a well-documented phenomenon(1). However, iCorticosteroid can cause a rise in IOP within a few weeks of commencement, but typically the pressures return to normal on cessation of treatment. Intra-articular corticosteroid injection causing elevated IOP is an extremely rare phenomenon , but has been previously documented in the literature(2, 3). To our knowledge, wWe describe present the firsta case of of a patient who received intra-articular glucocorticoids resulting in steroid-induced glaucoma. high IOP and permanent glaucomatous damage.

A 56-year-old male received multiple cervical spine facet joint injections of corticosteroid on 5 different occasions for cervical radiculopathy and referred shoulder pain secondary to a work-related injury over a 17-month period. Approximately 6 months after his 5th and final corticosteroid injection, he the patient presented with noted symptoms of blurred vision in the right eye. (RE) with associated frontal headache. He had no previous personal or family history of glaucoma and optometric visits prior to corticosteroid treatment had recorded no ocular pathology. his IOP at the optometrist office previously were reported normal. On ophthalmic examination his visual acuities werey were RE 6/19 OD and Left Eye (LE) 6/6 OS. There was a right relative afferent pupillary defect, and the Goldmann tonometry revealed an IOP with Goldmann applanation tonometry was of RE 55mmHg OD and LE 31mmHg OS. There was

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~~a relative afferent pupillary defect (RAPD) in the RE. Corneal thicknesses were within normal limits.~~ Gonioscopy demonstrated bilateral open angles and there were no features of any other secondary glaucoma. ~~. The anterior segment examination was unremarkable in both eyes.~~ Fundoscopic examination revealed complete pathological cupping of the right optic disc and a 0.8 ~~cupping~~ cup-disc ratio on the left. (Fig~~ure~~ 1). Automated perimetry showed ~~Visual field showed~~ severe ~~significant~~ field constriction in the RE and ~~a~~ moderate glaucomatous ~~lesser degree of~~ loss in the left eye ~~LE~~ (Fi~~ggure~~ 2). ~~OCT scanning elicited significant thinning of retinal nerve fiber layer (RNFL) layers worse in the RE than the LE.~~ He was immediately commenced ~~started on~~on maximal medical IOP ~~pressure~~ lowering therapy including oral acetazolamide. ~~Diamox, Simbrinza (brinzolamide / brimonidine tartarate) and Duotrav (Travoprost/ Timolol) to control the IOP.~~

Within days~~One week later~~, his IOP in both eyes was in the low teens~~, had normalized to RE Acetazolamide13mmHg and LE 14mmHg. Diamox wa~~ was discontinued and the IOP remained at target pressure~~stable~~ on topical medical therapy. ~~with Simbrinza and Duotrav eye drops.~~ It is highly likely ~~speculated that o~~that this ~~ur~~ patient developed ~~developed~~ steroid-induced ~~elevated IOP which progressed to~~ glaucoma from the multiple intra-articular glucocorticoid injections.~~.~~

~~The pathophysiology of steroid use is well documented. Glucocorticoids, secreted by the adrenal glands were first discovered in the 1940s and were used for their anti-inflammatory properties. As the therapeutic use of glucocorticoids became more commonplace, possible side effects were also discovered such as the development of ocular hypertension in certain individuals.~~ Becker *et al*. showed that in a normal population there are three categories of

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steroid responders: s. 6% of individuals were high responders with a rise of >15mmHg in IOP after ocular steroid usage 4-6 weeks after initiation; m. Moderate responders had 6-15mmHg IOP rise, and non-responders had < 6mmHg elevation(4). Additional risks that contributes to high steroid response includes , diabetes, primary open angle glaucoma (POAG) sufferers andand family history of relatives of those with primary open angle glaucoma (POAG). There is considerable evidence to support the concept that corticosteroids increase the aqueous outflow resistance by altering the extracellular matrix composition of the trabecular meshwork, (5) and there is evidence for genetic susceptibility. However, the individualized IOP response to steroids remains poorly understood. W

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It is generally accepted that steroid induced elevated IOP is a direct result of altering trabecular meshwork (TM) ultrastructure. Firstly, there is a dysregulation and excessive extracellular matrix deposition in the cribriform region and adjacent trabecular beam. Steroid activate Cross-linked actin cytoskeleton (also known as CLANS), precursors to stress fibers which can link across TM structure and activate to reduce overall aqueous outflow and increase IOP. In addition, steroid cause increased accumulation of basement membrane like material deposited in the outer trabecular meshwork beams. Immunohistology shows these cells to have characteristics of myofibroblasts, cells strongly associated with fibrosis. This change in the TM ultrastructure is unique to the eyes with steroid induced glaucoma (SIG) and is not seen in aging eyes or those eyes with POAG(5).

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Glucocorticoid controls gene expression for inflammation and complement activation and its response varies considerably from individual to individual. The initiation of this effect is via the glucocorticoid receptor, which is genetically encoded by gene NR3CQ. This receptor

~~resides intracellularly alongside of the multiprotein complex which includes chaperone proteins and immunophilins. The primary goal of glucocorticoid is to control gene expression.~~

~~Myocilin (MYOC) is also known as the trabecular meshwork inducible glucocorticoid response (TIGR) gene product isolated by Polansky and Colleagues as a gene candidate for the outflow obstruction/regulation in glaucoma. The expression of MYOC in trabecular meshwork has been shown to be steroid induced. This gene and its mutations are charted into a database online and accounts for 4-5% of POAG. It is hoped that this may provide insight into idiopathic POAG and other causative genes. Further studies could provide a definitive answer to the question about whether MYOC protein plays any role in SIG(5).~~

~~We hope that genetic profiling in precision medicine of Ophthalmology may protect the steroid responsive patients in the future by tailoring medical treatment to fit the characteristics of the individual patient. Before that is a reality, w~~We recommend that clinicians ~~physicians and surgeons communi~~communicate the risk of elevated IOP ~~intraocular pressure~~ to patients receiving repeated intra-articular corticosteroid injections~~.~~ and consider baseline and ongoing o~~O~~phthalmic examination whilst receiving treatment. ~~is also recommended in these patients to prevent irreversible blindness from SIG.~~

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Figure 1: Colour Fundus photograph showing the optic disc in the right and left eye

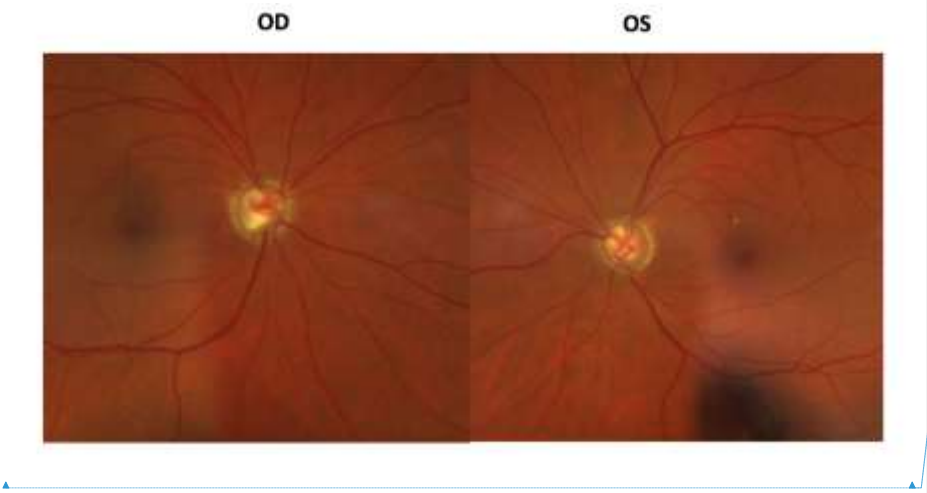

Figure 2: Figure showing the Humphrey Visual Field Defect in the Right and left eye

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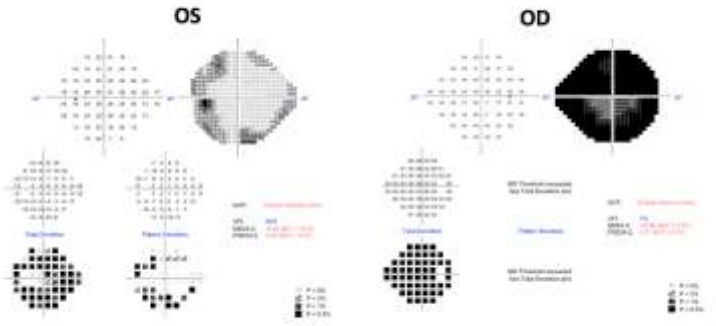

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