Methods: A 16-month-old female patient who suffered a severe attack by a big-sized dog (Rottweiler) in the midface area was managed with surgery/PFD combination and followed up for 20 months to evaluate the efficacy to control, prevent, and improve injury sequels.
Results: Surgery/PFD combination offered a good complementary therapy downregulating inflammatory activity, improving blood supply, and activating cytokine modulation and collagen synthesis/biosynthesis (scar control). No side effects were reported in this case report.
Conclusions: Surgery/PFD management for severe facial dog bites represents a safe and effective therapeutic option to protect and improve a patient's quality of life, minimizing long-time sequels.

Key Words: Pirfenidone, dog bites, severe face trauma, PFD, TGF-β, trauma surgery, pediatric trauma, scar prevention, scar management

Dog bite injuries in children remain an under-recognized and under-reported public health problem. Epidemiological data indicates that in the USA, 4.5 million people are bitten by dogs each year; on average, 1 person in 100 is a victim of a dog bite needing medical attention with children twice as likely to be hospitalized than adolescent or adults.[1] In Mexico, the incidence reported in 2007 was 110 dog attacks for every 100,000 inhabitants. Dogs cause the majority (80%–90%) of animal bites requiring medical attention.[2–4] Victims are more commonly young males, with a peak incidence between 5 and 9 years of age.[5]

Dog bites most commonly affect the extremities, while 15%–27% of bite wounds occur in the head and neck.[2,6] Nose, ears, lips, and cheeks are the most commonly injured sites. Younger victims tend to be smaller in size, and therefore dog bites more frequently affect the head and neck in young children.[2]

Morbidity from acute bite trauma can include substantial blood loss, large soft-tissue defects, lacerations, abrasions, infection, and bone fractures. Scars and psychological damage are the long-term reminders of these events. Although mortality is less frequent, several deaths are reported each year worldwide as a result of severe dog maulings.[7,8]

Pirfenidone (PFD) is a wide-spectrum antifibrotic and anti-inflammatory drug that modulates diverse cytokines action, ie, TGF-β, TNF-α, EGF, PDGF, VEGF, IGF-1, FGF, IFN-γ, IL-1, IL-6, and IL-8, which has proved good effects in in vitro and in vivo settings.[9–12]

The aim of this study was to assess the effectiveness of PFD as a concomitant therapy with surgery in the treatment of severe facial trauma in pediatrics.

PATIENTS AND METHODS

Patient and Initial Management

A 16-month-old female patient who suffered a severe attack caused by a big-sized dog (Rottweiler) in the midface area.

After the attack, the patient was first attended in a primary care institution but, due to its severe injuries and critical condition, was transferred to Tacubaya Pediatric Hospital. Emergency service received the patient starting its stabilization and management, but due to the injury magnitude, her immediate enrollment in Pediatric Plastic and Reconstructive Surgery Service was necessary.

Clinical and radiological evaluations were performed founding a patient with ventilatory support, and several facial injuries included bilateral cheek and oral avulsion, bilateral facial nerve damage, superior and left inferior alveolar fracture, left zygomatic arch fracture, left comminuted parasymphyseal mandible fracture, and parotid and submandibular salivary glands exposure (Fig. 1).

Empiric antimicrobial coverage with ampicillin/sulbactam and administration of rabies prophylaxis was necessary due to the characteristics of the injury and the unknown vaccination antecedent of the dog, respectively.

Surgical and Postsurgical Management

Bite-wound care began 4 hours after attack in the operative room with exhaustive surgical cleanup using copious irrigation and debridement of devitalized tissue, and irrigation with 1% povidone-iodine was necessary as antiseptic prevention, continuing with left-sided mucosal closure and mandible fracture stabilization using 2-0 nylon suture; proximal branch of the left facial nerve was neurotized to orbicularis oris muscle 2 cm from the left lip commissure because distal section was missed, continued by closure by layers. Alveolar fracture reduction and closure of oral mucosa, nasal exploration and reimplantation of right cheek flap, and injuries affecting the floor of the mouth were corrected using closure by layers (Fig. 2).

Epidermolysis and scar development where evident 5 days after surgery, then salivary fistula was diagnosed at the seventh day. Fistula management consisted in closed drainage and octreotide resolving in 5 days. Once fistula was corrected, pirfenidone gel at 8% was applied t.i.d. for 6 months to improve scar progress and epithelization.

RESULTS

After 14 days of hospitalization, the patient was discharged; management and follow-up as outpatient were supplied by a multidisciplinary medical group consisting in rehabilitation, ophthalmology, pediatric odontology, and psychology services to improve and limit any psychological or functional damage.

Schedule for rehabilitation was twice a week the first month and once a week the succeeding visits. Neuromuscular rehabilitation required electrostimulation twice a week for 1 year. Also, pediatric odontology assessment was necessary to improve dental occlusion.

At discharge, the patient showed a left facial nerve paralysis, which compromised ocular closure, and presence of sialorrhea. Scar treatment by PFD application was continued at home.

One month after the attack, the right cheek developed lymphatic trapping due to the semicircular lesion leading to localized edema; it improved gradually until complete recovery after 1 year of treatment with PFD t.i.d.

FIGURE 1. Initial evaluation of the patient. We can observe the severity of the damage produced by the dog attack.

After 20 months of follow-up, results showed an excellent scar improvement, orthopantomography revealed an adequate fracture consolidation and conservation of teeth germ, dental occlusion has been corrected, and good self-perception has been obtained until this moment (Fig. 3).

DISCUSSION

Actually, the primary goal in the management of head and neck bite wounds is to achieve rapid healing while minimizing the risk of infection. This case report supports the findings published by Wu et al where primary repair of pediatric facial dog bite injuries, including complex soft-tissue injuries, is safe when performed in conjunction with antibiotic administration.[13]

In case of empiric antibiotic therapy or prophylaxis for cat and dog bites, guidelines recommend protection against *Pasteurella*, *Streptococcus*, and *Staphylococcus* species as well as anaerobes. It is known that the most suitable single agent to cover the pathogens of concern is oral amoxicillin and clavulanate, or if intravenous therapy is required, ampicillin and sulbactam. Alternative regimens for pediatric patients include clindamycin plus trimethoprim-sulfamethoxazole. For rabies control, current Centers for Disease Control and Prevention guidelines establish that prophylaxis includes immediate administration of antirabies immune globulin followed by a 5-dose course of rabies vaccine. Tetanus prophylaxis is recommended for animal and human bites if the patient has had fewer than 3 tetanus toxoid doses or more than 5 years have elapsed since the last immunization.[14]

After dog bites, complications like granuloma telangiectaticum, lymphangitis, endocarditis, meningitis, brain abscess, sepsis, and extensive intravenous blood clotting are always latent.[15] However, physical and psychosocial consequences of being attacked by a dog as a child can be devastating and cannot be minimized.[8] Facial scarring after severe dog attacks should be considered as one of the most under-reported and significant sequels due to its capacity to alter self-perception.

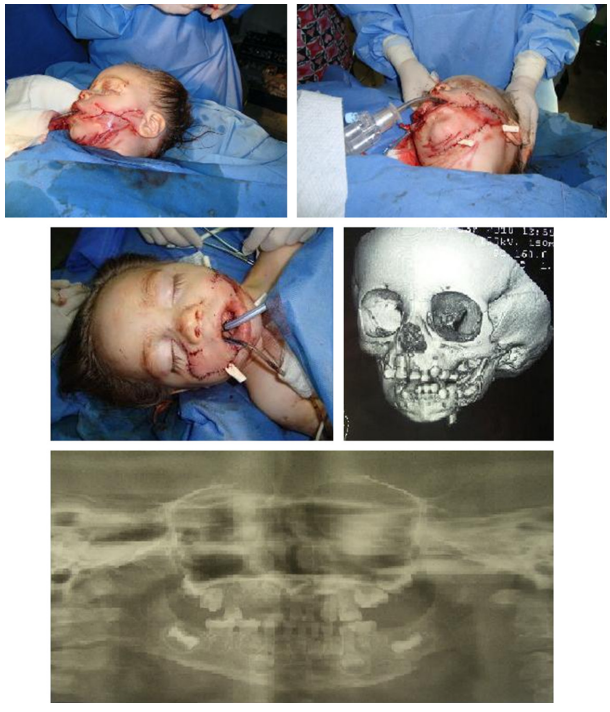

FIGURE 2. The first 3 photos show the post-surgical state of the patient with Penrose drainage in the suture area. A CT is provided to show the mandible injury after attack. Last image shows an orthopantomography where the left comminuted parasymphyseal mandible fracture is evident with no damage in dental pieces.

FIGURE 3. Up to now, the patient has this appearance; a good quality of her scar is clearly seen with no serious consequence in her quality of life or self-perception.

PFD is a pyridone derivative with wide-spectrum antifibrotic, cytokine, and extracellular matrix (ECM) degradation modulator drug. Recent studies have demonstrated that PFD is highly effective to regulate fibroproliferative disorders like cirrhosis, breast capsular contracture, focal segmental glomerulosclerosis, pathological skin scarring, and others, no matter the stage of the scar.[11,12,16] This knowledge was applied to offer a new preventive and therapeutic option to patients with high pathologic scarring risk.

In this study, we evaluated the effectiveness of surgery plus PFD in the management of severe facial trauma due to dog attack. Our results showed that despite good technical skills and opportune management, PFD offered a good complementary therapy down-regulating inflammatory activity which leads to control edema and blood supply improvement in the damaged area; cytokine modulation was critical in the regulation of wound healing and collagen synthesis/biosynthesis (scar control). No side effects were reported during PFD administration.

CONCLUSIONS

Pediatric dog bite injuries are a common phenomenon with a highly increasing incidence, and medical services like wound care and repair, tetanus prophylaxis, and antibiotic treatment for infection prevention present an increasing demand. Current severe dog-bite management is based on corrective surgery, and no previous reports have elucidated potential therapies to improve and prevent its outcomes. PFD and its anti-inflammatory and antifibrotic activity had proved to be a good therapy to avoid long-time sequels, improving quality of life and minimizing alterations in self-perception.

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REFERENCES

1. Meints K, de Keuster T. Brief report: don't kiss a sleeping dog: the first assessment of "the blue dog" bite prevention program. *J Pediatr Psychol* 2009;34:1084–1090
2. Griego RD, Rosen T, Orengo IF, et al. Dog, cat, and human bites: a review. *J Am Acad Dermatol* 1995;33:1019–1029
3. Ruskin JD, Laney TJ, Wendt SV, et al. Treatment of mammalian bite wounds of the maxillofacial region. *J Oral Maxillofac Surg* 1993;51:174–176
4. Goldstein EJC. Bite wounds and infection. *Clin Infect Dis* 1992; 14:633–638
5. Taplitz RA. Managing bite wounds. Currently recommended antibiotics for treatment and prophylaxis. *Postgrad Med* 2004;116:49–59
6. Stefanopoulos PK, Tarantzopoulou AD. Management of facial bite wounds. *Dent Clin North Am* 2009;53:691–705
7. Sacks JJ, Sinclair L, Gilchrist J, et al. Breeds of dog involved in fatal human attacks in the United States between 1979 and 1998. *J Am Vet Med Assoc* 2000;217:836–840
8. Kaye AE, Belz JM, Kirschner RE. Pediatric dog bite injuries: a 5-year review of the experience at The Children's Hospital of Philadelphia. *Plast Recontr Surg* 2009;124:551–558
9. Babovic-Vuksanovic D, Widemann BC, Dombi E, et al. Phase I trial of pirfenidone in children with neurofibromatosis 1 and plexiform neurofibromas. *Pediatr Neurol* 2007;36:293–300
10. Raghu G, Johnson WC, Lockhart D, et al. Treatment of idiopathic pulmonary fibrosis with a new antifibrotic agent, pirfenidone. *Am J Respir Crit Care Med* 1999;159:1061–1069
11. Macias-Barragan J, Sandoval-Rodriguez A, Navarro-Partida J, et al. The multifaceted role of pirfenidone and its novel targets. *Fibrogenesis Tissue Repair* 2010;3:16
12. Armendariz-Borunda J, Lyra-Gonzalez I, Medina-Preciado D, et al. A controlled clinical trial with pirfenidone in the treatment of pathological skin scarring caused by burns in pediatric patients. *Ann Plast Surg* 2012;68:22–28
13. Wu PS, Beres A, Tashjian DB, et al. Primary repair of facial dog bite injuries in children. *Pediatr Emerg Care* 2011;27:801–803
14. Ambro BT, Wright RJ, Heffelfinger RN. Management of bite wounds in the head and neck. *Facial Plast Surg* 2010;26:456–463
15. Kuvat SV, Bozkurt M, Kapi E, et al. Our treatment approaches in head-neck injuries caused by animal bites. *J Craniofac Surg* 2011;22:1507–1510
16. Veras-Castillo ER, Cardenas-Camarena L, Lyra-Gonzalez I, et al. Controlled clinical trial with pirfenidone in the treatment of breast capsular contracture: association of TGF-β polymorphisms. *Ann Plast Surg* 2013;70:16–22