Anophthalmic Syndrome: A Review of Management

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Purpose: To review and summarize current management of anophthalmic syndrome—enophthalmos, superior sulcus syndrome, lower eyelid laxity, and upper eyelid ptosis.

Methods: The authors performed a PubMed search of all articles published in English on the management of anophthalmic socket syndrome.

Results: A review of 37 articles demonstrated that anophthalmic syndrome occurs in a significant proportion of this patient population. Primary prevention through careful selection of primary orbital implant is ideal. Residual mild deficits can then be corrected through prosthesis modification. When modification of the prosthesis is no longer sufficient, specifically targeted procedures become necessary.

Conclusions: Ocularists and oculoplastic surgeons should work together closely to treat anophthalmic syndrome. Future studies should establish uniform measurement criteria as the next step in validating the benefit and limitation of each technique.

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Anophthalmic syndrome, as defined by Vistnes[1] in 1976, consists of enophthalmos, superior sulcus syndrome, lower eyelid laxity, and upper eyelid ptosis. While not always simultaneously present, components of this syndrome are often encountered in the course of anophthalmic rehabilitation (see Fig. 1A,B). Proposed etiologies of anophthalmic syndrome include atrophy of orbital fat, migration of muscle cone, traumatic bony loss, an unrecognized orbital wall fracture with subsequent herniation of orbital fat, volume loss after globe removal, levator disinsertion, malposition of superior rectus muscle, and long-standing gravitational burden of orbital implant and prosthesis.[2] Regardless of its etiology, when present, this undesirable outcome can ultimately lead to patient dissatisfaction and necessitate both surgical and nonsurgical interventions to provide adequate anophthalmic rehabilitation.

Literature on patients with anophthalmic syndrome predominantly focuses on long-term follow-up studies of orbital implants and complications, mechanisms and management of extrusion, preference for implant type or technique, and treatment of a contracted socket.[3,4,5,6] Despite not being a primary focus of anophthalmic literature, a subset of data and experience on the approach to components of anophthalmic syndrome have been published. Understanding the underlying pathomechanics and unique corrective techniques available enables ocularists and oculoplastic surgeons to devise a cohesive strategy for the management of anophthalmic syndrome. This review aims to discuss current management of enophthalmos, superior sulcus deformity, lower eyelid laxity, and upper eyelid ptosis in patients with anophthalmic syndrome.

METHODS

The authors performed a PubMed search of all articles published in English on the management of anophthalmic socket syndrome. Searches included a combination of the following words: "anophthalmic socket," "anophthalmic orbit," "anophthalmos," "lid ptosis," "superior sulcus deformity," "superior sulcus," "orbital implant," and "socket contracture." From the resulting articles, the references were then reviewed for pertinent articles.

RESULTS

Prevalence of Anophthalmic Syndrome. A review of 37 articles demonstrated that anophthalmic syndrome occurs in a significant proportion of this patient population. Of the 162 patients seen by Sergott and Vistnes[7] between 1972 and 1985, 50% presented with superior sulcus syndrome and enophthalmos, 70% with lower eyelid laxity, and 20% with upper eyelid ptosis. A 1995 survey of members of American Society of Ophthalmic Plastic and Reconstructive Surgery (ASOPRS) regarding outcomes with orbital implant reveals superior sulcus syndrome in 7.5% to 22.8% of patients, cosmetically significant enophthalmos

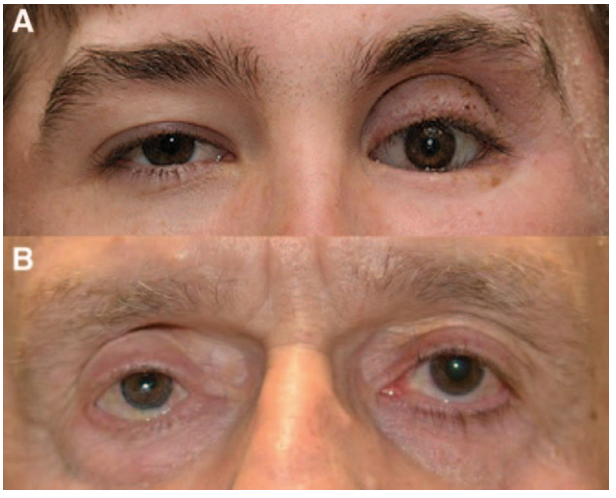

FIG. 1. **A**, Enophthalmos and deep superior sulcus of left orbit (photo courtesy of Dr James C. Fleming, Memphis, TN.). **B**, Slight upper eyelid ptosis and lower eyelid laxity of OD. Component of occult upper eyelid ptosis as tightening of lower eyelid would lift prosthesis up and worsen upper eyelid ptosis.

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(>2 mm) in 4.2% to 17.3% of patients, and lower eyelid malposition in 0.5% to 24%, depending on the type of orbital implant.[6] Most recently in 2012, a long-term study of 314 cases of porous polyethylene orbital implants found blepharoptosis (n = 33; 10.5%) to be the most common complication in their patients regardless of the type of surgery performed, or whether they were from primary enucleation, evisceration, or secondary orbital implantation.[5]

Primary Prevention. As with any disease process, primary prevention without need for added surgical or nonsurgical intervention is the ideal outcome. The average volume of the native eye ranges from 6.9 to 9.0 ml depending on the variability of axial length.[8] During enucleation, the eye is removed (6.9 to 9.0 ml) along with any additional soft tissue (approximately 4 ml), which is subsequently replaced by a spherical implant (20-mm implant = 4 ml) and a prosthesis (additional 1.5 to 4.0 ml), leaving a variable amount of volume deficit.[2] Depending on the ability of the oculoplastic surgeon to select an appropriately sized orbital implant and the ability of the anophthalmic socket to accommodate a prosthesis of sufficient volume, a volume deficiency with resulting cosmetic deficits may ensue. Kaltreider et al.[9] in a retrospective study of 59 patients with anophthalmic syndrome found that greater enophthalmos and superior sulcus deformity was present in those with inadequate volume replacement compared with those with 100% or more volume replacement.

Through Kaltreider et al.'s[9] work with A-scan to measure axial length of the contralateral healthy eye to approximate implant size, the authors were able to prospectively test the validity of an algorithm for the selection of implant size for enucleation and evisceration. This formula (implant diameter = axial length–2 mm; axial length = A-scan+1 mm) was able to provide mean volume replacement of 101%, limit sulcus deformity, and minimize clinically significant enophthalmos (mean 1.2 mm) in the 54 patients studied.[8] Adequate intraorbital volume can even correct a degree of ptosis by providing an optimal implant diameter to support the levator muscle, obviating the need for other surgical intervention.[10] In addition, by maximizing orbital volume replacement, the size of prosthesis can be minimized, thus reducing future secondary eyelid problems from a bulkier prosthesis.[8]

Prosthetic Modification. From an ocularistry perspective, Bethke[11] provided an outline for evaluating prosthetic eyes for the patient with anophthalmic syndrome, which took in consideration many issues still current. The ocular implant—its diameter, material, and surgical positioning—has the greatest influence on the cosmetic outcome for the patient with anophthalmic syndrome. While the surgical procedure of implant placement lays the foundation for the prosthetic restoration that follows, there are limitations to all procedures.

An ocular prosthesis should complement the orbital implant in replacing the volume lost from the enucleated eye; however, it should not be a substitute for insufficient posterior volume replacement. Compensation for volume-deficient orbits results in a larger, bulkier prosthesis, which has been associated with both ptosis and lower eyelid laxity in enucleated adult patients.[12,13] Per Kaltreider[12] in her review of 70 patients with anophthalmic syndrome, an ideal volume of 2.2 ml was believed to be a reasonable end target with 4.2 ml as the proposed upper limit of prosthetic volume. This again illustrates the importance of careful selection of orbital implant size to optimize posterior volume replacement to prevent downstream complications. In patients with anophthalmic syndrome, modification of the prosthesis does afford the ocularist with some options to correct enophthalmos, superior sulcus deformity, and upper eyelid ptosis.[14]

Superior Sulcus Syndrome and Enophthalmos. By maximizing prosthesis size without exceeding a critical volume or weight, enophthalmos and superior sulcus syndrome can be reduced. Early reports on modern ocularistry outline the standards for obtaining the desired prosthetic shape.[15] As ocularists Allen and Webster[16] described in 1969, an alginate impression helps to determine the size (volume) of the prosthetic eye, although simply filling the socket cavity does not necessarily solve potential problems.

When modification of the prosthesis is no longer sufficient, specifically targeted procedures become necessary. Deficits in orbital volume contents in patients with anophthalmic syndrome are recognized as the cause of superior sulcus syndrome and enophthalmos. Postulated etiologies of superior sulcus syndrome include levator disinsertion, atrophy of orbital fat, loss of volume when the globe is removed, depression in the orbit floor from unrecognized fracture, and malposition of superior rectus muscle.[7,17,18] When enophthalmos and superior sulcus syndrome are still present, numerous corrective surgical procedures have been described in literature, such as orbital implant exchange, placement of autologous tissue or alloplastic material, and the use of tissue expanders.[2,7,17,18,19,20, 21,22,23,24,25,26,27,28]

Historically, replacement of lost volume has been through subperiosteal implants in the floor of the orbit–autogenous bone, autogenous cartilage, glass wool, plastic wedges, inflatable silicone prosthesis, glass beads, and room-temperature vulcanized silicone.[7,17] The rationale is to selectively displace tissue forward and upward with the intention of obliterating sulcus defect and reducing enophthalmos. Superior sulcus syndrome is generally the most difficult challenge for both ophthalmologists and ocularists and usually requires more aggressive surgical interventions. Iverson et al.[17] in 1973 compared glass beads, silicone beads, and room-temperature vulcanized silicone in reducing enophthalmos and superior sulcus syndrome and found room-temperature vulcanized silicone to offer the most reduction in preoperative enophthalmos (5.7 mm preoperatively to 0.3 mm postoperatively) and to produce the best cosmetic correction in superior sulcus syndrome (average grade, 3.8 out of 4; normal appearance, 4). Following this in 1987, Sergott and Vistnes[7] showed room-temperature vulcanized silicone to be a reliable and safe procedure with excellent long-term results and without serious complications.

Since then, several approaches to enophthalmos and superior sulcus deformity have emerged. Van Gemert and Leone[25] published a clinical series on a technique that used autogenous dermis-fat graft in the preaponeurotic space of the upper eyelid to reduce the superior sulcus deformity. Autogenous grafts offer better integration in adjacent tissue with fewer tendencies for migration and inflammatory reaction. Drawbacks, however, include unpredictable absorption rate of the graft, potential for creating ptosis, and harvest site morbidity. In a different venue, Adenis et al.[24] proposed the implantation of hydroxyapatite tricalcium phosphate ceramic implants in the orbital fat as an alternative to traditional subperiosteal location. They postulated that the supraperiosteal position of the blocks allowed for a greater vector force on the orbital implant with more of a net forward displacement. Correction of enophthalmos and superior sulcus syndrome was obtained in 70% and 90% of cases, respectively.[24]

While the aforementioned techniques reduce superior sulcus syndrome and enophthalmos, they rely on preoperative estimates of volume needed for replacement and risk-inadequate correction postoperatively. Honda et al.[27] published a case report on the use of a tissue expander behind the orbital implant, which enabled adjustments in intraorbital volume according to the degree of postoperative enophthalmos. Most recently, literature on orbital volume augmentation has moved toward injectable calcium hydroxyapatite as a viable option for correction of anophthalmic syndrome.[20,22,28] Of the 15 patients studied by Vagefi et al,[20] there was a mean reduction of 2.4 mm enophthalmos per syringe of filler. Previous attempts at injectable fillers with cross-linked collagen, silicone oil, autologous fat, and hyaluronic acid over the past 20 years were subject to a short half-life, unpredictable volume restoration, inflammation, migration, and extrusion. Calcium hydroxyapatite, however, has demonstrated lasting improvement with little loss of effect over 1.5 years, features a less invasive technique with ease of application, allows for a titratable volume replacement through successive injections, and enables to perform this procedure in the clinic setting.[20]

Lower Eyelid Laxity. Because the lower eyelid supports the prosthetic eye, the pathomechanics of lower eyelid laxity is thought to be secondary

to gravitational forces on the ocular prosthesis, resulting in altered vectors of force on the lower eyelid and orbital septum.[29,30] Consequently, a larger, heavier prosthesis sits more anteriorly, contributing to sagging of the lower eyelid and reduction in the depth of the inferior sulcus and impaired retention of the prosthesis.[30] Of equal importance, lower eyelid laxity can mask an occult upper eyelid ptosis (see Fig. 1B). With sagging, the prosthesis appears to be appropriately positioned relative to the upper eyelid; however, when the prosthesis is pushed up with tightening of the lower eyelid, the new location of the prosthetic's pupil relative to the upper eyelid makes an occult ptosis to become apparent.[10] Depending on the degree of eyelid laxity and medial or lateral canthal involvement, lower eyelid malposition is typically corrected with a lateral tarsal strip.[3] For optimal surgical correction, the prosthesis in place preoperatively should make no attempt to compensate for enophthalmos, lower eyelid laxity, or upper eyelid ptosis.[29]

Upper Eyelid Ptosis. In the anophthalmic orbit, the etiology of upper eyelid ptosis can fall in 1 of 3 main categories: trauma from initial event that precipitated enucleation, iatrogenic from enucleation surgery itself, or by creation of an anatomical or pathomechanical situation, which disturbs the natural balanced mechanisms. As ptosis still occurs in eviscerated cases and patients with retained microphthalmic globes, it would appear that creation of an anatomical or pathomechanical imbalance and not solely trauma from surgical enucleation is a plausable etiological explanation. Per Vistnes,[1] there is a functional "lengthening" of the levator muscle, which contributes to a lower position of the eyelid margin when the pivot point is effectively lowered and more posterior after enucleation and placement of an orbital implant.

Thus, ocularists are able to compensate for mild ptosis by augmenting the shape of the superior portion of the prosthesis or by adding fullness to the corneal apex and upper limbal to add volume and shift the levator pivot point forward and upward.[1,12,13] Unfortunately, once the prosthesis exceeds a critical size threshold, this often creates the appearance of a bulging eye that may not close. Moreover, the increased size and weight of the prosthesis can draw down the lower eyelid. Another nonsurgical approach can be through camouflaging a drooping eyelid, superior sulcus deformity, or both by using eyeglasses with a bold frame style. The frame can be positioned to lie horizontally in front of the upper eyelid, providing a visual distraction for the casual observer. In addition, eyeglasses have the added benefit of protecting the remaining healthy eye. In cases of small fissure and enophthalmos, a single cosmetic optic lens, as used to improve the appearance of a blind eye, can help improve the appearance of a prosthetic eye.

When such nonsurgical solutions and ocular prosthesis modifications are unable to correct moderate to severe ptosis with a satisfactory aesthetic result, there is still utility in adjustment of the prosthesis in the preparation for surgery. Mombaerts and Groet[13] demonstrated the importance of preoperative prosthetic modifications to vertically align the pupils without any correction of ptosis. This allowed for debulking of the prosthesis at the expense of worsened ptosis upfront, but with the advantage of a technically easier ptosis surgery and less risk of overcorrection. With this method, symmetrically corrected ptosis with contralateral eye occurred in 19 of 29 patients (66%), 1 mm residual ptosis in 6 patients (17%), and 2 mm residual ptosis in 4 patients (14%).[13]

Traditionally, an external approach with levator resection is preferred for surgical correction of ptosis in patients with anophthalmic syndrome to preserve maximal conjunctival tissue and prevent socket contracture.[31] When using the external or anterior approach, resection of the skin and especially preaponeurotic fat should be avoided or kept to a minimum as this can worsen superior sulcus syndrome.[13] Recent literature, however, has shown that an internal conjunctiva or Muller's muscle resection can be used to correct mild ptosis in the patients with anophthalmic syndrome without complications related to shortened superior fornix.[27,32,33] Regardless of approach, care should be taken to avoid surgically overcorrecting the upper eyelid as this cannot be fine-tuned with the prosthesis.[13]

Socket Contracture. While not part of the anophthalmic syndrome, socket contracture has since been incorporated in an updated syndrome called postenucleation socket syndrome—enophthalmos, superior sulcus syndrome, ptosis or eyelid retraction, lower eyelid laxity, and shallowing of the lower fornix.[3] Contracted fornices can result in problems with retaining a prosthesis and subsequently may require an ocularist to fabricate progressively larger conformers, a technique used in prosthetic treatment of microophthalmia, in which conformers are placed to condition and expand the eye socket. Conformers are upsized until the socket reaches the desired size, at which point a custom prosthesis can then be placed. If severe enough, this can result in the inability to use an ocular prosthesis. Depending on the grade of socket contracture, a number of techniques exist: anterior lamellar repositioning; grafting of mucous membrane, skin, dermis, fat, auricular cartilage or amniotic membrane; and free vascularized radial forearm flap.[3,34,35,36,37]

Worldwide, mucous membrane grafting is the preferred surgical technique for contracted socket. The major drawback of any graft procedure is the need for harvesting of tissue from a separate site on the patient. As the patient may require a repeat procedure in the future, there exists a need for an ideal tissue that is abundant and readily available. Amniotic membrane offers a promising alternative, as it has been shown to give cosmetically and functionally acceptable results in cases of mild to moderate grades of anophthalmic socket contracture comparable to mucous membrane grafting. Some beneficial characteristics of amniotic membrane over mucous membrane are its epithelialization properties, ability to reinforce adhesion of basal epithelial cells, and prevention of epithelial apoptosis by producing several growth factors. A limitation is the fact that amniotic membrane is a substrate graft and requires the presence of healthy conjunctival cells to differentiate and multiply over it, thus necessitating careful patient selection, such as avoiding use in patients who have received radiation to the orbit.[35] In the event of severe socket contracture after enucleation, more technically demanding approaches such as local advancement or pedicled rotation flaps may become necessary.[36]

When patients have concomitant socket contracture and lower eyelid malposition, techniques using a posterior lamella spacer are ideal. A variety of homologous (i.e., sclera), synthetic (polyester mesh, porous polyethylene, polytetrafluoroethylene), and autogenous materials (fascia lata, oral mucosa, nasal cartilage, palatal mucosa, upper eyelid tarsus, and auricular cartilage) have been previously used as spacers. Auricular cartilage is an ideal spacer material as it not only elevates the retracted lower eyelid and lengthens the retracted conjunctival fornix, but it also provides robust support for the prosthesis. Smith and Malet[34] achieved successful correction in 92.6% of the 54 cases with a mean follow up of 19.7 months (95% correction in moderate retraction, 86% correction in severe retraction) using auricular cartilage. If lower eyelid laxity and fornix contracture are only mild and upper eyelid ptosis is present, an upper eyelid tarsectomy with use as a lower eyelid spacer is also an excellent alternative as a spacer substrate.[37]

DISCUSSION

As intraorbital implants have evolved over the years, so too has the management of anophthalmic syndrome. Given the breadth of entities encompassed in anophthalmic syndrome or postenucleation socket syndrome, it is imperative that ocularists and oculoplastic surgeons work collaboratively. Nolan and Vistnes[29] rightly proposed an optimal sequence of operative procedures: 1) correction of enophthalmos and superior sulcus deformity, 2) correction of lower eyelid laxity, and 3) correction of upper eyelid ptosis. Ocularists should then be relied on for both pre- and postoperative troubleshooting. By following these steps, the patient with anophthalmic syndrome can hopefully

get maximal benefit with the minimum amount of surgery. For instance, by maximizing orbital volume, the prosthesis bulk may be reduced and thus relieve some or all the future sagging of the lower eyelid, sparing potentially unnecessary downstream surgical corrections.

Most of the data regarding the management of anophthalmic socket derives from small clinical case series and at best small cohort studies. Given the small sample sizes, these studies are particularly susceptible to making a type II error—they lack sufficient power to determine if a true difference exists between techniques. While the nature of anophthalmic socket does not lend itself easily to larger studies, a more uniform or standardized set of objective criteria can allow for pooling of data.

Proposed criteria on enophthalmos, superior sulcus deformity, ptosis, and socket contracture are as follows. Enophthalmos is to be graded from 1 to 4 (grade 1 = no postoperative improvement; grade 2 = improvement <2 mm but remained enophthalmos; grade 3 = improvement ≥2 mm but remained enophthalmos; and grade 4 = no enophthalmos) compared with unaffected side.[2] Superior sulcus syndrome is to be graded on a scale of 0 to 4 (grade 0 = none; grade 1 = trace, medial only, barely visible; grade 2 = mild, medial, easily detected; grade 3 = moderate, medial to central; and grade 4 = severe, extending medial to lateral; see Fig. 2A–C).[8,9] Ptosis is to be evaluated as successful when eyelid position is within 1 mm of the normal side in primary gaze.[12] Socket contracture is to be graded from 1 to 5 (grade 1 = shallow or shelved lower fornix; grade 2 = loss of both upper and lower fornices, preventing retention of artificial eye; grade 3 = loss of upper, lower, medial, and lateral fornices; grade 4 = loss of all fornices with reduction in palpebral aperture; and grade 5 = recurrence of contraction after repeated trial of reconstruction).[35]

As the approach to the anophthalmic syndrome continues to expand, it remains critical that both ocularists and oculoplastic surgeons together tailor a step-wise approach to correcting these cosmetic defects. There exists a fine balance between the ability of the prosthesis to correct deficits alone and a critical point in which it can instead complicate the surgical picture. Communication between the oculoplastic surgeon or ophthalmologist, ocularist, and the patient is essential to defining realistic patient expectations. The ophthalmologist is typically the initial point of contact with the patient with anophthalmic syndrome and usually dictates the course of action for prosthetic restoration. Conversely, the ocularist can play an important role in educating the patient about nonsurgical and prosthetic options and help navigate any necessary compromises between surgical and nonsurgical management. Lastly, defining uniform measurement criteria will be an important next step in validating the benefit and limitation of each technique.

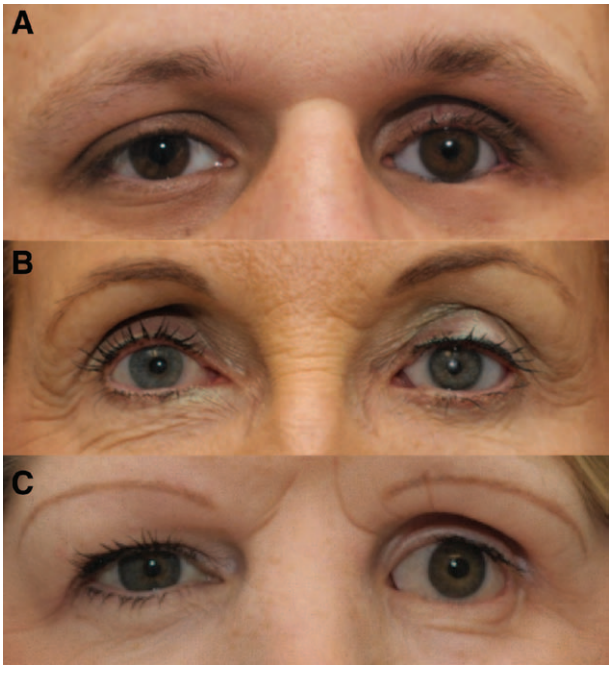

FIG. 2. **A**, Grade 2 superior sulcus syndrome, OS. **B**, Grade 3 superior sulcus syndrome, OS. **C**, Grade 4 superior sulcus syndrome, OS (photos courtesy of Dr James C. Fleming, Memphis, TN.).

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