Review Article

Pararamosis: Disease of the Rubber Plantations

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Abstract. Pararamosis is a medical condition, described in the latex extracting areas of the Amazon (rubber tree regions), resulting from contact with the caterpillar of the *Premolis semirufa* moth. The disease can present itself in an acute form—similarly to other erucisms (injuries caused by moth larvae in humans)—or in a chronic form, typically characterized by the occurrence of changes in the joints of the hands. Because of its importance, in the context of tropical diseases, the objective of this article was to review the main facets of the disease, emphasizing the different pathogenic aspects of the interaction between the arthropod and man.

INTRODUCTION

Pararama is the popular name given to the caterpillar form of an insect native to the Amazon region, the moth known as *Premolis semirufa*. Repetitive contact with the insect's bristles in its caterpillar or cocoon form can cause a disease known as pararamosis, "disease of the rubber plantations" ("doença dos seringais"), "disease of the rubber trees" ("doença das seringueiras") or "rheumatism of the rubber tappers" ("reumatismo dos seringueiros"). Although some authors refer to the disease as pararama, this term is preferred to describe the animal, using the word pararamosis to name the illness (such standard will be adopted in this article). It is a particular class of erucism—nomenclature used to describe caterpillar accidents^{1,2}—that initially causes symptoms such as pain, itching, burning sensations, and erythema, and can, with repetitive contact, cause interphalangeal morphological changes due to the thickening of the synovial membrane of affected joints.^{3–7}

The disease, which manifests properties of a chronic inflammatory reaction, is characterized as an occupational disease because of its intimate relation to the labor activities of rubber tappers, explaining its greater prevalence in areas with bountiful rubber trees, such as the Amazon rain forest, especially in the state of Pará.^{4,7–9}

In this article, the main aspects of pararamosis, its etiology, and pathogenesis, as well as its clinical, therapeutic, and prophylactic aspects, will be addressed, aiming to contribute information for a better comprehension regarding the disease and for the appropriate planning of healthcare actions.

ETIOLOGY

Pararamosis is caused by the contact with the *P. semirufa* caterpillar, commonly called "pararama" or "pararama caterpillar," pertaining to the Erebidae family and Arctiinae subfamily. The arthropod (Table 1) has been described in Brazil, but it can also be found in Ecuador, French Guiana, Panama, and Peru.^{7,10–12}

Biological cycle and morphological aspects. *Premolis semirufa*, similar to other members of the Lepidoptera order,

has a biological cycle composed of four stages: egg, caterpillar, cocoon, and adult (Figure 1). The caterpillar of this species measures approximately two to three centimeters in length, whereas the adult specimen reaches two centimeters in length and has a wingspan of around 2–5 cm.^{7,11}

In its caterpillar phase, the insect is diurnal and feeds on the leaves of *Hevea* spp., rubber tree native to Brazil, partially characterizing the insect's niche. Its body is covered in numerous bristles of various sizes composed of chitinous material, divided in small, medium, and large bristles.^{7,11,13,14} According to Dias and Azevedo,⁶ the larger bristles measure approximately 2–3 cm and emerge from small protuberances on the lateral surfaces of the caterpillar's abdominal and thoracic segments. The medium-sized bristles, in turn, measure up to 1 cm and are found in two pairs of tufts on the dorsal surface of the first and seventh abdominal segments. The smaller bristles, that measure from 1.5 mm to 2 mm, are located on the dorsal face of the second to eight body segments as pairs of tufts.⁶ The exact composition of the substances found in the interior of the glands attached to the bristles is still not known, let alone their molecular mechanisms when interacting with the human organism.^{7,15}

In experiments with mice, it has been proven that it is the smaller bristles that cause acute and/or chronic inflammatory reactions when they come into contact with the human skin. Furthermore, bristles of all sizes are found surrounding *P. semirufa*'s cocoon, except on its flat side, where the arthropod attaches itself to surfaces in this stage. This cocoon has a brownish-gray color and is the shape of a spindle, and its small bristles are arranged perpendicularly, which gives it a velvety appearance.⁶

ECO-EPIDEMIOLOGY

Bergillos and Rivas, in a work published in 2013, estimated the occurrence of approximately 60 annual cases of pararamosis.¹⁶

TABLE 1
Taxonomic classification of the *P. semirufa*

Kingdom	Metazoa
Phylum	Arthropoda
Class	Insecta
Order	Lepidoptera
Family	Erebidae
Genus	<i>Premolis</i>
Species	<i>Premolis semirufa</i>

Source: U.S. National Library of Medicine-NCBI Taxonomy. Available at: <https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id=695210>.

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FIGURE 1. Adult (above) and caterpillar (below) forms of *Premolis semirufa*. Photograph by Rafael Marques Porto (Instituto Butantan). Image kindly provided by the author. This figure appears in color at www.ajtmh.org.

Currently, the cases of pararamosis concentrate, primarily, in areas within the Brazilian Amazon region plentiful with rubber tree plantations, most prevalent in the state of Pará.^{7,11,12} Because of its relation to laboral activities, the most affected population is that of the rubber tappers who are injured during sap collection, representing more than 90% of cases. The initial symptoms are restricted to dermatological manifestations, including itching and burning sensations. Consequently, the affected population tends not to resort to professional help, which increases the number of underreported cases. Contact with the caterpillar yields manifestations that occur unilaterally or bilaterally in the patients' hands, with the right hand being the most commonly affected, with the third interphalangeal joint of the middle finger usually being the most compromised. This is due to the fact that the rubber tappers generally use their fingers to facilitate sap collection of the *Hevea* spp., which puts them at risk of coming into contact with the bristles of *P. semirufa*, especially when they do not use protective equipment, such as gloves, correctly.^{10–12,17}

In addition, studies highlight a correlation between the number of incidents involving pararamosis and the months in which latex extraction is most significant in Brazil. The occurrence of accidents was observed during all months

throughout the year, and a decrease was noticed during the months of November, December, and January, corresponding to a period of less extraction.^{9,10}

PATHOGENESIS: ACTION OF THE BRISTLES

Human contact with the smaller bristles of the *P. semirufa* caterpillar initiates the pathophysiological process of pararamosis, and its evolution varies with the local immune/inflammatory response. After the initial contact, the release of mediators, such as histamine and serotonin, occurs, which, associated with substances contained within the glands attached to the hollow bristles, increases vascular permeability.^{9,13}

Furthermore, it was observed that the toxins within the bristles presented elevated hyaluronidase activity, degrading hyaluronic acid—an abundant component of the intercellular matrix of the skin, cartilage, and synovial fluid—that serves to stabilize and lubricate the joints. The toxins also have gelatinolytic activity, due to the metalloproteases and serum proteases that can degrade collagen types IV, V, VII, and XI, found in the bone and in the cartilaginous joints, regulating their remodeling.¹¹

In addition, the toxic products synthesized by *P. semirufa* have proteolytic activity with the potential to activate the complement system of the human organism and trigger the hydrolysis of C3, C4, and C5, generating biologically active components, such as anaphylatoxins.^{7,12,18} Although the complement system is especially linked to the innate immune response, its excessive activation, resulting in the production of anaphylatoxins, can cause an important inflammatory disorder that occurs in humans after poisoning, which manifests itself in the lesion and in tissue degradation.⁷ In cases of accidents with pararamosis, the toxins decrease the action of the alternative and lecithin pathways of the complement system, due to the excessive activation of these pathways and/or the continuous consumption of the complement. It should be noted that in a study carried out with mice, a fraction containing serine protease was identified: Ps82, an enzyme that is involved in the proteolytic activity of the bristles and that has the ability to decrease the activity of the complement system's three pathways through consumption and/or induction of its high activity.⁷ In addition, it has the ability to induce the production of C3 and C4 and directly cleave C3, C4, and C5 to form anaphylatoxins.^{7,18} Thus, it is to be expected that the further identification and characterization of Ps82 may contribute to the development of future therapies for the prevention and specific treatment of pararamosis, which are still nonexistent.

In addition to the changes described, these substances induce differentiation and proliferation, especially of B lymphocytes, which, in turn, secrete IgG antibodies, especially those of the IgG1 subclass, indicating a predominance in the activation of the Th2 pattern, because this antibody subclass is mainly induced by cytokines with this immune response pattern, such as interleukin (IL) IL-4, IL-5, IL-10, and IL-13.¹¹ They also induce the activation of TCD4 and TCD8 lymphocytes by stimulating the expression of CD80 and CD86, the activation of antigen presenting cells, and the formation of memory B cells, promoted by the increased expression of the CD40 co-stimulator, characterizing the chronic nature of pararamosis.^{7,11,12}

The substances previously described are also responsible for activating the Th1 and Th17 immune responses, which

produce cytokines that act during and after inflammation, such as IL-1, IL-2, IL-4, IL-6, IL-10, IL-12, tumor necrosis factor alpha, interferon gamma, IL-23, and, mainly, IL-17, important cytokine involved in the development of rheumatoid arthritis (RA).^{7,11,12} The expression of the IL-17 receptor is also induced in several different cells, which causes the recruitment of neutrophils and other myeloid cells, contributing to the disease's profile.

The chronicity of pararamosis, responsible for the articular clinical manifestations, results from the infiltration of smaller bristles into the victim's tissues, mainly in the tendons, periosteum, perichondrium, and synovial bursa of the hands, along with the body's inability to absorb and eliminate these bristles, which causes an infiltration of neutrophils and macrophages accompanied by edema and/or the action of protein secretions from the glands attached to the bristles.^{10,15} Because of the continuous presence of the bristles in the victim's tissue, the acute inflammatory processes are replaced by a chronic granulomatous response, and, in this context, granulomas and giant cells are usually found to be accompanied by a varying proliferation of fibrosis of the peripheral connective tissue and of the periosteum sheaths involving the bristles.^{10,15,17}

NATURAL HISTORY AND CLINICAL FINDINGS

Acute alterations. Initially, contact of the patient's skin with the bristles of the *P. semirufa* caterpillar causes intense itching at the site and, in some cases, a burning sensation accompanied by signs of an acute inflammatory process, such as edema, erythema, pain, and heat of the affected area, which can persist for approximately 3–7 days after the first accident.^{7,10–12}

Chronic alterations. In situations of repeated exposure over time, the development of mono or oligoarticular synovitis can be observed, which occurs because of the thickening of the synovial membrane accompanied by the deformity of interphalangeal joints, consequence of the persistence, and progression of the initial edema, similar to the findings in RA.^{7,12} Periarticular fibrosis is the main component responsible for the progressive immobilization of the affected joint, which leads, in this limited group of individuals, to the final condition of ankylosis with functional disability.^{10,19,20} The chronic condition can be complicated by pyogenic arthritis, caused by direct infiltration or migration of bacteria to the joint, synovial pouch, or tendon sheath.¹¹ This may happen because of infection of the site after inoculation of bacteria present under the patient's nails, occurring when the patient scratches the region in response to the itching.

DIFFERENTIAL DIAGNOSIS

Because of the initial symptoms manifesting themselves as local dermatological reactions, the differentiation of the accident with *P. semirufa*, in acute injuries, should be established with allergic reactions and, especially, other types of eruptions. In the chronic phase, because of the similarity of the articular manifestations, the condition must be distinguished from RA. There are no specific tests for diagnosing the chronic condition of the disease; therefore, pararamosis is diagnosed based on clinical findings, the natural history of the disease, and epidemiological data.

RADIOLOGICAL EVALUATION

The radiological evaluation allows for the detection and monitoring of joint changes, as well as for the analysis of the arthropathy's degree of evolution. However, it is deficient in the perspective of unequivocally characterizing pararamosis.¹⁰ X-rays of the affected hand permit visualization of the swelling of soft tissues affected by the bristles, in addition to fibrosis of the juxtaarticular tissue and, also, the loss of joint space due to the thickening of the synovial membrane. In addition, deformities, such as the swan-neck deformity of interphalangeal joints, can be seen in some patients and resemble the manifestations observed in RA.²¹ In this case, dosing the rheumatoid factor or the autoantibodies against cyclic citrullinated peptide (CCP) can be used to differentiate the two diseases, especially anti-CCP, because of its high sensitivity and specificity for RA.^{22,23}

TREATMENT

Acute changes should be addressed with symptomatic agents, with emphasis on 1) washing the affected region with room temperature running water, 2) applying cold compresses with menthol or vinegar, and 3) elevating the affected limb.¹⁰ Furthermore, the use of oral antihistamines to control itching and topical corticosteroids, in addition to pain relievers to relieve symptoms presented in the early stages, are recommended.^{10,17}

Currently, there is no known specific therapy to treat patients with chronic pararamosis.^{10,11,19} Thus, the importance of specialized monitoring for analyzing the arthropathy's evolution is undeniable, indicating, in some more severe cases, the surgical removal of joint granulomas.^{10,24}

PROPHYLAXIS AND CONTROL

Pararamosis has relatively simple prophylactic measures to be complied with, in view of the seminal relation of the disease to the rubber tappers' labor activities. Therefore, the adequate use of personal protective equipment—such as gloves, boots, and glasses—represents an important prevention strategy, as they serve as barriers for the worker, preventing or, at least, making it difficult for the skin to contact the bristles of the *P. semirufa* caterpillar during the sap extraction of the *Hevea* spp.^{9,10,25} In addition, as pararamosis is classified as an occupational disease, the education of professionals who perform latex extraction represents an essential form of prophylaxis and would be undeniably helpful in an attempt to reduce the number of cases of this type of accident.

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REFERENCES

1. Branco MMP, Borrasca-Fernandes CF, Prado CC, Galvão TF, Silva MT, Mello De Capitani E, Hyslop S, Bucarechi F, 2019. Management of severe pain after dermal contact with caterpillars (erucism): a prospective case series. *Clin Toxicol (Phila)* 57: 338–342.
2. Sandoval-Mayen P, García-Rodríguez MI, Alonso-Pinedo YA, Mendoza-Arias MF, Mayorga-Rodríguez J, 2020. Erucism: a little frequent dermatosis? *Dermatol Rev Mex* 64: 64–69.
3. Seldeslachts A, Peigneur S, Tytgat J, 2020. Caterpillar venom: a health hazard of the 21st century. *Biomedicine* 8: 143.
4. Costa RM, 1981. Pararamose: uma reumatose ocupacional. *Rev Bras Reumatol* 21: 132–136.
5. Dias LB, 1989. Pararama. Instituto Evandro Chagas, 50 anos de contribuição às ciências biológicas e à medicina tropical. *Belém Fundação Serviço de Saúde Pública* 2: 799–809.
6. Dias LB, Azevedo MC, 1973. Pararama, a disease caused by mouth larvae: experimental findings. *Bullet Pan Am Health Organ* 7: 9–14.
7. Villas Boas IM, Pidde-Queiroz G, Magnoli FC, Gonçalves-de-Andrade RM, van den Berg CW, Tambourgi DV, 2015. A serine protease isolated from the bristles of the Amazonian caterpillar, *Premolis semirufa*, is a potent complement system activator. *PLoS One* 10: e0118615.
8. Costa RM, 1978. Pararamose: reumatismo exótico do seringueiro da Amazônia. *Rev Bras Reumatol* 18: 201.
9. Costa RM et al., 1993. Pararamose: an occupational arthritis caused by lepidoptera (*Premolis semirufa*). *Rev Paul Med* 111: 462–465.
10. Brasil, 2001. *Funasa. Manual de diagnóstico e tratamento de acidentes por animais peçonhentos*. Brasília, Brazil: Funasa, 67–74.
11. Villas-Boas IM, Gonçalves-de-Andrade RM, Pidde-Queiroz G, Assaf SL, Portaro FC, Sant'Anna OA, van den Berg CW, Tambourgi DV, 2012. *Premolis semirufa* (Walker, 1856) envenomation, disease affecting rubber tappers of the amazon: searching for caterpillar-bristles toxic components. *PLoS Negl Trop Dis* 6: e1531.
12. Villas-Boas IM, Gonçalves-de-Andrade RM, Squaiella-Baptistão CC, Sant'Anna OA, Tambourgi DV, 2013. Characterization of phenotypes of immune cells and cytokines associated with chronic exposure to *Premolis semirufa* caterpillar bristles extract. *PLoS One* 8: e71938.
13. Dias LB, Rodrigues MG, 1997. Pararamose. *Leão RNQ. Doenças Infecciosas: Enfoque Amazônico*. Belém, Brazil: CEJUP.
14. Rodrigues MG, 1976. Efeitos danosos da lagarta “pararama” em seringueiros no estado do Pará. *Boletim da Faculdade de Ciências Agrárias do Pará* 8: 5–31.
15. Costa RM, 1991. *Artropatia da pararamose: Epidemiologia, clínica e modelos experimentais*. [Tese de Doutorado em Reumatologia]. São Paulo, Brazil: Escola Paulista de Medicina.
16. Bergillos F, Rivas MA, 2013. *Toxinologia clínica. Lesiones por picaduras y mordeduras de animales*. Madrid, Spain: Bubok Publishing.
17. Cardoso AEC, Junior VH, 2005. Acidentes por lepidópteros (larvas e adultos de mariposas): estudo dos aspectos epidemiológicos, clínicos e terapêuticos. *An Bras Dermatologia* 80: 571–578.
18. Siqueira-Batista R, Gomes AP, Bastos CA, Santos EP, Azevedo SFM, Mendes TA, Oliveira AP, Cerqueira FR, Paula SO, Geller M, 2015. The complement system: importance in clinical practice. *Rev Bras Med* 72: 95–100.
19. Artemenko SRT, 1998. Araneísmo, escorpionismo e outros animais peçonhentos. Schechter M, Marangoni DV, eds. *Doenças infecciosas: conduta diagnóstica e terapêutica*. Rio de Janeiro, Brazil: Guanabara Koogan.
20. Fraiha H, Ballarini AJ, Leão RNQ, 1986. Síndrome hemorrágica por contato com larvas de mariposa (Lepidoptera, Saperiniidae). *Instituto Evandro Chagas, 50 anos de contribuição às ciências biológicas e à medicina tropical*. Belém, Brazil: Fundação Serviço de Saúde Pública, 811–818.
21. Barcelos A, Nour D, Silva JAP, 2001. Radiografia das mãos: elementos típicos em artropatias comuns. *Acta Reum Port* 27: 201–209.
22. Alarcon RT, Andrade LEC, 2007. Anticorpos antiproteínas citrulinadas e a artrite reumatóide. *Rev Bras Reumatol* 47: 180–187.
23. Atzeni F, Talotta R, Masala IF, Bongiovanni S, Boccassini L, Sarzi-Puttini P, 2017. Biomarkers in rheumatoid arthritis. *Isr Med Assoc J* 19: 512–516.
24. Torres-Filho SR, 2015. Acidentes humanos com venenos animais. Tavares W, Marinho LAC, eds. *Rotinas de diagnóstico e tratamento das doenças infecciosas e parasitárias*, 2nd Edition. São Paulo, Brazil: Atheneu, 226–231.
25. Siqueira-Batista R, Montenegro SSP, Santos SS, Santana LA, eds. *Parasitologia: fundamentos e prática clínica*. Rio de Janeiro, Brazil: Guanabara Koogan, 643–645.