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RESEARCH ARTICLE

A RETROSPECTIVE STUDY OF 16 CASES OF ACUTE COMPARTMENT SYNDROME FOLLOWING SNAKEBITE

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Abstract

Acute compartment syndrome after snakebite is considered to be quite rare and there is still a lot of controversy in regard to its diagnosis and management as it has been reported by the little available medical literature on the topic. It is in this context that our series assumes importance as we report our experience relating to management and outcome of 16 consecutive cases of compartment syndrome from snakebites. A 15-year retrospective study was conducted on all adult patients with compartment syndrome following snakebites, who were admitted between April 2005 and December 2019 in our institution. Due to non-availability of equipment to measure intracompartmental pressure, the diagnosis of compartment syndrome was based on clinical judgment. There were 10 (62.5%) male and 6 (37.5%) female, with a mean age of 32.1 ± 7.8 years. Bite site was mostly in the lower limbs (62.5%). Based on clinical severity, 2 (12.5%), 10 (62.5%) and 4 (25%) patients were classified into classes I, II, and III, respectively. FAV-Afrique® antivenom was administered to 12 (75%) patients in doses ranging from 1 to 5 vials by patients. Fasciotomy was performed in all cases and the median time from admission to surgery was 5.8 hours (range: 4–9 hours). The mean hospital stay was 16 days and follow-up of patients has shown good results: normal limb function was regained in all cases. In summary, acute compartment syndrome following snakebite is not rare in our context and must be treated by performing early fasciotomy without any delay after diagnosis.

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Introduction:-

Snakebites are a serious public health problem reaching high incidence rates and severity mainly in rural regions of tropical and subtropical countries situated in South Asia, Africa, and Latin America [1-3]. There are no available accurate statistics on snakebites worldwide, the epidemiology is poorly known and incidence estimates vary widely ranging from 1.8 million to 5.4 million bites globally per year [1, 4]. According to the World Health Organisation, snake envenomation leads annually to more than 100,000 deaths worldwide and causes permanent disability or disfigurement in about 400,000 cases [5].

In Morocco, almost 137 snakebites are recorded per year with an annual incidence of 0.46 bites per 100,000 inhabitants and a case-fatality rate of 4.1% [6]. Of the four medically important poisonous families of snakes

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(Elapidae, Viperidae, Atractaspidinae, Colubridae), the Viperidae (*Daboia mauritanica*, *Bitis arietans*, *Cerastes cerastes*, *Cerastes vipera*, *Echis leucogaster*, *Vipera latastei* and *Vipera monticola*) and the Elapidae (*Naja haje legionis*) remain the most common species of snakes responsible for most of the envenomation in our country [7]. Elapid venom is neurotoxic and absorbed rapidly into the blood stream causing rapid systemic effects [8], while Viper venom contains a complex mixture of high molecular weight proteins, mainly proteases, peptid hyaluronidase, and phospholipases whose effects are predominantly hemorrhagic and cytotoxic leading to coagulation abnormalities and severe local signs [9]. Acute compartment syndrome (ACS) after snakebite is considered to be quite rare and there is still a lot of controversy in regard to its diagnosis and management as it has been reported by the little available medical literature on the topic [10-12]. It is in this context that our series assumes importance as we report our experience relating to management and outcome of 16 consecutive cases of compartment syndrome from snakebites.

Material and Methods:-

After approval from our internal Institutional Review Board, a 15-year retrospective study was conducted on all adult (>18 years) patients with ACS following snakebites, who were admitted between April 2005 and December 2019 in our institution. Patients who did not have bite marks of a snake and any other forms of unknown bites that were not snakebites, were under 18 years old, and whose file records were inaccessible were excluded from the study. Among 138 patients who presented for snakebite during the study period, a total of 16 cases of ACS met our inclusion criteria and were included in this study.

A datasheet that has the parameters – age, sex, geographic origin, site of the bite, type of snake, time from snakebite to emergency department arrival, clinical presentation, laboratory values (hematologic and biochemical tests), severity of envenomation as determined by a traditional snakebite severity grading scale (Table 1), presence of systemic (rhabdomyolysis, venom-induced consumption coagulopathy, thrombocytopenia, and bleeding) or local (necrosis, infection) complications, treatment modalities (antivenom administration regimen, fasciotomy), length of hospitalization and outcome (recovered or died) - was used.

Diagnosis:

Due to non-availability of equipment, no intracompartmental pressure measurement was done. The diagnosis of ACS with the indication of fasciotomy was based on clinical judgment.

Specific treatment:

Immunotherapy was indicated in case of clinical and biological evidence of envenoming:

1. Systemic envenoming: haemostatic disorders, neurotoxic signs, cardiovascular abnormalities, acute renal failure, intravascular haemolysis or generalised rhabdomyolysis.
2. Local severe envenoming

FAV-Afrique® is the only antivenom available in Morocco since August 2012. It is a polyvalent antivenom composed of highly purified fragments of F (ab')² immunoglobulins against ten snake species among the most dangerous in Africa and belonging to families Viperidae and Elapidae. The dosage depends on the severity of envenoming. Initial dosage is 20 mL of antivenom (containing at least 20 LD50 mice per mL of each species valence) diluted to a total of 250 milliliters in isotonic fluid and infused over 30 to 60 min. Subsequent administrations depend on changes in the subject's clinical condition and the clinical response to the first infusion. Repeated doses are sometimes needed in severe cases.

Supportive treatment:

Tetanus prophylaxis and active tetanus immunization were given to all patients, as well as analgesics, antiallergics and serrapeptase. Frozen plasma and platelet concentrates had been used in case of severe bleeding.

Surgical management:

Fasciotomy, to fully decompress all involved compartments, was performed urgently in all cases, under general or locoregional anesthesia. The macroscopic appearance of muscle was carefully assessed and all non-viable tissue radically excised. Fasciotomy wounds were left open and were temporarily dressed with paraffin gauze, fluffed swabs and crepe bandages. The closure of fasciotomy incisions was carried out using Vacuum assisted closure (VAC), split skin grafting or healing by secondary intention.

The patients were followed-up for six months postoperatively on average (range: 4-14 mois) and functional recovery was assessed.

Statistical analysis:

All data were compiled using Microsoft Excel and analyzed using Statistical Package for Social Studies (SPSS 22.0 software). Categorical variables are reported as absolute numbers and percentages. Continuous variables are described as means \pm standard deviations for normally distributed data and as median values and interquartile ranges when data were not normally distributed.

Results:-

A total of 16 subjects were recruited for this study. Of these, 10 (62.5%) were male and 6 (37.5%) female, with a mean age of 32.1 ± 7.8 years (range: 21-48 years). Moreover, all patients (100%) were from rural areas. In terms of the type of snake, 4 (25%) subjects were bitten by *Daboia mauritanica*, 3 (18.7%) by *Cerastes Cerastes* and 2 (12.5%) by *Echis leucogaster*. In 7 (43.7%) cases, the patients could not identify the colour of the snake. Bite site was mostly in the lower limbs (62.5%) (Fig 1). The average time elapsed between being bitten by the snake and admitted in the hospital was 190.5 ± 160.5 minutes (range: 90 to 680 minutes). The most common findings from the physical examination (Fig 1, 2) of the patients were local swelling (100%), blistering (75%), tachycardia (75%), and hyperthermia (68.7%). Based on clinical severity, 2 (12.5%), 10 (62.5%) and 4 (25%) patients were classified into classes I, II, and III, respectively. The diagnosis of ACS was made only by clinical findings: intense pain exacerbated with passive muscle stretching, a tense compartment, sensory deficits or paresthesias. Motor deficit was not identified in any patient and pulses were intact. The hematological and biochemical laboratory abnormalities were: hemoconcentration (75%), anemia (50%), leukocytosis (43.7%), thrombocytopenia (43.7%), prolonged prothrombin time (37.5%) and increased CRP level (31.2%).

FAV-Afrique® antivenom was administered to 12 (75%) patients in doses ranging from 1 to 5 vials by patients. The average dose administered was 1.95 vials per patient. Fasciotomy was performed in all cases and the median time from admission to surgery was 5.8 hours (range: 4– 9hours). A limited lazy S shaped incision along the volar aspect of the forearm was used in case of ACS of the upper extremity. The dorsal compartment and the mobile extensor wad were released without the need for a dorsal incision. Two dorsal incisions centered over the second and fourth metacarpals were performed if there was an ACS of the hand. As for fasciotomy of the lower extremity, the dual-incision technique was used (Fig 3): a longitudinal skin incision in the anterolateral aspect of the leg, approximately 2 cm anterior to the fibula, and a posteromedial skin incision, approximately 2 cm posterior to the tibia. After this initial decompression and debridement of non-viable tissues, patients returned to the operating room in two to four days for additional assesment and debridement. The fasciotomy wounds have been managed with a VAC device in 10 patients and moistened dressings in 6 patients. The mean hospital stay was 16 days, with a minimum of 10 days and a maximum of 26 days. Follow-up of patients has shown good results: normal limb function was regained in all of cases treated.

Discussion:-

Snake bite is an acute life-threatening, time-limiting, medical emergency of villagers and is a neglected public health problem in tropical and sub-tropical countries [4]. Most of the literature is focused on snakebite mortality [13-14]. However, many survivor patients may suffer from permanent physical deformities because snake venom causes both systemic and local complications. Compartment syndrome is an extremely rare but severe complication with an incidence ranging from 0.20 to 1.36 % [10-12]. Til date, the medical literature contains only few case reports and case series describing this entity [15-21].

Snake venom is composed of a panoply of toxins and a complex mixture of proteins with cytotoxic, proteolytic, and/or neurotoxic enzymes which can initiate a significant amount of inflammation and edema in the bite site [22]. Within the limbs, muscles are organised into tightly packed compartments, each containing muscle, arteries, nerves and lymphatic vessels and surrounded by an inelastic connective tissue sheath [22]. The increasing edema following snakebite leads to rising pressure within the inextensible compartment, which affects the venous return system and results in decreased arterial pressure. This reduced transmural pressure gradient between microcirculation and interstitium induces ischemia within the affected compartment, creating a vicious cycle of cellular anoxia and leading to chemical mediators further increasing capillary permeability and fluid extravasation [22]. This vicious cycle must urgently be broken because high intracompartmental pressure (ICP) sustained for 6–8 hours results in

irreversible soft tissue damage [24]. The incidence of ACS was high (11.7 %) in the current study which may be related to the predominance of cytotoxic snakes in our country. Similar results were reported by Kim et al (10.8%) [25]. As to Hsu and co-workers, they had found an incidence of 6.6%, which is also relatively high [26].

Although much has been learned about compartment syndrome in recent decades, many questions and controversies surrounding its diagnosis and treatment have remained. Most studies consider measurement of the ICP as an important tool for diagnosis, with a pressure higher than 30 mmHg as significant of compartment syndrome [27]. Many authors recommend the use of a delta pressure (ΔP) which is defined as the difference between the diastolic blood pressure and measured compartment pressure. A ΔP of ≤ 30 mmHg is diagnostic of ACS [28]. Most of the centers in developing countries where snakebites are common, do not have the necessary equipment for measuring ICP and the diagnosis is made on the basis of clinical findings, especially pain which is severe, disproportionate to patient's clinical presentation, not relieved by painkillers, and worsen by passive stretch of compartment muscles [29]. Paresthesia, paresis/paralysis are late features and pulselessness is not used as a diagnostic criteria because peripheral pulses are usually present also when a high compartment pressure is diagnosed [30].

Management of ACS in snake envenomation, conservatively or by fasciotomy continues to be a controversial subject. Many authors support early fasciotomy in the treatment of all cases of envenomation. Our results were consistent with these findings and we suggest surgery improve outcome and should be performed early [31-32]. However, we agree that it should be avoided when the muscle is already dead. Fasciotomy in such instances provides no benefit and can increase the risk of infection [33]. On the other hand, others advocate that fasciotomy is the treatment for compartment syndrome from trauma or similar causes, but its effectiveness in snake bites envenomation is uncertain [34]. According to them, fasciotomy is never necessary when adequate antivenom has been administered because modern antivenoms both limit the spread of necrosis by inhibiting protease activity and reduce local swelling, leading to decreased risk of ACS. Moreover, some studies argue that combination of both fasciotomy and antivenom may improve functional outcome in severe snake bites. This leads to a question, what are the indications and advantages of early fasciotomy in the management of compartment syndrome? Specific indications for fasciotomy have been established. These are mainly based on clinical evaluation. Recent studies support that an increase of ICP up to 30- 45 mmHg is an absolute indication for fasciotomy [35]. Unfortunately, measurement of ICP is not always possible in a number of medical centers in developing countries, so that the diagnosis of compartment syndrome is always based on clinical standards. Ribeiro et al attempted to determine the risk factors for local complications: bites on extremities, especially the hand, the size of the snake, and the severity of envenomation [36]. In our series, all victims were treated by fasciotomy and 12 of them had received antivenom serum. After a mean follow-up of 6 months, no functional deficit was recorded in any of our patients.

Table 1:- Classification of the severity of snakebite.

Grade	Findings
0, No envenomation	Absence of local or systemic reactions, Fang marks (+/-)
I , mild envenomation	Fang marks (+), moderate pain , minimal local edema (0-15cm) , erythema (+), ecchymosis (+/-), no systemic reactions
II, moderate envenomation	Fang marks (+), severe pain, moderate local edema (15-30cm), erythema and ecchymosis (+), systemic weakness, sweating, syncope , nausea vomiting, anemia or thrombocytopenia
III, severe envenomation	Fang marks (+), severe pain , severe local edema (>30cm), erythema and ecchymosis (+),hypotension , paresthesia, coma, pulmonary edema, respiratory failure

Figures:



Figure 1:- Clinical photograph of the affected left lower limb showing severe local edema extending to the leg, knee, and thigh with haemorrhagic blisters on the dorsum of the foot.



Figure 2:- A 47-year-old woman presented with *Daboia mauritanica* bite on his right thumb, painful local edema with paresthesia was observed on the fingers and hand.



Figure 3:- Same patient as in Figure 1, double incision fasciotomy of the leg.

- (a) Antero-lateral fasciotomy of the leg and fasciotomy of the dorsum of the foot
 (b) Postero-medial incision of the leg

Conclusion:-

Compartment syndrome secondary to snake bite envenomation is not rare in our context and its management requires high vigilance. Early diagnosis and emergency fasciotomy coupled with administration of antivenom is limb saving.

Conflicts Of Interest:

The authors confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

Ethical Approval:

Approval has been taken from bioscience center.

Consent:

Written informed consent was obtained from the patients for publication of this article and any accompanying images.

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