

Neonatal Wells Syndrome Associated With Eosinophilic Gastroenteritis.

Diallo M*, Diop A, Diadie S, Ndiaye M, Dieng M.T and Kane A.

Department of Dermatology, Aristide LeDantec Teaching Hospital, University of Dakar, Senegal

*Corresponding author

Moussa Diallo, Department of Dermatology, Aristide LeDantec Teaching Hospital, University of Dakar, BP 6821 Dakar-Etoile, Senegal, Tel: 00 (221) 77 762 90 90

Submitted: 17 June 2017; Accepted: 25 June 2017; Published: 27 July 2017

Abstract

Background: Eosinophilic cellulitis (Wells syndrome) is an uncommon eosinophilic dermatosis of unknown pathogenesis, which signals undiagnosed infectious, malignant or systemic disease. It has been reported exceptionally in association with inflammatory bowel disease.

Case report: A 7-month-old female infant, whose parents had no particular medical history, was seen for pruriginous papulo-nodular lesions evolving since her birth. She was followed for evolutive intestinal pseudo-obstruction, diagnosed as Hirschsprung disease, and was treated by discharge colostomy after an obstruction. Biological examinations showed hypereosinophilia and anaemia. Skin histopathology revealed a dense eosinophilic infiltrate, with flame figures typical of eosinophilic cellulitis. Histopathology of the resected colon showed a dense eosinophilic infiltrate throughout the bowel wall, with the presence of ganglion cells and normal nervous plexus.

Discussion: This case of eosinophilic cellulitis is of particular interest because of its neonatal occurrence, nodular presentation and association with eosinophilic gastroenteritis. To our knowledge, this is the third reported association between eosinophilic cellulitis and eosinophilic gastroenteritis, which appear to have the same pathophysiology. Wells syndrome should therefore be added to the list of dermatosis associated with inflammatory bowel disease.

Keywords: Eosinophilic cellulitis, Wells syndrome, Eosinophilic gastroenteritis.

Introduction

Eosinophilic cellulitis, or Wells syndrome is an uncommon dermatosis of unknown pathogenesis, usually encountered in adults and whose interest is to reveal an underlying pathology. Thereby, Wells syndrome has been reported in association with numerous diseases especially infectious, malignant and systemic [1]. It has been reported exceptionally in association with inflammatory bowel diseases [2]. Primitive eosinophilic gastroenteritis correspond to an elective inflammation of the digestive tract related (gut) to a predominantly eosinophilic infiltrate in the lack of hypereosinophilia known cause [3]. We reported a case of neonatal Wells syndrome associated with primitive eosinophilic gastroenteritis.

Observation

A 7-month-old female infant was referred to the dermatology department for pruriginous papulo-nodular lesions on scalp and limbs evolving about since the first month of her birth with remissions and exacerbations. She was the only child of a healthy couple with unremarkable medical history. The mother, a 30-year-old primiparous didn't receive any medication during

her pregnancy. Classical serological tests made during pregnancy for (HIV, toxoplasmosis, viral hepatitis, syphilis, rubella) were negative. There was no family history of atopic disease. The child was born of a normal, well invigilated pregnancy of 40 weeks and 5 days, following eutocic vaginal delivery with a birth body weight of 2700 g and 8 points of Apgar score. There was no neonatal infection. She was fed exclusively breast milk since her birth. She was followed in pediatrics and surgery departments for bowel dysfunction type of obstinate constipation, bloating, bowel tenseness and abdominal distension evoked Hirschsprung disease after hydrosoluble enema and therefore had undergone a discharge colostomy after an obstruction. Clinical examination showed a child in good general condition, weighing 6 kg with a normal neurologic behavior and adapted reactions. Dermatological examination demonstrated erythematous subcutaneous nodular lesions localized on the forearm and the back of his right hand (Fig. 1). There were also excoriated erythematous papules and nodules scattered on the scalp (Fig. 2). Subungual hemorrhage, mucosal ulceration, cutaneous signs of vasculitis or Raynaud phenomena were not noted. Abdomen was soft, painless, without palpable mass, with erythematous, papular and oozing colostomy orifice (Fig 3).



Figure 1: subcutaneous nodular lesion of forearm

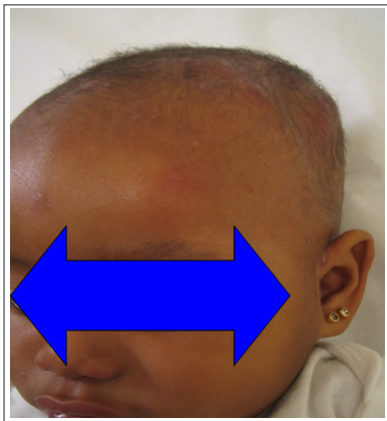


Figure 2: papulo-nodular lesions on scalp



Figure 3: colostomy orifice

The rest of the clinical examination, especially pulmonary, cardiac and lymph nodes was unremarkable. There was no clinical malformation detected.

A biopsy specimen from the nodular lesion of the forearm revealed a dense infiltrate of eosinophils within the entire dermis and the upper hypodermis with flame figures typical of Wells syndrome (**Fig 4**). There were no features of vasculitis or granulomatous. Special stains with periodic acid-Schiff and acid-fast revealed no evidence of specific pathogen. Topical corticosteroids was first tried on the few papulo-nodular lesions with a favorable evolution but followed by remissions and exacerbations.

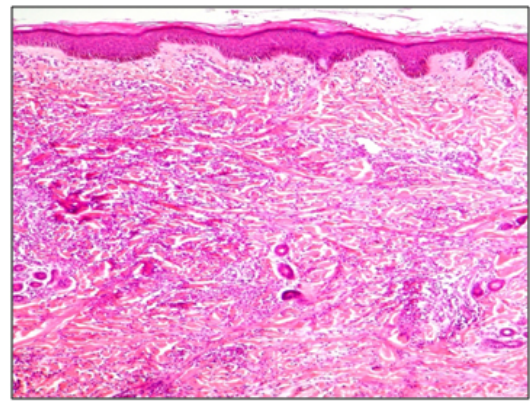


Figure 4: eosinophils infiltrate throughout the dermis with flame figures (hematoxylin-eosin, magnification 40).

Thereafter histological results of colectomy specimens showed a marked infiltrate extended to all layers of the bowel wall, consisting mainly of eosinophils and lymphocytes (**Fig. 5**). There were no granuloma or parasites or other microorganisms identified. Mesenteric and sub mucous nervous plexus was normal, without schwann's sheath hyperplasia and with the presence of ganglion cells.

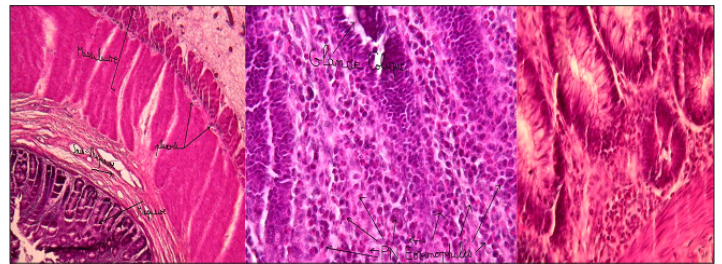


Figure 5: histopathology of colectomy specimens revealing a dense eosinophilic infiltrate and the presence of the nervous plexus (hematoxylin-eosin, magnification 40).

Investigations demonstrated a total white blood cells (WBC) count of 8900/mm³ with 2790/mm³ neutrophils, 2340/mm³ eosinophils, 40/mm³ basophiles, 4890/mm³ lymphocytes, 100/mm³ monocytes. Platelets were at 388.000/mm³. Hemoglobin: 10, 8 g/dl, mean corpuscular volume (MCV): 73μ3, mean corpuscular hemoglobin concentration (MCHC): 32, 6 g/100 ml, mean corpuscular hemoglobin (MCH): 23, 9 pg. The hyper eosinophilia and anaemia were also present on previous complete blood count. Total serum immunoglobulin E (IgE) levels were 825 KU/l (IU/ml) (*n* < 20). The total serum protein was 63 g/l with a rate of IgG: 7,10 g/l (*n* = 2-12), IgA: 0,39 g/l (*n* = 0,27-0,86), IgM: 0,96 g/l (*n* = 0,20-1,40). Vitamin B12 was 869 ng/l (*n* = 141-489). The immunophenotyping of blood leukocytes was normal. Antinuclear, DNA and antineutrophil cytoplasmic antibodies were negative.

Serological tests for Bilharzia, HIV, toxoplasmosis, hepatitis B and stool examination for ova, cysts, or parasites were negative. Repeated infectious etiologic investigations including (thick blood, hemocultures, urine culture, radiographies) were negative. Blood tests results for glucose level, serum electrolytes, urea, creatinine, transaminase, alkaline phosphatase (ALP), gamma-glutamyltranspeptidase (GGT), bilirubins, prothrombin time, activated partial thromboplastin time (APTT) were all within the physiological range. The Erythrocyte sedimentation rate was 30 mm/hour and C-reactive protein at 3mg/L. Electrocardiogram and chest X-ray were unremarkable.

After a short medical follow-up during which an improvement of skin lesions under topical corticosteroids was noted, the patient was lost to view.

Discussion

Described since 1973 by Kaijser, eosinophilic gastroenteritis correspond to an elective gastrointestinal tract inflammation related to a predominantly eosinophilic infiltrate [3,4]. Endoscopic, radiological and clinical features are highly variable and depend on the seat and especially the layer of the bowel wall involved by the infiltrate [3-6]. Eosinophilic gastroenteritis may result in obstructive syndrome in case of muscular layer infiltration and leading to a pseudo-Hirschsprung presentation which is difficult to distinguish clinically and radiologically with true Hirschsprund disease [3,7-9]. Definitive diagnosis of eosinophilic gastroenteritis requires the evidence of an significant eosinophilic infiltrate whose rate is above 20 eosinophils per high-power field at histopathological examination [3,6]. The gastrointestinal symptoms observed in our patient are related to eosinophilic gastroenteritis as evidenced by the density of the infiltrate, the presence of nerve plexus and ganglion cells. We didn't perform an endoscopy in our patient in order to evaluate precisely the digestive extent of the infiltrate because we already had digestive histology.

The neonatal forms are exceptional, but nevertheless reported [10,11]. It is rare conditions whose incidence is unknown, but are predominant between 30 and 50 years [12,13]. Eosinophilic gastroenteritis is probably primitive in our patient, in the absence of known causes for eosinophilia such as drug injury, malignant, eosinophilic, infectious or systemic disease found [3,4,7,12]. Several studies suggest a relationship with a specific food allergy as evidenced by the elevation of IgE levels [3,4,7,12].

Extraintestinal involvements (biliary, pancreatic, hepato-splenic, pleural and pericardial) have also been described in eosinophilic gastroenteritis [3,9]. However, no skin manifestation is classically described, although an association with skin diseases has been reported [2,14-22]. Eosinophilic cellulitis (WS) is an eosinophilic dermatitis characterized by recurrent polymorphous clinical manifestations but classically resembling "cellulitis" which histology reveals a dermal infiltrate of eosinophils, associated with "flame figures" characteristic but non specific [23]. Our patient presented a Wells syndrome as evidenced by the histology of the nodular lesion of the forearm and persistent blood eosinophilia. It is special because of its papulonodular presentation and its occurrence in the neonatal period, during which it is exceptional [24,25]. However, several clinical features have been described, including the rare papulonodular presentations already reported by Wells since his original article [26-28]. As in our case, these nodular forms and scalp localization seem more frequent in pediatric cases [29]. Wells syndrome is considered as a hypersensitivity reaction in response to various exogenous and endogenous stimuli. Thus, it has been described in association with arthropod bites, medications, viral, parasitic, fungal, bacterial infections, malignancies, and vaccinations [24,30-35]. Although all parasitic serology tests were not performed in our patient but the neonatal onset of the disease and the negativity of the repeated infectious investigations in a child in exclusive maternal diet eliminate an infectious origin. There was no drug injury or malignancy found. The skin histological findings with flame figure were not indicative of a hypereosinophilic syndrome. In the same way, a systemic disease could not be accepted in the lack of granuloma or vasculitis changes at histopathology and in view of the negativity of the immunological results. In our patient, the Wells

syndrome seems, as has already been observed, to be related to the eosinophilic gastroenteritis. Although the clinical relations of these two diseases are so far not yet documented, they probably share the same physiopathological mechanism. Indeed, the role of interleukin 5 in the production, activation, adhesion and degranulation of eosinophils, already known in the Wells syndrome has also been documented during eosinophilic gastroenteritis [2]. Although several skin diseases have been described during inflammatory bowel diseases, to our knowledge, apart from intestinal parasitosis, only three cases of Wells syndrome associated with chronic gastrointestinal diseases have been reported. It was an association in two cases with eosinophilic colitis, and in one case, the Wells syndrome was revealing of colon cancer [2,14,15]. The two cases associated with eosinophilic colitis were all atypical by their bullous presentation. In one case, Wells syndrome had occurred in a patient with known eosinophilic colitis and in the other case, the diagnosis were concurrent. In these two patients, effective treatment of colitis had resulted in the disappearance of cutaneous manifestations of Wells syndrome. In addition, a simultaneous recurrence of both diseases was observed. Our observation is the third case of Wells syndrome associated with eosinophilic gastroenteritis and is particular by its occurrence in neonatal period.

Originally, Wells syndrome has been described as a distinct dermatological entity. However, the variability of conditions and circumstances associated must consider Wells syndrome as a mode of skin reaction common to many diseases and lead the preference of "Wells phenomenon" term. All these conditions lead to this Wells phenomenon by a common mechanism based on a recruitment and differentiation of eosinophils secondary to interleukin 5 production by CD4 + T cells activated by these stimuli [36,37].

Conclusion

The Wells phenomenon in our case is of particular interest because of its neonatal onset, nodular presentation and especially association with eosinophilic gastroenteritis. This observation is the third reported case of association between eosinophilic cellulitis and eosinophilic gastroenteritis. Therefore, Wells syndrome should be added to the list of dermatosis associated with inflammatory bowel disease.

References

1. Chamailard M, Beylot-Barry M, Cogrel O, Bouabdallah K, Debarruel F, et al. (2005) Maladie de Vaquez révélée par un syndrome de Wells. *Ann DermatolVenerol* 132: 147-150.
2. Sakaria SS, Ravi A, Swerlick R, Sitaraman S (2007) Wells' syndrome associated with ulcerative colitis: a case report and literature review. *J Gastroenterol* 42: 250-252.
3. Oh HE, Chetty R (2008) Eosinophilic gastroenteritis: a review. *J Gastroenterol* 43: 741-750.
4. Okpara N, Aswad B, Baffy G (2009) Eosinophilic colitis. *World J Gastroenterol* 15: 2975-2979.
5. Freeman HJ (2008) Adult eosinophilic gastroenteritis and hypereosinophilic syndromes. *World J Gastroenterol* 14: 6771-6773.
6. Furuta GT, Forbes D, Boey C, Dupont C, Putnam P, et al. (2008) Eosinophilic Gastrointestinal Diseases Working Group. Eosinophilic gastrointestinal diseases (EGIDs). *J PediatrGastroenterol Nutr* 47: 234-238.
7. Yun MY, Cho YU, Park IS, Choi SK, Kim SJ, Shin SH, et al. (2007) Eosinophilic gastroenteritis presenting as small bowel obstruction: a case report and review of the literature. *World J*

- Gastroenterol 13: 1758-1760.
8. Velchuru VR, Khan MA, Hellquist HB, Studley JG. (2007) Eosinophilic colitis. *J Gastrointest Surg* 11: 1373-1375.
 9. Sheikh RA, Prindiville TP, Pecha RE, Ruebner BH (2009) Unusual presentations of eosinophilic gastroenteritis: case series and review of literature. *World J Gastroenterol* 15: 2156-2161.
 10. Ohtsuka Y, Shimizu T, Shoji H, Kudo T, Fujii T, Wada M, et al. (2007) Neonatal transient eosinophilic colitis causes lower gastrointestinal bleeding in early infancy *J Pediatr Gastroenterol Nutr* 44: 501-505.
 11. Murray SM, Woods CJ (1981) Disseminated eosinophilic infiltration of a newborn infant, with perforation of the terminal ileum and bile duct obstruction. *Arch Dis Child* 56: 66-71.
 12. Yan BM, Shaffer EA (2009) Primary eosinophilic disorders of the gastrointestinal. *Tract Gut* 58: 721-732.
 13. Méndez-Sánchez N, Chávez-Tapia NC, Vazquez-Elizondo G, Uribe M (2007) Eosinophilic gastroenteritis: a review. *Dig Dis Sci* 52: 2904-2911.
 14. Utikal J, Peitsch WK, Kemmler N, Booken N, Hildenbrand R, et al. (2007) Bullous eosinophilic cellulitis associated with ulcerative colitis: effective treatment with sulfasalazine and glucocorticoids. *Br J Dermatol* 156: 764-766.
 15. Hirsch K, Ludwig RJ, Wolter M, Zollner TM, Hardt K, et al. (2005) Eosinophilic cellulitis (Wells' syndrome) associated with colon carcinoma. *J Dtsch Dermatol Ges* 3: 530-531.
 16. Suresh E, Doherty V, Schofield O, Goddard C, Dhillon V (2005) Eosinophilic fasciitis and eosinophilic colitis: a rare association. *Rheumatology* 44: 411-413.
 17. Ogden S, Denyer ME, Wilkinson SM (2007) Erythema nodosum and eosinophilic oesophagitis: more than a chance association? *Br J Dermatol* 156: 1388-1389.
 18. Anderson RD, Patel R, Hamilton JK, Boland CR (2006) Cronkhite-Canada syndrome presenting as eosinophilic gastroenteritis. *Proc* 19: 209-212.
 19. Kumar A, Teuber SS, Naguwa S, Prindiville T, Gershwin ME (2006) Eosinophilic gastroenteritis and citrus-induced urticaria. *Clin Rev Allergy Immunol* 30: 61-70.
 20. Squires KA, Cameron DJ, Oliver M, da Fonseca Junqueira JC (2009) Herpes simplex and eosinophilic oesophagitis: the chicken or the egg? *J Pediatr Gastroenterol Nutr* 49: 246-250.
 21. Ojetti V, De Simone C, Aguilar Sanchez J, Capizzi R, Migneco A, et al. (2006) Malabsorption in psoriatic patients: cause or consequence? *Scand J Gastroenterol*. 41: 1267-1271.
 22. Schultz ES, Diepgen TL, Schuler G, von den Driesch P (1998) Rezidivierende Angioödem mit Gastroenteritis bei Blut- und Gewebseosinophilie *Hautarzt* 49: 566-570.
 23. Consigny S, Courville P, Young P, Richard C, Gauthier V, et al. (2001) Formes anatomocliniques du syndrome de Wells. *Ann Dermatol Venereol* 128: 213-216.
 24. Gilliam AE, Bruckner AL, Howard RM, Lee BP, Wu S, et al. (2005) Bullous "cellulitis" with eosinophilia: case report and review of Wells' syndrome in childhood. *Pediatrics* 116: 149-155.
 25. Kuwahara RT, Randall MB, Eisner MG (2001) Eosinophilic cellulitis in a newborn. *Pediatr Dermatol* 18: 89-90.
 26. Caputo R, Marzano AV, Vezzoli P, Lunardon L (2006) Wells syndrome in adults and children: a report of 19 cases. *Arch Dermatol* 142: 1157-1161.
 27. Wells GC, Smith NP (1979) Eosinophilic cellulitis. *Br J Dermatol* 100: 101-109.
 28. Ghislain PD, Van Eeckhout P (2005) Eosinophilic cellulitis of papulonodular presentation (Wells' syndrome) *J Eur Acad Dermatol Venereol* 19: 226-227.
 29. Garty BZ, Feinmesser M, David M, Gayer S, Danon YL (1997) Congenital Wells syndrome. *Pediatr Dermatol* 14: 312-315.
 30. Livory M, Wechsler J, Revuz J, Bagot M, Chevalier X, et al. (2008) Cellulite de Wells et dermohypodermite bactérienne nécrosante induites par l'anakinra. *Ann Dermatol Venereol* 135: 839-842.
 31. Boura P, Sarantopoulos A, Lefaki I, Skendros P, Papadopoulos P (2006) Eosinophilic cellulitis (Wells' syndrome) as a cutaneous reaction to the administration of adalimumab. *Ann Rheum Dis* 65: 839-840.
 32. Toulon A, Bourdon-Lanoy E, Hamel D, Fraitag S, Leruez-Ville M, et al. (2007) Wells' syndrome after primoinfection by parvovirus B19 in a child. *J Am Acad Dermatol* 56: 50-51.
 33. Bassukas ID, Gaitanis G, Zioga A, Boboyianni C, Stergiopoulou C (2008) Febrile "migrating" eosinophilic cellulitis with hepatosplenomegaly: adult toxocariasis - a case report. *Cases J* 1: 356.
 34. Renner R, Kauer F, Treudler R, Niederwieser D, Simon JC (2007) Eosinophilic cellulitis (Wells' syndrome) in association with angioimmunoblastic lymphadenopathy. *Acta Derm Venereol* 87: 525-528.
 35. Spinelli M, Frigerio E, Cozzi A, Garutti C, Garavaglia MC, et al. (2008) Bullous Wells' syndrome associated with non-Hodgkin's lymphocytic lymphoma. *Acta Derm Venereol* 88: 530-531.
 36. España A, Sanz ML, Sola J, Gil P (1999) Wells' syndrome (eosinophilic cellulitis): correlation between clinical activity, eosinophil levels, eosinophil cation protein and interleukin-5. *Br J Dermatol* 140: 127-130.
 37. Weiss G, Shemer A, Confino Y, Kaplan B, Trau H (2001) Wells' syndrome: report of a case and review of the literature. *Int J Dermatol* 40: 148-152.

Copyright: ©2017 Moussa Diallo, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.