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Jyoti Ranjan Parida

Department of Immunology,
IMS and SUM Hospital, Siksha
"O" Anusandhan University
(Deemed to be), K8, Kalinga
Nagar, Bhubaneswar, Odisha,
India

Aishwarya Joshi

Department of General Medicine,
IMS and SUM Hospital, Siksha
"O" Anusandhan University
(Deemed to be), K8, Kalinga
Nagar, Bhubaneswar, Odisha,
India

Srikant Kumar Dhar

Department of General Medicine,
IMS and SUM Hospital, Siksha
"O" Anusandhan University
(Deemed to be), K8, Kalinga
Nagar, Bhubaneswar, Odisha,
India

Chandan Das

Department of General Medicine,
IMS and SUM Hospital, Siksha
"O" Anusandhan University
(Deemed to be), K8, Kalinga
Nagar, Bhubaneswar, Odisha,
India

Debasmita Tripathy

Department of General Medicine,
IMS and SUM Hospital, Siksha
"O" Anusandhan University
(Deemed to be), K8, Kalinga
Nagar, Bhubaneswar, Odisha,
India

Nalinikanta Sahoo

Department of General Medicine,
IMS and SUM Hospital, Siksha
"O" Anusandhan University
(Deemed to be), K8, Kalinga
Nagar, Bhubaneswar, Odisha,
India

Correspondence

Srikant Kumar Dhar

Department of General Medicine,
IMS and SUM Hospital, Siksha
"O" Anusandhan University
(Deemed to be), K8, Kalinga
Nagar, Bhubaneswar, Odisha,
India

Etiological and histological profile of erythema nodosum in a tertiary care hospital at eastern India

Jyoti Ranjan Parida, Aishwarya Joshi, Srikant Kumar Dhar, Chandan Das, Debasmita Tripathy and Nalinikanta Sahoo

Abstract

Erythema nodosum is a large, violaceous, erythematous, non-ulcerative, subcutaneous nodule with variable tenderness having every possible site of occurrence and are diagnosed clinically. It has been reported in various granulomatous as well as non-granulomatous conditions and the etiology/etiopathogenesis still remains unclear. Our study included 24 patients with erythema Nodosum who were clinically evaluated for signs of infectious, granulomatous, cancerous and inflammatory conditions and subjected to routine work up followed by relevant investigations. Biopsy of the lesion revealed Panniculitis and Perivascular inflammatory deposits. They were followed up until completion of treatment and resolution of EN. 12 cases had tuberculosis, 6 were idiopathic, 2 had CTD, 1 had leprosy, 1 had sarcoidosis, 1 had RA and 1 with oligoarthritis. Treatment with/without NSAIDs and that of the underlying cause effectively settled EN in all cases.

Keywords: Erythema nodosum, tertiary care hospital and Etiological and histological.

Introduction

Erythema nodosum (EN) is commonly considered as a benign and self-constraining hypersensitivity reaction which might be idiopathic or related with benign infections, sarcoidosis, rheumatologic sickness, meds, inflammatory bowel disease, autoimmune disorder, pregnancy and some malignancies [1, 2]. It is the most well-known clinicopathological variation of septal panniculitis typically first apparent as outcropping of erythematous delicate knob found predominantly over the extensor part of the lower extremities. Panniculitis is portrayed by inflammatory modification influencing essentially the subcutaneous adipose tissue which can get granulomatous in the histiocytic stage [3, 4]. The standard clinical introduction of EN is abrupt beginning appearance of symmetrical, tender, erythematous, warm nodules generally situated in the extensor surfaces on the shins, lower leg and knees which are bilaterally disseminated frequently. Ulceration of the knobs is surprising and they recuperate without decay or scarring. It is often preceded by non-specific prodromal symptoms of 1-3 weeks, which may include fever, malaise and symptoms of upper respiratory tract infection. It is usually self-limiting and last for two to six weeks. Diagnosis of EN is mainly based on clinical features, but in doubtful cases biopsy of the lesion may be helpful [5, 6, 7, 8]. Treatment of erythema nodosum should be directed to the underlying associated condition, if identified. Usually, nodules of EN regress spontaneously within a few weeks, and bed rest is often sufficient treatment. Aspirin and non-steroidal anti-inflammatory drugs may be helpful to enhance analgesia and resolution [9] EN is not a very uncommon condition and often it is associated with some underlying secondary condition, which remain undiagnosed if no proper evaluation is done. Even idiopathic erythema nodosum may be over investigated in some cases. The objective of the present study was to identify the underlying cause and associated co morbidities in case of EN and to evaluate the clinical presentation and variations in our patients.

Material and Method

All consecutive cases of erythema nodosum that came to rheumatology OPD still 30 April 2016 were enrolled. Detailed history of past events, family relevance, drug intake were taken. Thorough general and systemic clinical evaluation to look for signs of attributable

disease done. Routine tests in all patients: CBC, UREME, ESR, CRP, USG abdomen and pelvis, CXR. Relevant investigations to individual patients like ANA, ACE, Mantoux, ASO titre, slit skin smear, HRCT thorax. Skin biopsy of all patients from the lesion. Treatment of the underlying cause with or without NSAIDs and NSAIDs alone in patients without an evident disease. Written informed consent was obtained from the patients and the study protocol was approved by Institutional Ethics committee for human research from our institute.

The statistical software SPSS version 20 has been used for the analysis. An alpha level of 5% has been taken, i.e. if any P value is less than 0.05 it has been considered as significant

Results

All cases had EN for the first time. Age of presentation ranged from 15y to 57y. The duration of EN ranged from 1m-24m. Other significant mentions have been made in the table below (Table 1). Total 24 patients of Erythema nodosum were included in our study.

Table 1: Demographic data associated with the EN patients

Features	EN patients		P value
Sex	Male	11	0.410
	Female	13	
Age	Mean age 34.12		0.5
	Fever	75%	0.037
	Arthralgia	79.16%	0.037
	SOB/Cough	20.8%	0.240
	Malaise	54.16%	0.201
Site	LL	70.8%	
	UL+LL+T	12.5%	
	LL+T	8.3%	
	UL	4.1%	
	UL+LL	4.1%	
Size	5mm-5cm	66.6%	
	<5mm	20.8%	
	>5cm	12.5%	

Out of 24 EN patients 11 were male and 13 were female having mean age of both the gender 34.12 year. P value is less than 0.05 it has been considered as significant and the value we got here is 0.5. 75% out of 24 were having symptom of fever, 79.1 Arthralgia, 20.8% people were

revealed about SOB/Cough. 54.16% malaise. The size we found is maximum in between the range of 5mm-5cm i.e. 66.6% followed by the size of <5mm and >5cm, 20.8% and 12.5% respectively.

Table 2: Other clinical finding and diagnosis reports

Parameters	Results	No of patients
Drug intake	Steroid	3
	NSAID	4
	None	17
Other findings	Gangrene distal phalanges	1
	Thickened nerves	1
	B/L pedal edema	1
	None	21
Diagnosis	TB	12
	Idiopathic	6
	CTD	4
	Sarcoidosis	1
	Leprosy	1
	RA	1
	Oligoarthritis	1
HRCT THORAX	Parenchymal changes with mediastinal and hilar lymphadenopathy.	6
	Tubercular	4
	Sarcoid	1
	Idiopathic	1
Skin Biopsy	S/O EN	23
	S/O ENN	1

In table 2, we got other some clinical findings that revealed the basic cause/precipitating factor of EN in Eastern India is Tuberculosis followed by idiopathic variety. Out 24 patients drug was in taken by 7 patients (3 steroids, 3 NSAIDs). Similarly some others finding was like Gangrene distal phalanges in one patient, Thickened nerves having in

1 patient, B/L pedal edema in 1. Interestingly we got 50% patients were diagnosed with TB positive, Idiopathic 6 and CTD 4. Beside that we also found one sarcoidosis, one Leprosy, one RA and one Oligoarthritis patients out of 24 patients. HRCT THORAX revealed 6 patients having parenchymal changes with mediastinal and hilar

lymphadenopathy. Tubercular 4 patient and 1 from each confirm the sarcoid and idiopathic.

Discussion

In our study, total 24 cases of clinically diagnosed EN were evaluated and a detailed comparison was done on the basis of clinical and laboratory parameters our main objectives were to identify the etiology of EN, to find out the associated clinical profiling of these 24 patients

In our study, we have found male to female ratio of 1:1 almost. The mean age of the patients was 34.12 years This is in accordance with the previous studies which demonstrated that EN the sex ratio is approximately equal before the pubertal age group^[10]. It has been reported that EN occurs between the second and fourth decades of life, with the peak incidence between 20 and 30 years of age, probably because of the high incidence of sarcoidosis at this age^[6, 7, 11]. The diagnosis of EN can usually be made clinically, with no need for histopathological examination for the diagnosis.

Erythema nodosum has been associated with a variety of infectious diseases, most notably tuberculosis, streptococcal infections, *Yersinia enterocolitica*, *Y. pseudotuberculosis*, cat-scratch disease, tularemia, acute upper respiratory tract infections, Q fever, and epidemiologic internal organ mycoses (histoplasmosis, coccidioidomycosis etc).^[12, 13, 14, 15, 16] Chronic inflammatory conditions includes Behcet's disease, Reiter disease, systemic lupus erythematosus, inflammatory bowel disease, and sarcoidosis, malignant diseases, and exposure to certain medications can be involved in the etiology of EN^[17, 18, 19, 20, 21, 22]. Streptococcal infection was reported as the most common cause of EN in the pediatric as well as adult population^[12]. In our study group we have found parenchymal changes with mediastinal and hilar lymphadenopathy and tubercular as the most common cause EN (10 patient).

The most common etiologic factors in our study were tuberculosis. It has been reported that EN can be the first and only presentation of tuberculosis in a patient with/without evidence of active disease^[23]. Tuberculosis should be investigated and excluded, especially in endemic areas, as an underlying etiology of EN. EN, in Anna Nagar, Chennai. And found 7 cases were of tubercular, which indicates that tuberculosis is a common cause of EN in our country where there is high prevalence of tuberculosis^[24]. In our case we got maximum 12 patient out of 24 were TB positive patients.

Erythema nodosum is associated with sarcoidosis in 10 to 35% of cases^[8, 11]. Psychos DN *et al.* in one prospective study in Greece found that out of 132 cases of erythema nodosum 28% was associated with sarcoidosis^[25]. Mert A *et al* had evaluated 100 cases of EN in Istanbul where they had found 10% of cases were associated with sarcoidosis^[26]. There is variation according to geographical distribution. We have found less (1 patients) may be as because it has reported that sarcoidosis is less in prevalence in South East Asian countries. In our study, we found significantly increased occurrence of features like history of sore throat, Arthralgia, fever, weeks, arthritis, cough, Malaise. Some studies state Tuberculosis the leading cause worldwide while others consider it Idiopathic. The pathogenesis is believed to be due to deposition of immune complex in the venules of subcutaneous fat, production of

oxygen free radicals, TNF-alpha and granuloma formation in response to endogenous antigens leading to type IV hypersensitivity reaction. However, vasculitis is clearly evident to be a component in addition to septal panniculitis in EN. Numerous bacteria, viruses, parasites, fungi, malignancies, drugs and even pregnancy have been probable precipitating entities as we discussed before.

Conclusion

The leading cause/precipitating factor of EN in Eastern India is tuberculosis followed by idiopathic variety. Nonspecific arthralgia is a very frequent association even in the absence of inflammatory arthritis. In addition to septal panniculitis, vasculitis is frequently seen our patients with EN. Erythema nodosum rarely involves the face. Mantoux test might be considered in the initial investigation algorithm in patients presenting with EN. So all patients of erythema nodosum need detailed evaluation to find out any underlying systemic disease. Further Indian studies may be needed on this topic to find out etiological factors & predictors EN.

Conflict of interest: Nil

Fund for the study: Nil

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