CUTANEOUS VASCULITIS AS A PARANEOPLASTIC SYNDROME IN CHILDHOOD

Christina Feitosa Pelajo,* Sheila Knupp Feitosa de Oliveira,**
Marta Cristine Félix Rodrigues,*** Juliana Maia Torres*

Abstract

Introduction: In children, vasculitis as a paraneoplastic syndrome has never been reported before. In this work we report a vasculitis syndrome as a neoplasm onset manifestation in a child and we discuss our case regarding the data from literature.
Case report: A 7-year-old girl presented with hand and foot ulcerations, fixed cyanosis and pallor. During investigation, a central nervous system (CNS) rhabdomyosarcoma with metastasis on multiple sites was diagnosed.
Discussion: Rhabdomyosarcomas represent 5 to 8% of childhood neoplasms, although the CNS seldom is the primary site. In the indexed English language literature there were no published cases of vasculitis associated with rhabdomyosarcoma in any ages, neither of vasculitis as a paraneoplastic syndrome in childhood, which suggests that the described report is the first being published. Awareness of this possible coexistence could allow to an earlier diagnosis of neoplasms expressed by vasculitis, leading to an earlier treatment and a longer survival.

Keywords: Vasculitis; Rhabdomyosarcoma; Paraneoplastic Syndrome; Childhood.

Resumo

Introdução: A ocorrência de vasculite como expressão de uma síndrome paraneoplásica nunca foi descrita em crianças. Relatamos o caso de uma criança com vasculite paraneoplásica e discutimo-lo, correlacionando-o com os dados da literatura.
Caso clínico: Menina de 7 anos que iniciou um quadro caracterizado por úlceras nas mãos e nos pés. A investigação diagnóstica revelou um rabdomiossarcoma do sistema nervoso central (SNC) com metástases em múltiplas localizações.
Discussão: Os rabdomiossarcomas representam cerca de 5 a 8% das neoplasias na infância. A localização primária no SNC é rara. Não encontrámos relatos publicados na literatura em língua inglesa indexada de vasculite associada a rabdomiossarcoma em nenhuma faixa etária, nem de vasculites como síndrome paraneoplásica na infância, o que nos leva a crer que este seja o primeiro caso descrito. O alerta para esta possibilidade tem como objectivo estimular o diagnóstico mais precoce de neoplasias que se manifestem como vasculite, permitindo um tratamento mais precoce e um aumento da sobrevida.

Palavras-Chave: Vasculite; Rabdomiossarcoma; Síndrome Paraneoplásica; Infância.

Introduction

The prevalence of malignancies in adult patients with vasculitis has been estimated in 3 to 8%.[1] Hematological malignancies are the most frequently observed.[2-6] Lung and colic tumors are the most frequent solid tumors reported.[1] Vasculitis may be the initial presentation of a neoplasm otherwise completely asymptomatic.[7-10] Vasculitis manifestation varies from 25 months before to 9 months after the cancer diagnosis.[1] The most frequently described vasculitis in these cases are leukocytoclastic and polyarteritis nodosa.[4,11,12] Hypotheses suggested to explain coexistence of neoplasms and vasculitis involve treatment, tumor antigen leading to immu-

*Médica pediatra - Especialização em Reumatologia Pediátrica – Instituto de Puericultura e Pediatria Martagão Gesteira – Universidade Federal do Rio de Janeiro.
**Médica pediatra, reumatologista pediátrica, chefe do Serviço de Reumatologia Pediátrica – Instituto de Puericultura e Pediatria Martagão Gesteira – Universidade Federal do Rio de Janeiro, pHD.
***Médica pediatra, reumatologista pediátrica – Serviço de Reumatologia Pediátrica do Instituto de Puericultura e Pediatria Martagão Gesteira.

Figure 1. Cyanosis and ulceration in the palms.

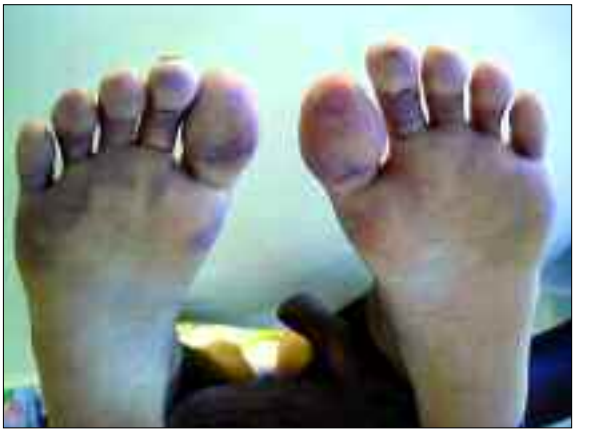

Figure 2. Cyanosis and ulceration in the soles.

ne complex formation, lymphokines and other vasoactive substances.[1,13] Treatment of malignancy often results in regression of the subjacent rheumatologic disease.[12,14] In children, vasculitis as a paraneoplastic syndrome has never been reported before. In this work we report a child's case and discuss it with regard to the literature data.

Case Report

A 7-year-old female child presented with an ischemic, painful lesion, which evolved with ulceration of the second left toe, followed by similar lesions in fingertips of the hands. She had enlargement of a cervical node, measuring 1.5 cm, which was soft and painless and presented also with fixed cyanosis, pallor areas and reddish palmar and plantar regions (Fig. 1 and 2). Laboratorial assessment revealed hematocrit = 25%, hemoglobin = 9g/dL (12--18g/dL) leukocyte count = 25,000 (45% neutrophil, 39% lymphocyte), platelet count = 671 $\times$ 10^3 (150-450 $\times$ 10^3) CRP = 98mg/L (<6mg/L), C3 = 263mg/dL (7-150mg/dL) and C4 = 44mg/dL (10--40mg/dL); prothrombin time, partial thromboplastin time, fibrinogen, biochemistry and urine were normal. Antinuclear antibodies (ANA), antineutrophil cytoplasmic antibodies (ANCA), anti-DNA and anticardiolipin antibodies were negative. Serologies for toxoplasmosis, rubella, hepatitis B and C, HIV and HTLV I and II were negative. Skin biopsy was not performed. She was treated with intravenous methylprednisolone (30mg/kg) for three days, and then oral prednisone (60mg) and low--weight heparin. New ulcerations on finger tips appeared although anemia improved and leukocyte number rose to 33,000. Echocardiogram, abdominal ultrasound and chest X-ray were normal. Doppler ultrasound showed superior and inferior limbs arteries with a high-resistance flow pattern, suggestive of distal vasoconstriction. Videocapillaroscopy showed capillary loops in palisade, narrowed capillaries, slow blood flow and loss of capillaries, suggesting hypertensive stasis. Methotrexate, pentoxifylline and nifedipine were added to treatment and subsequently buflomedil, because of inadequate response to nifedipine. There was improvement of cyanosis, which was substituted by reddish areas.

After one month, she presented night headaches, which woke her up and worsened when she lay down. This picture was followed by vomits, drowsiness and anisocoria. Computed tomography (CT) scan showed a large mass, measuring 8,4×6,5×5cm (91cm^3) in the right occipitotemporal area.

She was submitted to a tumor resection surgery and a marked improvement of cutaneous lesions was observed. Tumor histology and immunohistochemistry proved to be a rhabdomyosarcoma. After further investigation tumor dissemination in retroperitoneum, bladder, lungs and cervical nodes was detected. Radiotherapy was initiated, but she died after one month due to sepsis.

Discussion

Despite the absence of systemic involvement on admission and of a biopsy confirming vasculitis, the severity of the cutaneous lesions and the pos-

sibility of fingers gangrene were considered indications for treatment with corticosteroids, heparin and vasodilators. Since vasculitis as a paraneoplastic syndrome is not a complication described in children as it is in adults, this hypothesis was not considered. Neurological symptoms began 1 month after treatment of vasculitis was started. Immunohistochemistry revealed a CNS rhabdomyosarcoma, a tumor not related to vasculitis as paraneoplastic syndrome, even in adults.

Vasculitis is one known rheumatologic paraneoplastic syndrome, but other conditions such as hypertrophic osteoarthropathy, dermatomyositis/polymyositis, fasciitis, panniculitis, erythema nodosum, Raynaud's syndrome, erythromelagia and lupus-like syndromes can occur. Rheumatologic manifestations suggesting an occult neoplasm include rapid onset of an unusual inflammatory arthritis or diffuse bone pain in a patient older than 50 years of age, unexplained chronic vasculitis, refractory fasciitis, Raynaud's syndrome irresponsive to vasodilator therapy, rapidly progressive digital gangrene or Eaton-Lambert's myastenic syndrome.[14]

Rhabdomyosarcomas represent around 5 to 8% of childhood neoplasms and the central nervous system is seldom the primary site.[15,16] These tumors origin from embryonic mesenchyme of striated muscle cells. Main sites of metastasis are lungs, lymph nodes, bones, liver and brain.[17]

In this case, it was impossible to establish the primary site, since the disease was already disseminated when diagnosed. Nevertheless, based on the dimensions of the CNS mass, we consider that this could be the primary site. Medium survival in cases of CNS primary rhabdomyosarcoma is 8 to 10 months, despite aggressive chemotherapy and radiotherapy.[16] In our case, survival was three months after the vasculitis onset.

Paraneoplastic syndromes described in association with rhabdomyosarcomas, independently of their location, are anti-Hu syndrome,[18] membranous nephropathy,[19] retinopathy,[20] and hypercalcemia.[21] In the indexed English language literature we did not find any report of coexistent vasculitis and rhabdomyosarcoma at any age, or of vasculitis as paraneoplastic syndrome in childhood, which suggests that this is the first published case. Awareness of this possible coexistence could allow an earlier diagnosis of neoplasms expressed by vasculitis, leading to an earlier treatment and a longer survival.

Correspondence to:
Christina Feitosa Pelajo
Instituto de Puericultura e Pediatria Martagão Gesteira
Universidade Federal do Rio de Janeiro.
Av. Brigadeiro Trompowsky, s/ n. Ilha do Fundão
Rio de Janeiro – RK – Brasil
E-mail: chrispelajo@oi.com.br

References

1. Beji M, Khedher I, Ayadi n, Azouzi H, Hamza M. Periarteritis nodosa associated with lung cancer. A new observation. Tunis Méd 1999;77:585-588.
2. Sanchez NB, Canedo IF, Garcia-Patos PE, de Unamuno Perez P, Benito AV, Pascual AM. Paraneoplastic vasculitis associated with multiple myeloma. J Eur Acad Dermatol Venereol 2004;18:731-735.
3. Mita T, Nakanishi Y, Ochiai A et al. Paraneoplastic vasculitis associated with esophageal carcinoma. Pathol Int 1999; 49:643-647.
4. Hayem G, Gomez MJ, Grossin M, Meyer O, Kahn MF. Systemic vasculitis and epithelioma. A report of three cases with a literature review. Rev Rhum Engl Ed 1997;64:816-824.
5. Farrell AM, Stern SC, El-Ghariani K et al. Splenic lymphoma with villous lymphocytes presenting as leucocytoclastic vasculitis. Clin Exp Dermatol 1999; 24:19-22.
6. Blanco R, Gonzalez-Gay MA, Ibanez D et al. Henoch-Schönlein purpura as clinical presentation of a myelodysplastic syndrome. Clin Rheumatol 1997;16:626-628.
7. Ducarme G, Rey D, Bryckaert PE, Reguiai Z, Bernard P, Staerman F. Paraneoplastic urticarial vasculitis and renal carcinoma. Prog Urol 2003;13:495-497.
8. Wang CC, Chen MJ, Ho HC, Hong HS. Urticarial vasculitis and dermatomyositis in a patient with nasopharyngeal carcinoma. Cutis 2003;72:399-402.
9. Odeh M, Misselevich I, Oliven A. Squamous cell carcinoma of the lung presenting with cutaneous leukocytoclastic vasculitis: a case report. Angiology 2001;52:641-644.
10. Ponge T, Boutoille D, Moreau A, Germaud P, Dabouis G, Baranger T. Systemic vasculitis in a patient with small-cell neuroendocrine bronchial cancer. Eur Respir J 1998;12:1228-1229.
11. Diez-Porres L, Rios-Blanco JJ, Robles-Marhuenda A, Gutierrez-Molina M, Gil-Aguado A, Vazquez-Rodriguez JJ. ANCA-associated vasculitis as paraneoplastic syndrome with colon cancer: a case report. Lupus 2005;14:632-634.
12. Hutson TE, Hoffman GS. Temporal concurrence of vasculitis and cancer: a report of 12 cases. Arthritis Care Res 2000;13:417-423.
13. Pertuiset E, Liote F, Launay-Russ E, Kemiche F, Cerf-Payrstre I, Chesneau AM. Adult Henoch-Scönlein purpura associated with malignancy. Semin Arthritis Rheum. 2000;29(6):360-367.
14. Fam AG. Paraneoplastic rheumatic syndromes. Baillieres Best Pract Res Clin Rheumatol 2000;14:515-533.
15. Dropcho EJ, Allen JC. Primary intracranial rhabdomyosarcoma: case report and review of the literature. J Neurooncol 1987;5:139--150.
16. Tomei G, Grimoldi N, Cappricci E et al. Primary intracranial rhabdomyosarcoma: report of two cases. Childs Nerv Syst 1989;5:246--249.
17. Shimada H, Newton WA Jr, Soule EH, Beltangandy MS, Maurer HM. Pathology of fatal rhabdomyosarcoma. Report from Intergroup Rhabdomyosarcoma Study (IRS-I and IRS-II). Cancer 1987;59:459-465.
18. Schilstra A, van Tuiji JH, van Suylen RJ, Faber CG, ten Velde GP. Unclassified rhabdomyosarcoma in a patient with anti-Hu syndrome. Acta Clin Belg 2005;60: 248-251.
19. Tourneur F, Bouvier R, Langue J et al. Membranous nephropathy and orbital malignant tumor. Pediatr Nephrol 2000;14:53-55.
20. Hammerstein W, Jurgens H, Gobel U. Retinal degeneration and embryonal rhabdomyosarcoma of the thorax. Fortschr Ophthalmol 1991;88:463-465.
21. Leblanc A, Hartmann O, Pons G et al. Hypercalcemia associated with tumors in children. 20 cases. Arch Fr Pediatr 1984;41:551-555.