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Inflammatory myopathies in Nigerians: case series and literature review

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Abstract

Background: Idiopathic Inflammatory myopathies(IIM) are rare connective tissue diseases and have been rarely reported among Nigerians.
Objective : To study the clinical, laboratory and electromyographic characteristics of Nigerian patients with polymyositis and dermatomyositis.
Method: In a retrospective study, patients attending a private practice rheumatology clinic in Lagos and fulfilling the Bohan and Peter's criteria for polymyositis and dermatomyositis were examined and common causes of proximal muscle weakness were excluded. Haematological, biochemical, serological and electromyographic studies were carried out. Patients were treated with standard drugs.
Results: Fourteen patients(F-13, M-1) were diagnosed with Polymyositis(PM) and Dermatomyositis(DM). Seven had probable PM, 4 with possible PM and 3 with probable DM. Mean age was 35 years (range 22-54) ESR was markedly raised mean 105/min(26-150) .Muscle and liver enzymes were raised in all patients. Creatinine kinase median 1134(29-10,166); lactic dehydrogenase median 477(209-787); ALT 43(19-233); AST 136(25-725). Serology for ANF was positive in eight patients; Anti Jo1 in 1 out of 9 while Anti Mi2 was negative in all tested.EMG in 6 tested showed myopathic pattern.
Conclusion: Inflammatory myopathies are rare among Nigerians but a heightened awareness is needed for diagnosis and management.

Keywords- *Idiopathic Inflammatory myopathies, Nigerians clinical, laboratory features*

Résumé

Contexte: Les myopathies inflammatoires idiopathiques (IIM) sont des maladies des tissus conjonctifs rares et ont été rarement signalés chez les Nigérians.
Objectif: Etudier les caractéristiques cliniques, biologiques et électromyographiques des patients nigérians atteints de la polymyosite et de la dermatomyosite.
Méthode: Dans une étude rétrospective, les patients faisant l'objet d'une pratique clinique de rhumatologie privée à Lagos et à l'accomplissement de la Bohan et les critères de Peter pour la polymyosite et la dermatomyosite ont été examinés et les causes communes de la faiblesse des muscles proximaux ont été exclues. Les études hématologiques, biochimiques, sérologiques et électromyographiques ont été réalisées. Les patients ont été traités avec des médicaments standards.
Résultats: Quatorze patients atteints de polymyosite (PM) et la dermatomyosite (DM) (F-13, M-1) ont été diagnostiqués. Sept PM sont probables, possible avec 4 PM et 3 DM.
L'âge moyen était de 35 ans (extrêmes: 22-54). L'ESR a été nettement relevé signifie 105/min (26-150). Des muscles et des enzymes hépatiques ont été augmentés de volume chez tous les patients. La créatinine kinase médiane 1134 (29-10,166); le médiane déshydrogénase lactique 477 (209-787), ALT 43 (19-233); AST 136 (25-725). La s,k,kkérologie pour ANF a été positive chez huit patients; Jo1 Anti dans 1 cas sur 9, tandis que Anti Mi2 était négatif dans tous les cas après leur analyse. Six (6) EMG testés ont montré des traits myopathiques.
Conclusion: Les myopathies inflammatoires sont rares chez les Nigérians mais une prise de conscience est nécessaire pour le diagnostic et la gestion.

Introduction

Idiopathic Inflammatory Myopathies/Myositis (IIM), a connective tissue disease, consist of a group of chronic, immune mediated muscle diseases characterized by muscle inflammation, progressive muscle weakness and decreased muscle endurance [1]. Three main subsets of myopathies have been identified based on their clinical and histopathological features. These are namely, Polymyositis (PM), Dermatomyositis (DM) and Inclusion body myositis (IBM). Their diagnoses and classification are based on the Bohan and Peter's diagnostic criteria [2]. These criteria consist of- 1] proximal muscle weakness. 2] positive muscle biopsy 3] elevated muscle enzymes and liver enzymes (CK, AST, ALT, LDH, aldolase). 4] myopathic pattern on electromyogram (EMG). 5] characteristic skin rashes in dermatomyositis. Polymyositis and

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dermatomyositis are the most commonly reported types of myopathies [3,4] IIM are rare, with a prevalence rate of 1-6/ 100,000/year and an incidence of 0.1-1/100,000/year in the general population [1]. Even then, there have been suggestions that IIM is probably overdiagnosed [5]. Inflammatory myopathies affect women more frequently than men, with a ratio of 2: 1. Peak incidence exhibits a bimodal pattern of disease with peaks at 5-15 years and 45-65 years of age [6]. IIM, however, tend to occur at a younger age among African Americans. PM and DM occur more frequently in African Americans than Caucasians with a ratio of 5:1 and 3:1 respectively. The five year mortality rate is 20% [6].

The onset of inflammatory myopathies is usually heralded by difficulties with such routine tasks as stair climbing, getting up from lying or sitting position, combing the hair, brushing the teeth, as well as other tasks that require the use of proximal skeletal muscle groups. Other muscle involvement may lead to difficulty in chewing, swallowing and even breathing. There may also be such joint manifestation as polyarthritis or polyarthralgia. Smooth muscle involvement may result in myocardial infarction and cardiomyopathy. Also, skin involvement in patients with dermatomyositis could be characterized by intense skin itching and photosensitivity.

The pathogenic mechanism is poorly understood and various mechanisms have been suggested such as genetic, as well as environmental factors such as infections with viruses like coxsackie, influenza, echo, HTLV – 1. There are also suggestions of auto – immunity, with consequent abnormalities of cellular, and humoral systems.

Inflammatory myopathies have been rarely reported among black Africans, including Nigerians. One of the earliest reports was from Nigeria, a three case report in 1960 by Barnard *et al* [7]. There have also been other case reports from South Africa [8,9] and case series from Tunisia [10] and Senegal [11]. There are, however, no recent case series report from Nigeria.

The objective of this study was to highlight the clinical, biochemical, serologic and electromyographic characteristics of inflammatory myopathies among Nigerian patients, as well as to review relevant literature and discuss the management.

Materials and methods

This was a retrospective study of all patients fulfilling the Bohan and Peter criteria for IIM Table 1 attending Arthrimed Specialist Clinic, a private practice rheumatology clinic located in Ikeja, Lagos .History was taken to exclude statin and corticosteroid usage as well as thyroid disease, these being common causes of myositis or myalgia. Patients had complete physical examination with particular reference to the musculoskeletal and central nervous systems. Blood samples were taken and sent to laboratories for heamatological, biochemical and serology tests. Blood was also taken for HIV serology to exclude common infective cause of polymyositis. Electromyographic studies were requested for patients who could afford it. Classification of the inflammatory myopathies was based on modified Bohan and Peter by Vincze *et al* [1] as follows:- **Polymyositis**- *Definitive*- presence of 4 criteria; *Probable*-presence of 3 criteria; *Possible*- presence of 2 criteria. **Dermatomyositis**: *Definitive*-presence of 3 criteria(+skin rashes); *Probable*-presence of 2 criteria(+skin rashes); *Possible*- presence of 1 criterion(+skin rashes). Patients were treated appropriately with corticosteroids and immune suppressive drugs.

Results

A total of 14 patients with IIM were seen in the clinic between the period January 2001 to April 2012. This represented 0.5% out of the total number of 2882 new rheumatology patients seen during this same period. There were 13 females and one male patient. The demographic characteristics of the patients are as in Table 1. Physical examination showed Grade 2-4 muscle power of the proximal muscles, normal distal muscle power and normal reflexes in all the patients. Other systems were essentially normal.

Table 1: The demographic characteristics of 14 IIM patients

Age (years)	Range 22 – 54 Mean 35
Sex	Female – 13 Male – 1
Duration of Symptoms (months)	0.5 – 78 mean - 4

Using the Vincze criteria, seven patients (53.9%) were classified as 'Probable' polymyositis while 4 patients (30.7%) were classified as 'Possible', Three patients(15.4%) had probable dermatomyositis.

The characteristic erythematous skin rashes of dermatomyositis and the diagnostic Gottron's lesions in one of the patients with dermatomyositis are as shown in Figures 1-3.

The erythrocyte sedimentation rate (ESR) was elevated in eleven patients with range of 26 – 150 mm/hr and a mean of 105 mm/hr. The mean of the haematocrit was 36.3% with range of 31-40%. White cell count had a mean of 7,077 per cu mm(range

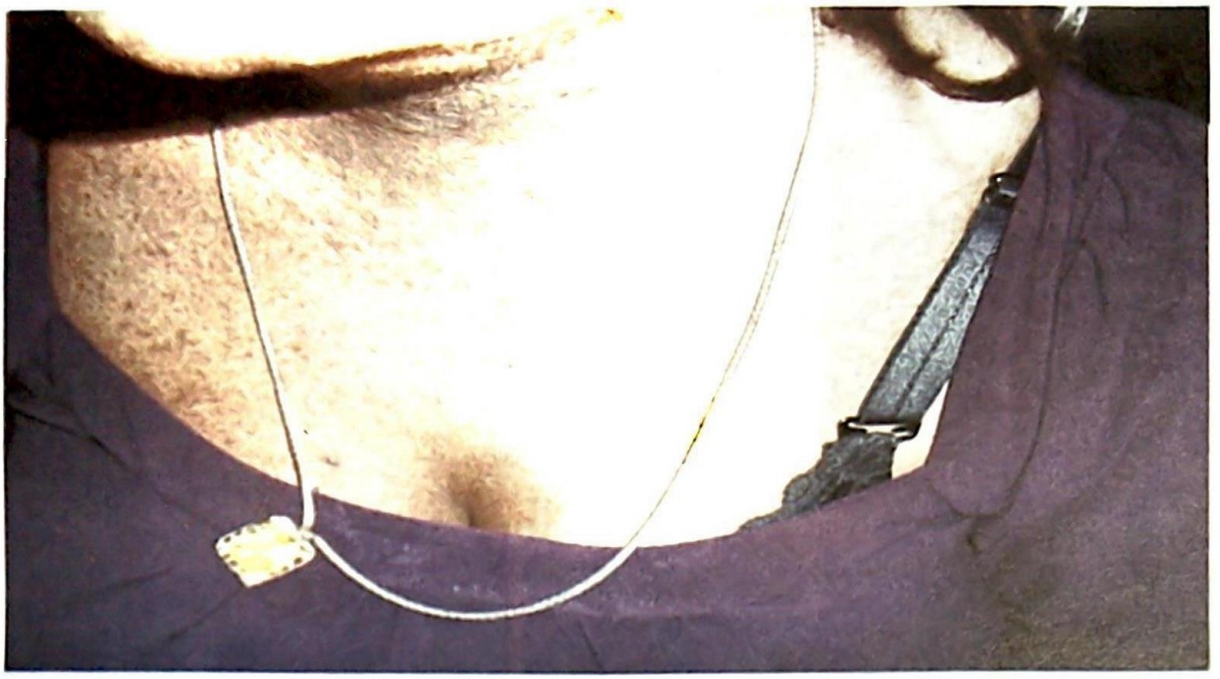

Fig 1: Showing the erythematous skin rashes in a patient with Dermatomyositis

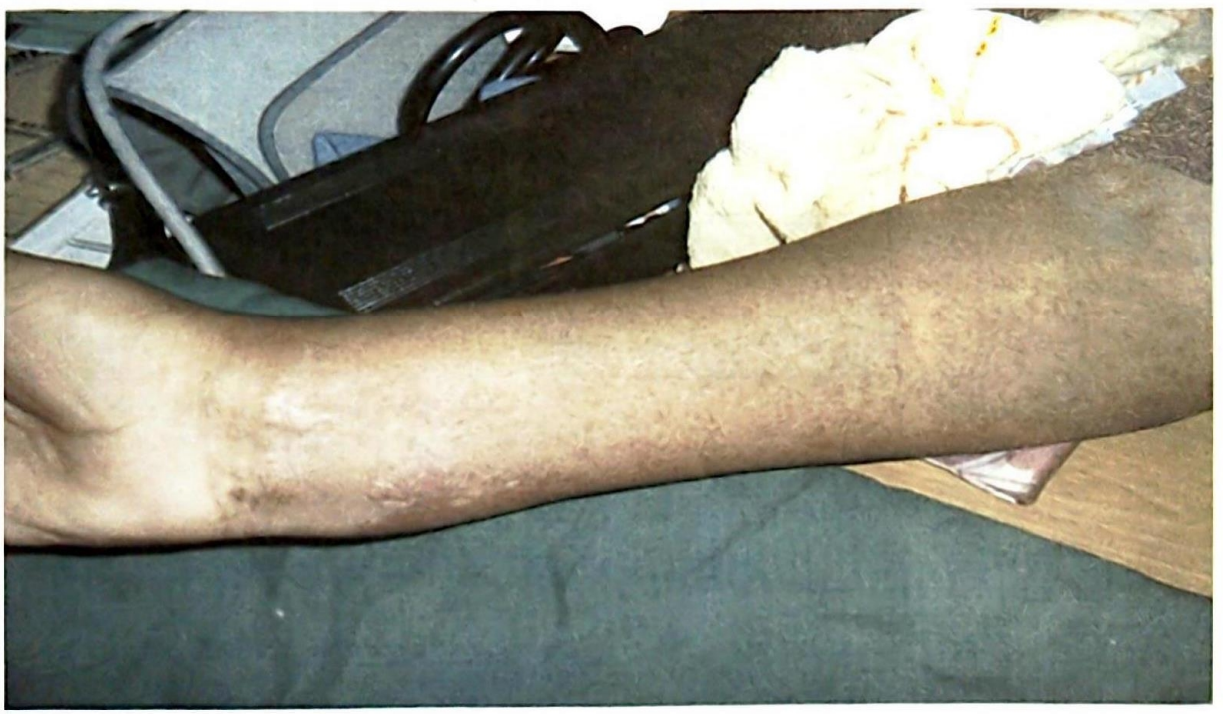

Fig 2: Showing erythematous skin rashes on the fore-arm of a patient with dermatomyositis

4,000 to 16,700) and normal differential count. Chest radiographs were available in 7 patients and were all reported as normal. ECG showed sinus arrhythmia and left axis deviation in 2 patients out of the 8 that had the investigation. The other 6 were reported as normal.

Muscle/ liver enzymes

The result of the muscle and liver enzymes are as shown in Table 2. These were markedly raised in most of the patients especially, the creatinine kinase and lactic dehydrogenase.

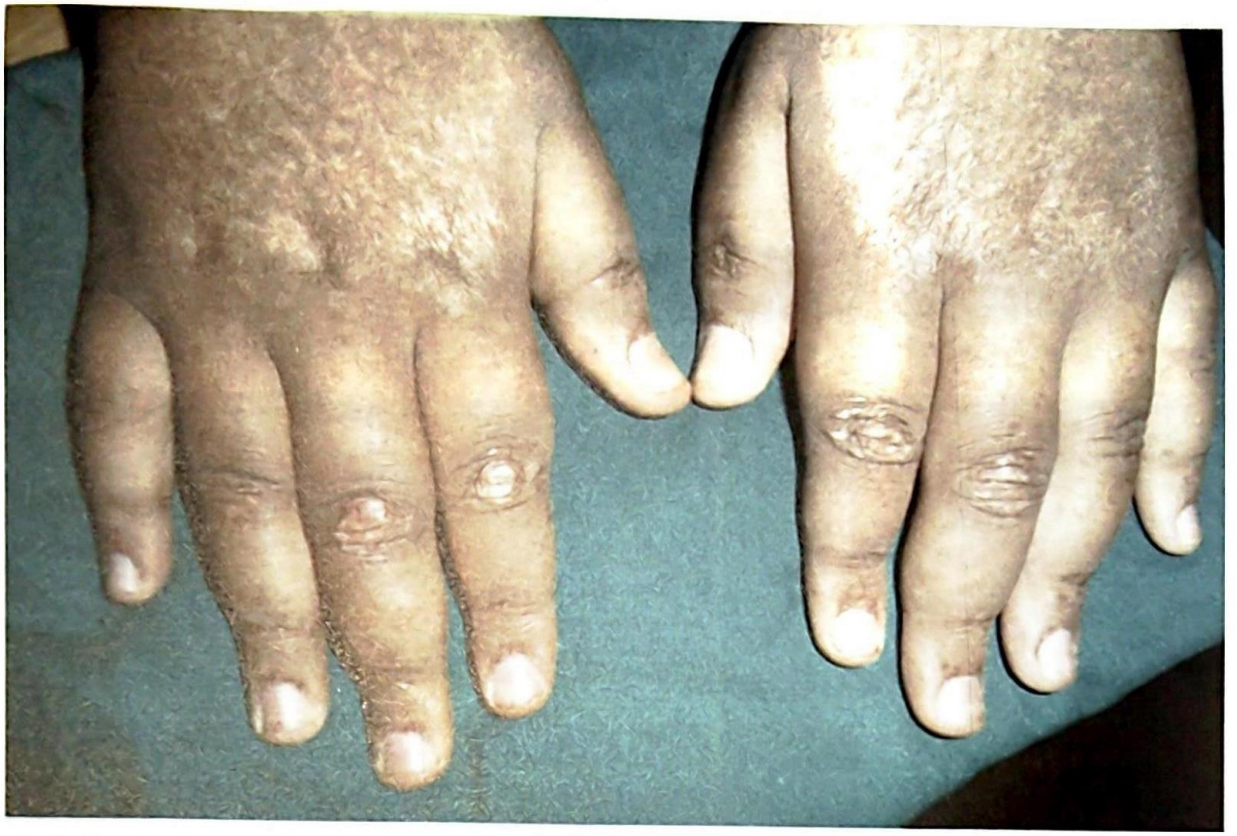

Fig 3: Showing Gottron's lesions on the proximal interphalangeal joints of a patient with DM

Table 2: Muscle and Liver enzymes in patients with IIM

Enzymes	Range (Median)	Laboratory reference range
Creatinine kinase	297 – 10,166 (1134)	15 - 170
Lactic dehydrogenase	209 – 787 (477)	117 – 258
ALT	19 – 233 (43)	10 – 40
AST	25 – 725 (136)	10 – 40

Serology

Ten patients had serology for anti nuclear antibody, of which 8 were positive, all with a speckled staining pattern. Anti Jol was carried out in 9 patients of which only one was positive in a female. Serology for Anti Mi2 was done in 9 patients with all being negative. HIV serology was negative in all the eleven cases tested.

Electromyogram

Six patients had EMG. They all showed the characteristic changes of short duration small amplitude, polyphasic motor units fibrillation and positive sharp waves.

Muscle Biopsy

Only one patient had muscle biopsy whose histology was reported as 'necrotic myofibres, regenerating muscle fibres, atrophic muscle cells, and evidence of inflammatory exudates'.

Treatment

All the patients had initial three day course of pulse methylprednisolone at presentation. This was followed with prednisolone at 1-2 mg/kg body weight in divided doses and Azathioprine 2-3mg/kg body weight. Two patients who did not respond to Azathioprine were placed instead on methotrexate tablets – 12.5 mg – 20mg weekly, as well as folic acid supplements.

Discussion

The fourteen patients here reported among 2882 patients seen in a private practice rheumatology facility indicate that inflammatory myopathies are rare as reported elsewhere. The younger age, mean of 35 years, at presentation is similar to the pattern among Africans American subjects .This is in contrast to the older age among Caucasians. The mean age of 52 years among the Senegalese patients also contrasts with the younger age in our report. There is a marked female preponderance among our patients (F – 13, M -1). This is in sharp contrast to

the ratio of 2.5:1(F:M) reported in other studies. The reason for this difference is not clear. It is instructive to note that of the three cases reported by Barnard, two of the subjects were female and one was male.

In an eighteen year multicentre retrospective study among Tunisians, 20 cases of polymyositis and 50 cases of dermatomyositis were identified showing a predominance of dermatomyositis [10]. The predominance of dermatomyositis is also seen in the report from Senegal with dermatomyositis ratio DM 15;PM 6. The preponderance of dermatomyositis seen in the Senegalese and Tunisian series is in contrast with predominance of polymyositis among our patients (DM 3 PM 11). It has been suggested that the ratio between PM and DM correlates with the intensity of the ultraviolet light radiation. It has been hypothesized that among Europeans the relative prevalence of DM and PM exhibits a latitudinal gradient and as such DM is more frequent closer to the equator [12]. The cause of this gradient is not definitely known but has been attributed to environmental and genetic factors [13]. Nigeria is nearer the equator than Tunisia and one would have expected the contrary in terms of higher frequency of DM.

Recent reports from South Africa have shown an association of PM with HIV [14]. However, eleven of our patients who were tested for HIV were negative. It is possible that this association among South Africans may be a reflection of the high prevalence of HIV/AIDs in the South African population.

Muscle enzymes are important in the diagnosis of both PM and DM. The patients in our study had very high levels of creatinine kinase, lactic dehydrogenase and AST. Studies have shown marked elevation of these enzymes in at least 90% of patients with inflammatory myopathies. Creatinine kinase is the most sensitive [15]. Serum aldolase which is usually elevated in IIM even in the presence of normal CK was however not available during this study.

Acute phase proteins such as ESR and CRP are recognized as markers of inflammation in auto-immune diseases. Only ESR was however done as this was more readily available and affordable. All the patients had elevated ESR with range of 26 – 150 and a mean of 105mm/hr. Though the ESR may be elevated in other conditions, its elevation in patients with proximal muscle weakness may be a pointer to the diagnosis of IIM. This is probably more relevant in the setting of Nigeria where serology, EMG and muscle biopsy are not readily available or affordable.

Myositis associated antibodies (MAA) are frequently detected in myopathies, especially Anti – Ro/SSA and La/SSB. Nonsynthetase Myositis specific antibodies (MSA) such as Mi2, on the other hand, are associated with unique clinical phenotype; these auto-antibodies being mostly detected in patients with immune mediated myopathy and anti synthetase syndrome. Eight auto-antibodies against different synthetases have been isolated, though most of them are still experimental. Anti Jo1,an antisynthetase myositis specific autoantibodies (MSA), is the most common, being present in 11 – 33 % of patients with PM or DM. Anti Jo 1 has been associated with the anti synthetase syndrome of erosive arthritis, Raynaud's phenomenon, fever and interstitial lung disease [16-18]. Of the nine patients in our study that had serology for anti Jol, only one was positive. None of the patients, however, showed the aforementioned features of the anti-synthetase syndrome. Mi 2 is mostly seen in dermatomyositis with skin rashes and usually indicates good prognostic and therapeutic outcomes. None of the nine patients tested in our study showed positive anti Mi2. Anti-nuclear antibody is a marker of systemic auto-immune diseases and is mostly seen in SLE patients but is seen in inflammatory myopathies and other connective tissue diseases. In our study six out of the 10 tested were positive for this autoantibody. Studies have shown presence of this auto- antibody in about 80% of patients with PM and DM [19].

Treatment of our patients was with corticosteroids, in addition to azathioprine or methotrexate. An open label study in 16 patients with IIM have previously shown that combination of corticosteroids and azathioprine had better long term outcome after 3 years than with corticosteroids alone [20]. All our patients did well on this regimen with improvement in muscle power and exercised tolerance. Follow up was however irregular for most of the patients. Various immune suppressives have been used in these conditions especially with the eventual strategy of steroid sparing. These include cyclophosphamide [21] cyclosporine [22], chlorambucil [23]. Biological agents have also recently been used in the management of inflammatory myopathies. However results with anti tumour necrosis factor agents such as infliximab have been disappointing. On the contrary, there are encouraging results from the use of rituximab in open label studies [24-26]. Intravenous immunoglobulins have also been found efficacious in the treatment of IIM [27,28].

The small numbers of patients seen in our study may be a reflection of the rarity of IIM. There is also the possibility that many more patients are seen by other specialists, especially neurologists,

dermatologists and orthopaedic surgeons. Although muscle biopsy is diagnostic for IIM, our patients objected to such intervention. Only one patient consented to open muscle biopsy. Most of the reported cases, including the Tunisian and Senegalese also did not have muscle biopsies. The cost of EMG in Nigeria(about 300 dollars) and its relative non-availability makes this diagnostic investigation unattractive to our patients. Serologic markers are also expensive for most of our patients. Such auto antibodies are not available in the Nigeria and sera are invariably sent to South Africa, with the attendant high cost and delay. Muscle and liver enzymes are however readily available and most of our patients had such. Although serologic markers are not included in the Bohan and Peter criteria, recent workers have proposed its inclusion for DM and PM [29,30]. This however is yet to be universally accepted.

Inflammatory myopathies especially polymyositis, though rare, is seen in Nigerians. Awareness of this condition is important, especially using the clinical presentation and muscle enzymes are important in order to make an early diagnosis and institute appropriate treatment.

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