

Evaluation and Approach of a Painful Quiet (Non-Red) Eye: A Comprehensive review for Primary Health Care Physicians

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Abstract

Different eye signs or symptoms seen in primary health care clinics and emergency departments may indicate the urgency for advanced and specialized care from ophthalmologists. Eye pain is one of the commonest complains encountered in various age groups and for that it is essential for health care providers to be aware of alarming features of eye pain and how to deal with it plus knowing when referral to an ophthalmologist is indicated. In many cases, isolated pain with no other signs and clear examination may lead to underestimation or misdiagnose of critical situation in which vision-saving can be a matter of time. Subsequently, this review article is provided to primary health care physicians and non-specialized caregivers who might face similar cases. In this review, differential diagnosis of pain in clear quiet eyes have been discussed briefly pointing out most relevant history and examination points, risk factors, treatment options and expected outcomes or prognosis of each differential.

Key words: Quiet Eye, painful, differential diagnosis, Saudi Arabia, normal examination.

Introduction

Eye pain is one of the most common complaints that present to primary care and family medicine clinics and emergency departments (1). Differential diagnosis of this kind of pain can be a true challenge, especially when the examined eye appears normal and with transient, mild, or no findings at all (1). A key important element in similar cases is taking a detailed history, which aids in reaching a proper diagnosis or at least recognizing critical cases that require immediate intervention or consultation from an ophthalmologist (1,2). Eye pain can also be a manifestation of a neurological problem or systemic disease; thus, practitioners are advised to thoroughly study the common causes of eye pain. (2,3). In this review, the discussion starts with covering the important items of history taking and physical examination for non-specialized doctors (3). Then, the most frequently encountered causes are divided into three main categories: orbital, ocular, neurological diagnoses, and other systemic diseases common in Saudi Arabia. A typical case from each division is presented, and key historical features of the disease are discussed. Additionally, important findings on examination and appropriate management are outlined according to national studies. The eye conditions presented in this review have been sorted based on their prevalence in Saudi Arabia since some similar articles were done in other foreign countries.

Evaluation and Approach

Initial evaluation should include several questions about vision loss or change in vision, foreign body sensation, photophobia and headache or presence or absence of eye redness either intermittent or constant (4). In all cases, potential sight-threatening conditions should be identified and dealt with as soon as possible. A careful examination can uncover these serious conditions:

Determine if the pain is in or around the eye. If the vision has changed, assess visual acuity. Check if the apparently white eye has any signs of inflammation, e.g. eye congestion localization whether it is diffuse, ciliary flush, localized or sectoral. Carefully examine the external eye, including those parts of the globe under the lids, for signs of occult trauma (subconjunctival hemorrhage), conjunctivitis, or foreign bodies. Serious sight-threatening causes of eye pain in the inflamed eye, in which the vision may or may not be reduced at the time of examination, include occult trauma, anterior uveitis, optic neuritis, acute angle closure glaucoma and, rarely, chronic glaucoma. In checking for these conditions, ask the following:

- Is there a history of recent or past trauma? (Pain after cataract or laser refractive surgery may rarely persist for weeks to months.)
- Is there evidence of trauma to the external eye and lids, e.g., in the pupil shape and reactions to light or sectoral or total iris loss?

- Examine with a bright pen torch and a direct ophthalmoscope, including the region of the globe under the eyelid. Evert the upper eyelid with a cotton bud (a useful check for foreign bodies). A retained sub-tarsal, periocular, or corneal foreign body can cause pain in an uninflamed eye. Some of the retained intraocular foreign bodies for a long period may alter the color of the iris (heterochromia).

- Is the pain of a dull, persistent, occasionally throbbing nature with headache?

This suggests migraine headache, chronic angle closure glaucoma or neovascular glaucoma, for instance, secondary to retinal vein occlusion or diabetic eye disease. Angle closure may occur in patients with shallow chamber and narrow angle.

- Is the pain of sudden onset or acute, especially on eye movement, and/or associated with visual loss?

This set of symptoms is pathognomonic for optic neuritis. Non-sight-threatening ophthalmic causes of eye pain are the most likely to present to general practice(5). These include optical causes (refractive error, eye strain), ocular surface disease (dry eye disease, Sjogren's syndrome), and a range of eyelid diseases(6).

When assessing for keratitis, clinicians should ask about several predisposing factors such as trauma and contact lenses. A contact lens history includes wearing schedule; overnight wear; contact lens hygiene protocol; use of tap water to rinse contact lenses; and swimming, using a hot tub or showering while wearing contact lenses. Bacterial and Acanthamoeba keratitis is associated with inappropriate contact lens use or care(2). Orbital cellulitis presents as unilateral erythema, swelling, proptosis and ptosis of the eyelid with associated pain with eye movement and decreased visual acuity(8). The eyelid and surrounding region should also be inspected for rashes or vesicles. Conjunctival or eyelid vesicles occur in about one-half of patients with Herpes Simplex Virus keratitis whereas herpes zoster ophthalmicus leads to associated pain and vesicular lesions appearing on a larger dermatome in a horizontal midline pattern(7). In the functional assessment, all patients presenting with eye pain should be tested for vision loss. Having the patient read a Snellen chart at a distance of 20 ft. (6 m.) is the standard test to evaluate visual acuity. Gross visual deficits are assessed using confrontational testing. The kinetic red test is performed by taking a five mm. red-topped pen and moving it inward from the boundary of each visual quadrant. This test may be combined with the more common static finger wiggle test to improve sensitivity for detecting visual field loss. This combination is the most sensitive way to assess for visual field deficit in the primary care setting (8). Determining more subtle differences such as whether vision loss is diffuse, central, or peripheral may require an ophthalmology referral for more precise testing (7). Primary care physicians are expected to examine the patient using the Snellen chart, tonometer, penlight, and fluorescein stain (7).

Ocular Causes

Dry Eye Disease

Dry eye disease, also known as dry eye syndrome or keratoconjunctivitis sicca, is a disease of the eye surface caused by underproduction or changes in the composition of lacrimal fluid or by increased evaporation. A diagnosis of dry eye accounts for nearly 20% of eye pain, and it represents the most common cause of eye pain(9). Dry eyes may lead to bilateral eye pain, foreign body sensation, tearing, photophobia, and occasional redness. Common causes of this condition include environmental factors (e.g., dry rooms and looking at computer screens for a long period of time), usage of contact lenses, eyelid abnormalities, and the use of medications (e.g., antihistamines, estrogens, Isotretinoin capsules and anticholinergics). Deficiencies in one of the three layers of the tear film (lipid, aqueous, and mucin) can be identified using the tear breakup time (TBUT) test(10). The general treatment is to avoid triggers (e.g., dry air), changing the environment (e.g., use of humidifiers), and the use of ocular lubricants or artificial tears in cases of aqueous or mucin layer deficiency(10). As for an inadequate lipid layer, warm compresses and fish oil supplements (e.g., Omega-3) can be used. Topical steroids and/or cyclosporin can also be used if the cause of the dryness is inflammatory(11).

Corneal Abrasion

A corneal abrasion is a scrape or a scratch on the surface of the corneal epithelium. Its symptoms can be eye pain, red eye, tearing, decreased visual acuity, photophobia, and/or a foreign body sensation (12). Corneal injuries can result from blunt force trauma or by sharp objects (e.g., with fingernails), wearing of contact lenses, foreign body entry, or chemical/radiation burns (12, 13). The patient's detailed history and an examination of the eye using fluorescein staining are the cornerstone for reaching the diagnosis of corneal abrasion(14). Fluorescein dye can aid in the visualization and properly estimate the depth and size of the suspected abrasion (15). Visual acuity should be checked with a Snellen chart(16). The goal of treatment is to prevent bacterial infections, speed up the process of healing, and provide symptomatic relief to the patient. Identifying such injuries and removal of any retained objects is crucial to the healing process. Antibiotic prophylaxis with lubricating ointments (e.g., erythromycin or bacitracin), topical drops (e.g., ofloxacin or moxifloxacin), or a combination of both therapies can prevent any pathogenic infections from growing on the epithelial defect. Pain relief options include oral analgesics and oral nonsteroidal anti-inflammatory drugs. Extended use of topical steroids is contraindicated on account of the risk of delaying stromal healing, especially in cases of HSV infection related abrasions, masking the development of a corneal ulcer, and causing toxicity to the corneal epithelium(13, 17). Also, topical steroids should be avoided in initial management. Recent studies have found that there is no advantage in using pressure eye patches or bandage contact lenses to reduce the abrasion area and pain. Small uncomplicated corneal abrasions should

heal within approximately 24–48 hours. Recurrent corneal erosions can occur as a complication(14).

Eye Strain

Eye strain is an emerging public complaint nowadays, especially with the digital devices being a part of daily life(18,19). A common presentation of patients is usually with an eye sore, frontal headache, and other ocular surface related symptoms like tearing and itchiness explained by the dryness of the eyes(1,18,19). Patients in some cases may suffer from other vision-related syndromes caused by viewing the computer display(18). Pains in eye strain were suggested to be muscular in origin by Duke-Elder and Tait and explained by the continuously overtaxing of the ciliary and extraocular muscles in order to maintain binocularity(19). However, other theories outweigh environmental and psychological factors(19).

Since dryness is a significant cause of eye strain, treatment options must include lubricating eye drops for mild cases(18). In some cases, oral supplements such as blueberry extract or omega-3 fatty acids can be used. Identifying any causative factors is important: in cases where eye strain is a result of computer vision syndrome or overuse of digital devices in general, it is important to initiate ergonomic practices as part of the management(18).

Post-Refractive Surgical Pain

The relation between dry eye syndrome and refractive surgeries is well established(1). Usually patients complain of discomfort, especially in the first few months (up to 6 months) following surgery. This dissatisfaction is found in about 90% of cases and is caused by dryness (1). In LASER assisted in-situ keratomileusis (LASIK) and other refractive procedures, disturbance of tear film, which acts as a defense barrier against ocular dryness, is due to direct damage to either the lacrimal glands or the corneal nerve plexuses, responsible for blinking rate control (1). Both injuries lead to decreased lacrimal clearance and therapy dryness and discomfort(1,20). The neuropathic pain following refractive procedures is usually described as being persistent and burning in nature or compared to the sensation of a foreign body due to allodynia(1,20). Patients are usually prescribed pain control medications and lubricants to manage the discomfort(1).

Intermittent Angle Closure

There are three types of primary angle closure glaucoma: intermittent, acute and creeping(1). Repeated episodes of rising intraocular pressure, which is characteristic of the intermittent subtype, can sometimes lead to chronic angle-closure glaucoma and other permanent complications of the anterior chamber if not identified early(21). Intermittent angle closure glaucoma is caused generally by the repeated papillary blockade and angle closure, which resolves spontaneously within 30–120 minutes and, thus, the usual physical examinations appear to be normal most of the time(1,21). An effective treatment option(21) appears to be a definitive surgical laser peripheral iridotomy with the

use of topical agents to decrease intraocular pressure. In some cases, selective laser trabeculoplasty may be used (21).

Posterior Scleritis

This is a disease of an autoimmune inflammatory process that affects the sclera and is mainly localized to restore muscle insertions(1,22). Pain in posterior scleritis is aching in nature and frequently described as deep and significant upon eye movements or pressure applied to the eye(22). Other features of the disease include loss of visual acuity or blurred vision(2). It is a relatively rare diagnosis and has a variable presentation. Moreover, physical examination may be normal in mild cases, and the slit lamp may not show any optic disc edema or any other abnormalities(22). Therefore, imaging modalities, especially ultrasonography, should be considered in suspected cases. An ultrasonogram is a useful tool in diagnosing posterior scleritis by revealing posterior scleral thickening(22). Other concurrent autoimmune diseases may raise the suspicion of posterior scleritis in patients with similar complaints. Treatment options are limited to oral steroids in most cases; however, recurrence is common(2,22).

Benign Essential Blepharospasm

This is a form of focal muscular dystonia that affects the co-inhibitory effect between protractor and retractor muscle groups in blinking and, thus, resulting in increased blink rate due to the continued spasms of the orbicularis oculi muscle(1,23,24). Patients usually complain of photophobia in the majority of cases accompanied by eye irritation or discomfort; women in their fifth to seventh decades are the most commonly affected individuals(23,24). The pathophysiology of the disease is still not well known; however, dysfunction of the thalamus, basal ganglia or brain stem is thought to play a part in this disease. Previously, botulism-type A toxin was used alone to treat benign essential blepharospasm. Nowadays, conservative measures like wearing sunglasses and dry eye treatments are effective in addition to oral medications prescribed for the underlying comorbidities, especially those of a psychological origin(24).

Microbial Keratitis

Microbial keratitis is characterized by a corneal epithelial defect with underlying stromal inflammation caused by replicating microorganisms. Patients often feel significant pain and distress which is rapidly progressive(25). Microbial keratitis appropriates considerable resources in ophthalmic acute care and requires aggressive treatment to halt the disease process and limit the extent of corneal scarring, which can cause loss of vision(26). Wearing contact lenses and trauma is the most common causes of microbial keratitis among other causes associated with ocular surface disease, previous herpetic eye disease and systemic disease(25). Treatment varies depending upon the type of microbial keratitis. In initial treatment, 'shotgun therapy' a combination of antibiotics is used on the basis of local epidemiological information and an intensive treatment using a single antibiotic as directed by the results of microbiological investigation(27). Soft

contact lens and chloramphenicol is used widely in United Kingdom for conjunctival and corneal disease as prophylaxis against bacterial infection and is commonly available without prescription(28). In the United States, concern about the precipitation of aplastic anemia has led to widespread use of fluoroquinolones in such scenarios, despite the paucity of evidence linking topical chloramphenicol use to the hematologic disorder(29). Fluoroquinolones are bactericidal antibiotics and inhibit 2 bacterial enzymes required for deoxyribonucleic acid synthesis. Second-generation compounds (ciprofloxacin, ofloxacin) inhibit DNA gyrase in gram-negative organisms better than topoisomerase IV in gram-positive bacteria, leading to poorer gram-positive cover(30).

Endophthalmitis

Endophthalmitis is a serious intraocular inflammatory disorder in result of an infection of the vitreous cavity. When infectious organisms gain entry to the eye by direct inoculation through intraocular surgery, penetrating trauma, or contiguous spread from adjacent tissues they cause exogenous endophthalmitis, whereas, endogenous endophthalmitis occurs when infectious agents are hematogenously disseminated into the eye from a distant focus of infection (31). Timing of therapy is an important factor in visual outcome of infectious endophthalmitis which can be diagnosed through various clinical presentations which helps to distinguish acute from chronic to determine an effective management plan (32). The prognosis in endophthalmitis is dependent on culture results (better prognosis for culture-negative cases), time of onset of the endophthalmitis (better prognosis for late-onset postoperative endophthalmitis), and the virulence of the pathogen (32). Patients receive either intravitreal antibiotics alone or in conjunction with steroids (33). The treatment modality is non-random in nature and based on the treatment preference of the various attending physicians (48). Intravenous antibiotics (maximum doses to allow intravitreal penetration) are considered mandatory in the treatment of endogenous endophthalmitis to treat both the eye infection as well as the original source of infection and bacteremia, if present (34). In general, intravenous antibiotics should be administered for 2 weeks for most infections, except in the case of endocarditis which usually requires at least 4 weeks of treatment (35). However, there has been considerable controversy over the use of more aggressive means in the treatment of endogenous endophthalmitis, in particular, intravitreal antibiotics and therapeutic vitrectomy (36,37).

Orbital causes

Graves' Ophthalmopathy

Graves' ophthalmopathy (GO) or orbitopathy is an autoimmune condition that is generally associated with Graves' disease (38). It is most associated with hyperthyroidism, but a state of euthyroid or hypothyroid may be present. Laboratory tests targeting thyroid malfunction as the cause may show decreased TSH, increased T3/T4, and, in the case of Graves' disease, increased TSH receptor antibodies (39). MRI or CT scan confirmatory

tests show exophthalmos, increased fat density and inflammation, and enlargement of the extraocular muscles. Photo documentation and imaging studies may also help in monitoring the progression of the disease. GO is usually a self-limiting disease, but intervention may be necessary in the case of severe symptoms (e.g., severe proptosis and lid retraction) or risk of complications (39,40). Treatment strategies for all patients include treating the underlying cause, e.g., hyperthyroidism, and conservative local measures such as eye protection and sleeping with the head of the bed elevated. In moderate to severe cases, high-dose IV steroids are used to reduce the production of glycosaminoglycans. Surgery is reserved for non-responders or if there is a threat to the vision of the patient (40).

Preseptal Cellulitis

Preseptal cellulitis, also known as periorbital cellulitis, is an infection of the eyelid and periorbital soft tissue without involvement of the orbital contents (41). Most commonly, it can occur as a result of a complicated bacterial rhinosinusitis infection. Other causes include acute inflammation of the lacrimal sac (dacryocystitis), trauma, ophthalmic surgery, and even hematogenous spread from distant locations (28). Symptoms include ocular pain, eyelid swelling, and, less commonly, chemosis and fever. It is primarily a clinical diagnosis. Laboratory investigations may show leukocytosis and positive culture, though they are generally unnecessary. A CT scan will show eyelid swelling only. Treatment options include oral antibiotics and close follow-up for mild, afebrile, non-systemic cases. Generally, the incidence of complications, especially life-threatening ones, is rare (41).

Orbital Cellulitis

Orbital cellulitis is an infection/inflammatory process that involves the tissues located posterior to the orbital septum within the bony orbit. The etiology is similar to preseptal cellulitis. The main symptoms are ptosis and ophthalmoplegia. Fever, malaise, eyelid swelling, and decreased visual acuity can also be seen. Clinical findings of reduced vision, diplopia, ophthalmoplegia, and ptosis make it distinguishable from preseptal cellulitis (42). It can affect all age groups. Like preseptal cellulitis, it is also primarily a clinical diagnosis. Laboratory investigations may show leukocytosis and positive culture results from the blood or tissue fluid. A CT scan of the orbit can confirm the diagnosis and unveil complications, e.g., orbital abscess or intracranial extension(42). Treatment options include empiric intravenous administration of antibiotics (vancomycin plus a third-generation cephalosporin or an aminopenicillin combined with a beta-lactamase inhibitor). Surgical drainage is indicated if there is an abscess(43).

Orbital Inflammatory Pseudotumor

Orbital pseudotumor, also known as idiopathic orbital inflammation, is a clinico-pathological entity that can present as unilateral or bilateral eye pain. The cause may be inflammation of muscle (myositis), the lacrimal glands (dacryoadenitis), the sclera (scleritis), or the

trochlea (trochleitis). Symptoms include external signs such as conjunctival injection and chemosis, ptosis, ophthalmoplegia, or proptosis (44). However, patients with isolated conditions such as myositis may only present with acute or subacute orbital pain on eye movement (2). Also, patients with trochleitis may present with focal tenderness in the superonasal orbit. Direct inspection and palpation of the trochlea and lacrimal gland areas should be performed in cases of eye pain, especially when localized superotemporally or superonasally (45). The diagnosis of orbital inflammatory pseudotumor is usually not clinically difficult. Orbital ultrasound or orbital imaging (CT or MRI) may demonstrate the characteristic findings. The patient with orbital myositis has enlarged, irregular muscles usually with tendinous insertion involvement (44). Treatment includes non-steroidal anti-inflammatory agents or corticosteroids for mild and moderate-severe cases respectively. Local injection of corticosteroids may also be helpful in selected patients. The illness is often monophasic although recurrent episodes may occur. Failure to respond to medications or recurrence is a "red flag" for possible alternative etiology. Biopsy should be considered in these cases (46-50).

Neurological causes

Migraine Headache

Migraine is a neurological disturbance of the sensory integration of the central nervous system resulting in visual and auditory symptoms in addition to headache (9,51). The pathophysiological pathway that relates eyes to migraine is still not well-understood, but theories suggest that the eye resembles the trigeminal input to pattern the disorder. A mainstay of diagnosis is that patients usually experience transient, recurrent episodes of headaches that are disabling in the majority of cases (9). Visual signs include redness and lacrimation while symptoms are usually photophobia, light-sensitivity, and blurry vision(9). Ophthalmoplegic migraine (OM) is a rare entity that is known to combine visual symptoms with migraine headache; however, more severe complications such as oculomotor paresis are present. Thus, investigation is essential rather than relying on clinical diagnosis (51). Treatment options vary depending on trigger factors and any other underlying causes(51).

Trigeminal Neuralgia

Trigeminal nerve transmission of direct and referred eye pain through its first branch, the ophthalmic, explains the eye involvement in many neurological conditions (9). Stabbing unilateral facial pain that is associated with numbness or other sensory symptoms is a typical presentation for patients with trigeminal neuralgia (9). Pain is usually episodic and severe and extends to involve other branches of the trigeminal nerve (9). Patients are in most cases treated with antiepileptics such as carbamazepine. If monotherapy fails, then a combination of two agents is preferred before surgical intervention (9).

Elevated Intracranial Pressure

High intracranial pressure (ICP) can arise due to different causes like space-occupying lesions, e.g., tumor or mechanical obstruction of cerebrospinal fluid flow and many other pathologies (9,51). Bilateral eye pain or ophthalmoplegia, due to retrobulbar pain and pain with eye movement, is a distinguishing feature of high ICP diagnosis. Imaging is of great use to establish diagnosis in such cases (52). Other patients' complaints can be generalized like seizures, loss of consciousness, or symptoms indicating focal deficits (52). In some cases, the pathophysiology is unclear and thus referred to as idiopathic (9,52). Approach to patients with high ICP can be started by investigating the underlying cause and then lowering intracranial pressure through medical therapy (52).

Optic Neuritis

Optic neuritis is an inflammation of the optic nerve that results in demyelination and can develop in patients with multiple sclerosis or be idiopathic (53). It is the most common neuropathy(53). Patients present with unilateral painful acute visual dysfunction complaining of poor color perception, central visual field defects, or relative afferent pupillary light defect (RAPD), which can be provoked or aggravated by eye movement. Treatment options vary depending on the cause (53). In cases where optic neuritis is a complication of multiple sclerosis, a neurological consultation is essential (53). In other cases, intravenous administration of steroids will aid in reducing optic disc edema and resolving the symptoms(53).

Cluster Headache

A cluster headache is a primary headache that is neurovascular in origin and thought to be a result of the continuous activation of the trigeminal autonomic reflex (9,51). This disorder is characterized by short-lasting attacks of severe headache(41). Patients tend to present complaining of unilateral worsening headache that is localized mostly to the first division of the trigeminal nerve, which is the ophthalmic division. It is important to not misdiagnose cluster headaches as migraines since different management approaches are designed for each disorder (54,55). Other symptoms include unilateral ptosis, miosis and rhinorrhea or facial swelling. These patients are usually managed by high flow oxygen supplementation (55).

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