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Original Research

Ulcerated hemangioma: Clinical characteristics, Microbiology and Response to adjunct antimicrobial therapy in children

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ABSTRACT:

Background: Hemangiomas are considered to be the most common congenital anomalies in the children. Though asymptomatic in most of the children, these vascular lesions can present with ulceration and superimposed bacterial or fungal infection and if left untreated the ulceration can further complicate by hemorrhage, scarring and disfigurement. Although there are various options for the treatment, no single option is found to be universally effective. The study aimed at studying the microbiological profile of the ulcerated hemangiomas and role of adjunct appropriate antibiotics as per the culture-sensitivity report. **Material and methods:** 50 children suffering from ulcerated hemangiomas were included as case group patients. Control group consisted of age matched 50 children from the available existing data. Nature of the lesions and superimposed ulcers were studied in detail. Case group patients underwent inoculation of the swab taken from the ulcerated region. Antibiotics were prescribed according to the culture-sensitivity report in addition to the definite medical management. Clinical response in the form healing of the ulceration and hemangioma was studied by following a strict follow up protocol. **Results:** *Methicillin Resistant Staphylococcus Aureus* (MRSA) was found to be the most common organism in the swab inoculation. *Candida albicans* growth was seen in 4 patients. The mean time of ulcer healing was 11.36±3.66 days in control group as opposed to statistically significant much lesser mean time in the case group i.e. 6.78±2.01 days (p value- 0.000). The hemangioma lesions too responded better when clinical response was studied. There were 24 non-responders in the control group in comparison to 10 children in the case group and good response was seen in three times patients in the case group (p value- 0.002). **Conclusion:** Our study demonstrated the all ulcerated hemangiomas should undergo microbiological profile and the appropriate antibiotics need to be added other than the definite medical management while treating these lesions.

Key words: Ulcerated hemangioma; Microbiological profile; Anti-microbiological agents; Clinical response

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INTRODUCTION:

Hemangiomas are the most common vascular soft tissue tumors during the infancy with a prevalence rate of 5% to 10%. [1] The natural history consists of a phase of initial rapid growth lasting for 3 to 6 months of life which can even extend for 24 months. It follows a period of stabilization of the lesion for the next few months and subsequently spontaneous involution proceeds usually occurring over several years.[2] These lesions can be extremely heterogeneous with size, location and their rate of proliferation. And therefore they carry a significant risk of complications in the form of ulceration and superimposed bacterial and/or fungal infection during the proliferative phase of the hemangioma life cycle. Lesions present at locations of visibility in infants are horrifying and they are really a source of concern to the parents.[3] Ulceration can further complicate in the form of pain, irritability, poor feeding, bleeding, scarring, and deformity of adjacent structures.[4] High risk hemangiomas include facial hemangiomas especially those lesions which are present in proximity to the eyes, lips, tip of the nose.[5]

Common organisms isolated from infected hemangiomas include *S. aureus*, Group A beta hemolytic streptococci *and Enterobacteriaceae* although anaerobic and mixed infections are also seen frequently.[6] Since the natural course is one of spontaneous regression, not all hemangiomas require medical intervention. But certain lesions warrant early and decisive initiation of treatment especially those with secondary ulceration or infection. Previous standard therapeutic options include physical measures (laser surgery, cryosurgery, excision) and systemic corticosteroids or β-blockers, all bearing the risk of serious side effects.[7] Ulcerated hemangiomas are generally treated with topical antibiotics, systemic antibiotics and analgesic for pain along with standard propranolol therapy. The purpose of this study was to review the bacteriological profile and antimicrobial susceptibility of various ulcerated hemangiomas. Appropriate antibiotics were administrated as adjunct to the definite medical management and clinical response was compared to those patients where no antibiotics were given in addition.

MATERIAL AND METHODS:

The study included 50 consecutive children presenting with features suggestive of ulcerated hemangioma in the Pediatric surgery out-patient department in a tertiary care institute. Equal number of age matched children constituted control group from the available existing data. Parents not giving consent for the study or having poor compliance, those already undergoing any form of physical intervention or systemic therapy with antibacterial and/or antifungal agents were excluded from the study. The children underwent detailed demographic analysis and the physical examination. For area calculation, measurements were taken in the largest dimension and in the direction perpendicular to that for both the hemangiomas and the overlying ulcers. Photographic documentation were taken using standard positioning and lighting at each visit. Tablet Propranolol in the dosage of 1mg/dL was started for all the patients on the day of presentation. Ointment Mupirocin was advised for the local application. Paracetamol suspension was prescribed for pain relief as per the requirement. Pus specimens were obtained by swabbing the purulent material from the deeper portions of the lesions after cleaning the surrounding skin with alcohol. Blood, Chocolate, and MacConkey agar plates were inoculated for aerobic organisms. The plates were incubated at 37°C aerobically to be examined later at 24 and 48 hours. For anaerobic bacteria, the material was inoculated on Robertson Cooked Meat broth (RCM) and incubated for seven days. Aerobic and anaerobic bacteria were identified by standard techniques.[6] Anti-microbiological agents were started as per the culture sensitivity report in addition to the definite medical treatment.

The patients were evaluated for time to ulcer healing on follow up visits. Hemangioma lesions were studied for change in their dimension, color and consistency at 7th day and subsequently after 2 weeks, 4 weeks, 8 weeks and 12 weeks. Responses in the lesions were graded as no response (<25% regression), partial response (>25% or 50% regression) and good response (>50% regression). Mere change in color and consistency without change in the dimension of the lesion was considered as a partial response.[8]

RESULTS:

The case group constituted 50 consecutive patients with ulcerated hemangioma. Equal number of children formed the Control where empirical treatment was given without microbiological examination. Both the groups were well matched in terms of age, gender and maturity of the children, duration and size of both the hemangioma lesions as well as the overlying ulcers (Table 1). On analysis of both the groups, male to female ratio was found to be 1:1.7 and the lesion was noted to be more among children born at term (58%). Two children in control group and one patient in case group were diagnosed to have the hemangioma in the third trimester antenatal ultrasonography. Three patients in either group were found to have multiple hemangiomas. Head and neck region was noted to be most affected in both the group as depicted in figure 1. Purulent discharge, pain and fever were the predominant symptoms among all the patients whereas few of the babies presented with bleeding in either group.

Variables		Controls (n-50)	Cases (n-50)	p value
Mean age (Months)		9.23±9.72	9.07±7.01	
Gender	Male	18	19	1.00
	Female	32	31	
Maturity	Term	32	26	0.31
	Preterm	18	24	
Mean age at detection of the lesion (Days)		8.06±2.27	8.02±2.49	0.93
Mean duration of the ulcer (Days)		15.12±7.58	15.02±7.46	0.91
Mean size of the lesion (cm^2)		12.71±4.33	12.57±4.95	0.88
Mean size of the ulcer (cm^2)		7.07±3.24	7.22±3.14	0.82

Table 1: Demographic data

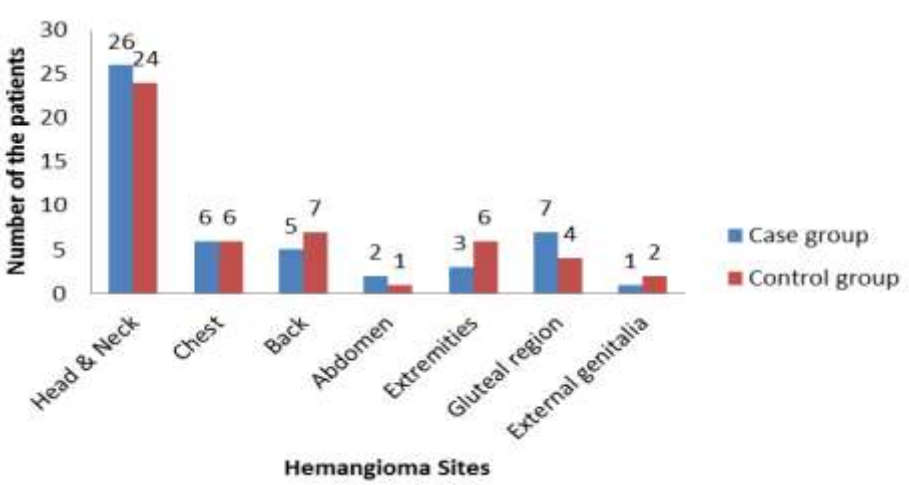

Figure 1: Various sites of the Hemangiomas

The nature of the ulcers was further compared in both the groups and the details are shown in table 2. Most of the ulcers were found to be pale colored and irregular in shape. Mean depth of the ulcers in either group was comparable (Table 2).

Variables		Controls (n-50)	Cases (n-50)	p value
Colour	Pale	32	32	1.00
	Pink	18	18	
Shape	Round	19	24	0.42
	Irregular	31	26	
Granulation tissue	Present	24	25	1.00
	Absent	26	25	
Erythema	Present	9	17	0.11
	Absent	41	33	
Discharge	Present	27	26	1.00
	Absent	23	24	
Temperature	Raised	11	22	0.03
	Normal	39	28	
Tenderness	Present	12	13	1.00
	Absent	38	37	
Consistency	Firm	25	27	0.84
	Soft	25	23	
Regional lymphadenopathy	Present	33	30	0.68
	Absent	17	20	
Mean depth of the ulcer (mm)		3.36±1.34	3.58±1.46	0.43

Table 2: Nature of the ulcers

Pus specimens were analyzed as per the standard protocols and inoculations revealed *Methicillin Resistant Staphylococcus aureus* (MRSA) as the most common organisms (28%) followed by *Methicillin Sensitive Staphylococcus aureus* (MSSA) in 14% of the children. One patient had polymicrobial growth and she grew MRSA and *Klebsiella pneumoniae* in her pus culture. There were four children who showed growth of *Candida albicans* on Blood Agar medium. The culture was sterile in eight children after 48 hours (Figure 2).

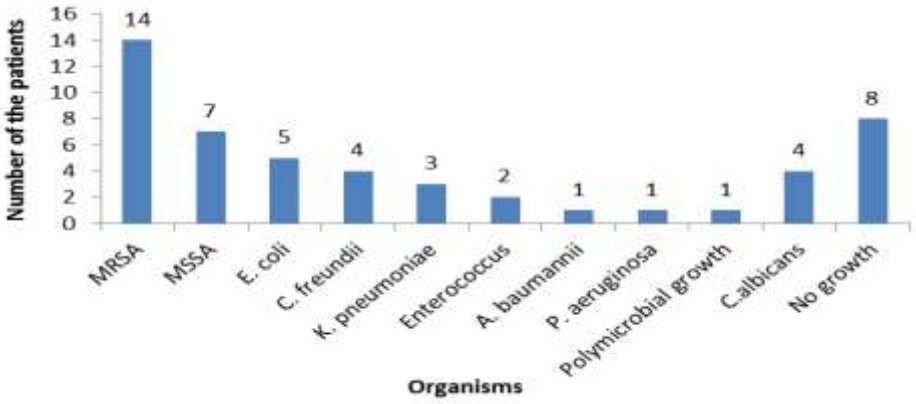

Figure 2: Microbiological profile

Treatment was initiated to all the patients in the out-patient department on very first visit using Tablet propranolol and local application of the ointment Mupirocin in the standard described dosage. Anti-microbiological agents were included further as soon the Microbiological profile and the culture-sensitivity report was received. Oral linezolid was the drug of choice in case culture grew MRSA and *Enterococcus* whereas a combination of oral Amoxycillin and Clavulanic acid was used for MSSA. The other antibiotics used were oral Ciprofloxacin for all Gram negative organisms, Injectable Amikacin in case of *Pseudomonas aeruginosa*. Fungal infection secondary to *Candida albicans* was treated with oral Fluconazole. Children who had sterile growth were not given antibiotics as the adjuncts.

All the children were called upon in the out-patient department and they were subjected to the clinical examination of the ulcer to look for its response to the anti-microbiological agents. The mean time for the ulcer healing was 6.78 days in case group whereas the mean duration in control group was 11.36 days. The response to the adjunct antibiotic in ulcer healing was found to be statistically very significant (p value- 0.000). The hemangiomatous lesion was examined at 7th day and subsequently after 2, 4, 8 and 12 weeks for the change in the colour, size and its consistency. The candidates in case group did well once the ulceration was resolved and started recovering faster as compare to the patients in the control group. After completion of 12 weeks of therapy; non-responders were 24 children in the control group as compare to only 10 patients in the case group. Partial responders were comparable and good response children outnumbered three times in the case group in comparison to control group babies. The detailed analysis has been shown in the table 3.

			Controls (n-50)	Cases(n-50)	p value
Mean time to ulcer healing (Days)			11.36±3.66	6.78±2.01	0.000
Characteristics of the Hemangioma on follow up	At 7 days	NR	50	50	
		PR	0	0	
		GR	0	0	
	At 2 weeks	NR	50	46	
		PR	0	4	
		GR	0	0	
	At 4 weeks	NR	45	28	
		PR	5	22	
		GR	0	0	
	At 8 weeks	NR	42	22	
		PR	8	28	
		GR	0	0	
	At 12 weeks	NR	24	10	
		PR	20	22	0.002
		GR	6	18	

Table 3: Clinical response (NR: No response, PR: Partial response, GR: Good response)

Ulcerated Right Cheek Hemangioma

DISCUSSION:

The definite cause of ulceration in haemangioma is unknown however maceration and frictional trauma are considered to be contributing factors or when the lesion outgrows its blood supply. On analysis, both the case and control group were noted to be well matched with regard to the age, gender, duration of the lesions and overlying ulcerations. The lesion in our study predominated among female patients (1.7 times). The result was similar to previous studies done by Ji y *et*

al, Pandey A *et al* and Wananukul and Chatproedprai.[1,3,9] This might be because of the estrogen hormone which is responsible for endothelial proliferation of the vascular system. In the present study, term babies were found to be more affected than the preterm babies as opposed to study done by Smolinski K N *et al*, where the lesions were more common among babies born before term. [10] Mean age at detection of the hemangioma (8.04 days) was found to be similar as depicted by Kim *et al*.[11] Mean size of the ulcerated lesion was also comparable with the study done by Kim. [11] Head and neck region was found to be the most commonly involved area in our study (50%). Similar results were obtained in the study done by Muneer *et al* (66%) Smolinski K N *et al*.[2,10] Most of the babies presented with purulent discharge (53%), pain (50%) and fever (46%). 16 out of the 100 patients presented with bleeding and history of trauma was revealed in few of these children. Pandey A described that hemorrhage can either occur spontaneously or following a trauma.[3] The ulcers present over the hemangiomas were studied in detail for various parameters i.e. color, shape and inflammatory signs. Mean depth of the ulcers in either group (3.58 mm and 3.36 mm in the case and the control group respectively) was comparable. No study in the searched literature has described the ulceration in such detail.

Most common isolate was found to be *S. aureus* (42%) with MRSA detected in 30% of these patients. This might be because of skin flora penetrating the site of hemangiomas and acting as a source of infection and ulceration. Members of Enterobacteriaceae family were most frequently encountered in perineal region lesions as they are the normal flora residing in rectal and vaginal canal. *C. albicans* isolation was more from the lesions present at the lip area which is a mucosal surface and it is more prone for the fungal infection. Similar growth pattern was observed by Brook *et al* in their study.[6]

A strict follow up protocol was established to know about the clinical response among children in both the groups. The ulcerations showed early resolution when appropriate antibiotics were prescribed for the case group patients. The hemangioma lesions also responded better and this can be related to the better penetration of propranolol in the lesions following recovery of the overlying ulcers. Similar results were found in a study done in California where treatment with systemic antibiotics led to decrease in duration of ulcerations and significant decrease in the pain and irritability.[11]

Our study highlights various demographic variables of the ulcerated hemangioma presenting at various locations. Also the nature of the overlying ulcer and its microbiological profile and culture sensitivity were stressed upon in detail. We found that if appropriate anti-microbiological agents are administered in addition to the definite management, the ulceration as well as the hemangioma recovers significantly faster. This will in turn prevent further complications in the form of bleeding, scarring and deformity of adjacent structures. Therefore, we propose use of appropriate antibiotics in addition to the definite standard medical treatment while dealing with the ulcerated hemangioma.

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