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Lymphadenitis "as rosary beads" - a diagnostic challenge

Linfadenitis "como cuentas de rosario": un desafío diagnóstico

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Resumen

Introducción: la linfangitis nodular (LN) puede ser manifestación de diversas condiciones infecciosas y no infecciosas, y se caracteriza por nódulos inflamatorios subcutáneos que se extienden desde el sitio del foco primario hasta los ganglios linfáticos regionales. Generalmente la LN constituye un desafío en la atención primaria de salud y estudios histopatológicos y microbiológicos son necesarios para establecer el diagnóstico definitivo. **Métodos:** reportamos un caso clásico de LN que se desarrolló en el miembro superior de un hombre de media edad después de un trauma en el pulgar derecho. **El objetivo**: fue enfatizar algunos aspectos del diagnóstico diferencial en un paciente con LN y reducir la tasa de diagnósticos erróneos en el escenario de la atención médica inicial. **Resultados:** las manifestaciones clínicas fueron inespecíficas, pero el estudio microbiológico reveló características típicas de esporotricosis. El tratamiento con itraconazol (200 mg diarios) durante seis meses se realizó con éxito completo. **Conclusión:** la LN constituye una condición desafiante y el diagnóstico temprano depende de un elevado índice de sospecha. Reportes de caso pueden reducir diagnósticos tardíos y resultados desfavorables.

Palabras clave: diagnóstico; linfangitis nodular; esporotricosis; trauma; úlcera.

Abstract

Introduction: nodular lymphangitis (NL) may be a manifestation of various infectious and non-infectious conditions, characterised by subcutaneous inflammatory nodules that extend from the site of the primary focus to the regional lymph nodes. NL usually constitutes a challenge in primary health care, and histopathological and microbiological evaluations are necessary to establish the definitive diagnosis. **Methods:** We report a classic case of NL that developed in the upper limb of a middle-aged man after trauma on the right thumb. **The objective**: was to emphasise some aspects of the differential diagnosis in a patient with NL and to reduce the rate of misdiagnosis in the scenery of initial medical attention. **Results:** the clinical manifestations were non-specific, but the microbiological study revealed typical characteristics of sporotrichosis. The treatment with itraconazole (200 mg daily) for six months was successful. **Conclusion:** NL constitutes a challenging condition and the early diagnosis depends on a high index of suspicion. Case reports may reduce late diagnoses with unfavourable results.

Keywords: diagnosis; nodular lymphangitis; sporotrichosis; trauma; ulcer.

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Introduction

Subcutaneous inflammatory nodules extending from the zone of *inoculum* to the regional lymph nodes of affected limbs (Tirado-Sanchez & Bonifaz, 2018) characterise nodular lymphangitis (NL). NL more often involves the upper limbs, and a heterogeneous group of microorganisms can play a causal role. The aetiology of NL includes fungi (*Sporothrix* spp., *Cryptococcus neoformans*,

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Coccidioides immitis, *Histoplasma capsulatum*, and agents of chromoblastomycosis); bacteria (*Nocardia* spp., *Staphylococcus aureus*, *Streptococcus pyogenes*, *Bartonella henselae*, *Burkholderia pseudomallei*, and *Francisella tularensis*); mycobacteria (*Mycobacterium tuberculosis and* non-tuberculous mycobacteria; and *Leishmania* spp. (Minadakis *et al*., 2011; Carvalho *et al*., 2017; Orofino-Costa *et al*., 2017; Secchin *et al*., 2017; Brito & Bittencourt, 2018; Sizar & Talati, 2018; Mora-Montes, 2018; Tirado-Sanchez & Bonifaz, 2018; Veasey *et al*., 2018). Because of clinical similarities favouring diagnostic pitfalls, Biopsies and microbiological cultures must be done. This report highlights some major causes of this challenging condition that is found in previously healthy as well as in immunocompromised individuals.

Case report

A 45-year-old man from the North-eastern Brazilian area had a trauma with a piece of wood on the second phalange of the right thumb, about a month before he searched for medical attention. A papular lesion appeared close to the site of trauma and evolved to ulceration with impaired healing. Furthermore, a sequence of non-tender subcutaneous nodules developed with a centripetal spreading, and involved the upper right limb from the wrist up to the ipsilateral axillary region. He was previously healthy and lived in a low-income area within a rural dairy farm environment, near of plants and in contact with domestic cats. He denied fever or systemic symptoms and did not use medications. On physical examination, the patient was eutrophic. There was a painless and hyperchromic irregular lesion in the first right fingernail plate; the ulcer on the same finger was shallow, irregular, and with elevated borders, and the lymph node chain had a linear pattern similar to rosary beads (Figure 1). The rest of the clinical findings, the results of routine laboratory determinations, and the images of plain chest radiographs were unremarkable. Histopathological studies for microorganisms in biopsy samples of the ulcer, including direct microscopy with potassium preparations, had negative results. The absence of malignant cells ruled out the initial hypothesis of malignancy, and the Mycobacterial cultures were negative. Additional evaluations allowed to correctly establishing the diagnosis of sporotrichosis based on the fungal cultures. Sabouraud dextrose agar with chloramphenicol was the medium utilised, and the agents isolated from the skin lesions and lymph nodes after 5 and 10 days, respectively, had characteristics of *Sporothrix spp*. The colonies appeared with a surface of membranous aspect, cream coloured and a dark halo. There was a transition from the mould to the yeast forms by culturing mycelia at 37ºC, and the agents had cigar-shaped bodies. The patient underwent a course of itraconazole (200 mg daily) during six months and obtained a complete improvement of the cutaneous lesions without any adverse drug effect. Currently, he is asymptomatic and remains under regular outpatient follow-up.

Discussion

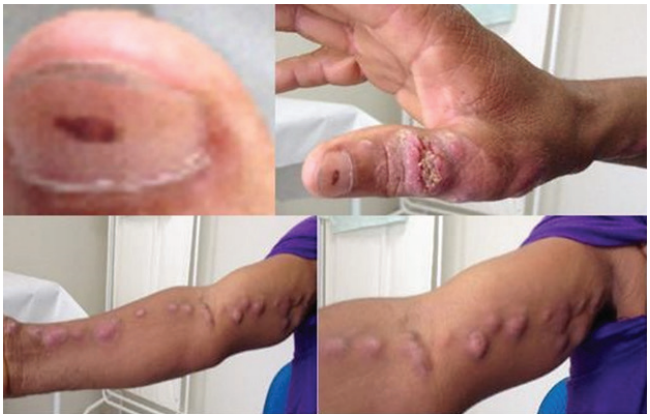

Figure 1: Hyperchromic change in the fingernail plate of the right hallux, and a shallow irregular skin ulcer with elevated borders on the same finger. In addition, numerous subcutaneous lymph nodes appear enlarged and disposed in a linear pattern similar to the "rosary beads".

The patient herein reported had melanonychia and ulceration in the right thumb, associated with subcutaneous nodules mimicking rosary beads in the upper limb. The main initial concerns were about either acral melanoma or the cat scratch disease, because of the concomitance of nail changes, ulcer with anfractuous borders, and the extensive regional lymph node involvement. He had an accidental trauma involving the first right-hand finger with subungual hematoma and a wound by a little piece of wood.

Acral melanoma can show a centripetal distribution of nodes in affected limbs. This tumour represents 4-5% of all the skin cancers, and nails are non-habitual areas (3-15%), but the prognosis is poor and late diagnoses is the leading cause of death (Santos *et al*., 2011). Because melanoma can have poor outcome if diagnosed at a late phase, the role of early diagnosis must be emphasised. Suspected skin or nail changes must always be assessed by a dermatologist before the biopsy procedure, because adequate management avoids the tumour spreading.

Cat scratch disease is an infectious disease caused by *Bartonella henselae*, usually inoculated in humans through a biting or clawing by infected cats, and rarely by tick bites. Typical manifestation is a tender unilateral lymph node enlargement after the initial skin lesions, which often appear as vesicles at the region of inoculation (Minadakis *et al*., 2011). Transmission by direct animal contact is not indispensable for suspicion, and approximately 50% of the patients have involvement of the upper limbs. The diagnosis is stablished with base on clinical data and the indirect fluorescent assay or ELISA serologic test. Azithromycin during five days is the treatment of

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choice for immunocompetent patients. In case of intolerance, other options may be clarithromycin, rifampicin, trimethoprim-sulfamethoxazole, ciprofloxacin, gentamicin, and doxycycline (Minadakis *et al*., 2011; Angelakis E & Raoult D, 2014). The cure of the lesions by itraconazole as in this patient report might be an indirect clue against the hypothesis of scratch cat disease because the infection is not responsive to azoles (Minadakis *et al*., 2011).

Sporotrichosis is frequent in South America and is the main subcutaneous mycosis in Brazil. Human infections often occur by inoculation of *Sporotrix schenkii* in the skin. In the vast majority of cases, the cutaneous implantation of this dimorphic fungus is secondary to trauma with plant material, but zoonotic transmission by infected cats also occur (Mora-Montes, 2018; Sizar & Talati, 2018; Tirado-Sanchez & Bonifaz, 2018). Interestingly, infected cats harbour a great number of transmissible forms of the fungus, with the possibility of repeated human inoculations and development of hypersensitivity. Characteristic features of the disease are solid and ulcerated lesions at the site of implantation followed by centripetal development of nodules, with ulceration or not. Pulmonary and disseminated manifestations are related to alcoholism, diabetes mellitus, chronic obstructive lung disease, and immunocompromised conditions (Mora-Montes, 2018; Sizar & Talati, 2018; Tirado-Sanchez & Bonifaz, 2018). Itraconazole (100 to 400 mg daily) during 2 to 3 months is the drug of choice, but for cases with systemic involvement, it is necessary to maintain the treatment from 6 to 12 months. Amphotericin B lipid complex or Liposomal Amphotericin B is the better choice for severe pulmonary or disseminated disease. Other options for treatment include potassium iodide, terbinafine. (Orofino-Costa *et al*., 2017; Mora-Montes, 2018; Sizar & Talati, 2018; Tirado-Sanchez & Bonifaz, 2018). Diagnostic pitfalls include the lymphadenitis caused by other agents but resembling sporotrichosis ("sporotrichosis" lesions).

The agents of Chromoblastomycosis (CBM) are fungi of the family *Herpotrichiellaceae* and the most prevalent species is *Fonsecacea pedrosoi* (90%), which predominates in tropical and subtropical regions, usually affecting male farm workers (Brito & Bittencourt, 2018). The initial lesions are usually papules in exposed areas of the limbs that may evolve by contiguity, lymphatic or haematogenous dissemination. Other clinical forms of CBM are verrucous, infiltrative, vegetative, and atrophic. The identification of hyphae and muriform bodies in histopathological samples and cultures in Sabouraud agar may confirm the diagnosis. Depending on the extension and chronicity, the treatment includes itraconazole (200-400 mg/day) and terbinafine (500-1000 mg/day) for 6-12 months, surgery, cryotherapy, thermotherapy, CO_2 laser, and immunoadjuvant compounds (Brito & Bittencourt, 2018).

Cutaneous leishmaniasis is a parasitic disease transmitted by the bite of a sand fly. Typical and atypical presentations of this entity occur in most of the South American regions. Clinical features and the course of infection depend on the host immune condition. The "sporotrichosis" lesions are more often found associated with decreased cellular immunity (Carvalho *et al*., 2017) and mainly due to infection by *L. brasiliensis* (Tirado-Sanchez & Bonifaz, 2018). Diagnostic mistakes occur with sporotrichosis if the skin lesions evolve from papules to nodes with proximal subcutaneous lymph node dissemination, as in that mycosis. Biopsy data are the gold standard for diagnosis. The severity of disease and the species of Leishmania guide the treatment, and vary from watchful expectation and intralesional therapy or cryotherapy for the mild cases to systemic drugs as sodium stibogluconate or liposomal amphotericin B for complex disease. Other drugs are itraconazole, ketoconazole, and allopurinol (Carvalho *et al*., 2017; Tirado-Sanchez & Bonifaz, 2018).

Mycobacterium tuberculosis and non-tuberculous mycobacteria (NTM) are important causes of "sporotrichosis" lymphadenitis (Tirado-Sanchez & Bonifaz, 2018; Veasey *et al*., 2018). The main agents of cutaneous NTM infections are *M. marinum*, *M. chelonae*, and *M. fortuitum*. Immunosuppressed individuals are more prone to these conditions. Mycobacterial infections were ruled out with the base on negative PPD test, absence of acid-fast bacilli in the lesions, and negative cultures. The NTM agents are often related to contact with contaminated water and fishes and may cause crusted ulcers and nodular lymphadenitis. They can also be acquired by inoculation through local trauma or surgical procedures (Tirado-Sanchez & Bonifaz, 2018; Veasey *et al*. 2018). The best options for treatment depend on the specific agent and may include rifampicin, ethambutol, clarithromycin or azithromycin, trimethoprim-sulphamethoxazole, and minocycline among others (Tirado-Sanchez & Bonifaz, 2018; Veasey *et al*., 2018).

Cutaneous nocardiosis usually occur following minor wounds contaminated with soil. Other ways of transmission are by infected cats or insect bites (Secchin *et al*., 2017). Infections by Nocardia can cause "sporothricoid" lesions in up to 25% of the immunocompetent patients (Secchin *et al*., 2017; Tirado-Sanchez & Bonifaz, 2018). Nocardia is a Gram-positive agent that may be mistaken by Mycobacteria in the Ziehl-Nielsen stain. Trimethoprim-sulphamethoxazole and minocycline are the best options for treatment of the cutaneous involvement (Tirado-Sanchez & Bonifaz, 2018).

Conclusion

Nodular lymphangitis is a challenging condition associated with infectious and non-infectious aetiologies, propitiating misdiagnosis because of similar clinical manifestations. As a whole, the definite

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diagnosis depends upon histopathological and microbiological data, which allows the prompt specific treatment and successful outcome. Many patients with this condition underwent initial empirical treatment before the correct diagnosis. The authors believe that case studies may contribute to reducing the amount of misdiagnosis.

Competing interests

The authors declare that they have no competing interests

Source of support

Nil

References

Angelakis E & Raoult D. (2014). Pathogenicity and treatment of Bartonella infections. *Int J Antimicrob Agents* **44**, 16-25.

Brito AC & Bittencourt MJS. (2018). Chromoblastomycosis: an etiological, epidemiological, clinical, diagnostic, and treatment update. *An Bras Dermatol* **93**, 495-506.

Carvalho LMV, Pimentel MIF, Conceição-Silva F, Vasconcellos ÉCFE, Valete-Rosalino CM, Lyra MR, Salgueiro MM, Saheki MN, Madeira MF, Mouta-Confort E, Antonio LF, Silva AFD, Quintella LP, Bedoya-Pacheco SJ & Schubach AO. (2017). Sporotrichoid leishmaniasis: a cross-sectional clinical, epidemiological and laboratory study in Rio de Janeiro State, Brazil. *Revista do Instituto de Medicina Tropical de São Paulo* **59**, e33.

Minadakis G, Angelakis E, Chochlakis D, Tselentis Y & Psaroulaki A. (2011). Cat-scratch disease in Crete: an update. *Infectious Diseases Reports* **3**, e15.

Mora-Montes HM. (2018). Special Issue "Sporothrix and sporotrichosis". *Journal of Fungi (Basel)* **4**, pii: E116.

Orofino-Costa R, Macedo PM, Rodrigues AM, Bernardes-Engemann AR. (2017). Sporotrichosis: an update on epidemiology, etiopathogenesis, laboratory and clinical therapeutics. *Anais Brasileiros de Dermatologia* **92**, 606-620.

Santos VM, Leal CT & Vasconcellos MJ. (2011). Late diagnosis of nodular melanoma of the foot in a 74-year-old Brazilian man. *Revista Médica de Chile* **139**, 1481-1483.

Secchin P, Trope BM, Fernandes LA, Barreiros G & Ramos-E-Silva M. (2017). Cutaneous nocardiosis simulating cutaneous lymphatic sporotrichosis. *Case Reports in Dermatology* **9**, 119-129.

Sizar O, Talati R. Sporotrichosis (Sporothrix schenckii). StatPearls [Internet]. Treasure Island (FL): StatPearls. Accedido en:https://www.ncbi.nlm.nih.gov/books/NBK532255/ el 06 de junio de 2018.

Tirado-Sánchez A & Bonifaz A. (2018). Nodular lymphangitis (sporotrichoid lymphocutaneous infections). Clues to differential diagnosis. *Journal of Fungi* (Basel) **4**, pii: E56.

Veasey JV, Monteiro NAS, Lellis RF & Klautau GB. (2018). Cutaneous atypical mycobacteriosis with sporotrichoid clinical presentation caused by automotive accident. *Anais Brasileiros de Dermatologia* **93**, 743-745.

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