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Paraneoplastic pemphigus associated with dendritic cell neoplasm and Castleman's disease: report of a new case and review of the literature

Case report

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Abstract: We report on a patient with longstanding multicentric Castleman's disease, hyaline-vascular type, who developed a follicular dendritic cell sarcoma, and finally presented a fatal paraneoplastic pemphigus. We review all four cases of such a triple association described in the literature so far.

Keywords: *Castleman's disease • Follicular dendritic cell sarcoma • Paraneoplastic pemphigus*

1. Introduction

Paraneoplastic pemphigus is an uncommon life-threatening mucocutaneous disease, generally presenting in patients with lymphoproliferative disorders [1]. We report on a new case of the disease, which occurred in a woman previously diagnosed with follicular dendritic cell sarcoma and multicentric Castleman's disease hyaline-vascular type.

2. Case Report

A 61-year-old woman presented with a three-day history of fever, cough with purulent sputum, worsening dyspnea and a mucocutaneous rash. Her past medical record was remarkable because of primary hypothyroidism, rheumatic heart disease, cholecystectomy, multicentric Castleman's disease, hyaline-vascular type, diagnosed eight years earlier, follicular dendritic cell sarcoma diagnosed three years earlier, and influenza associated myocarditis diagnosed three months earlier. For the treatment of Castleman's disease and follicular dendritic cell sarcoma she had undergone splenectomy three years earlier, because of persistent pancytopenia, and she had received four cycles of chemotherapy two months earlier, with no response.

On examination she was alert albeit moderately affected, and dyspneic. Temperature was 37.5 ºC, oxygen saturation while breathing room air was 93%, a grade 2/6 systolic murmur was heard in the aortic area, ronchi were auscultated in both lung fields, and signs of moderate ascites and mild pedal edema were also present. She had extensive erosions in her oral mucosa with hemorrhagic crusts covering her lips (Figure 1) and

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Figure 1. Extensive erosions and pseudomembranes in the lips.

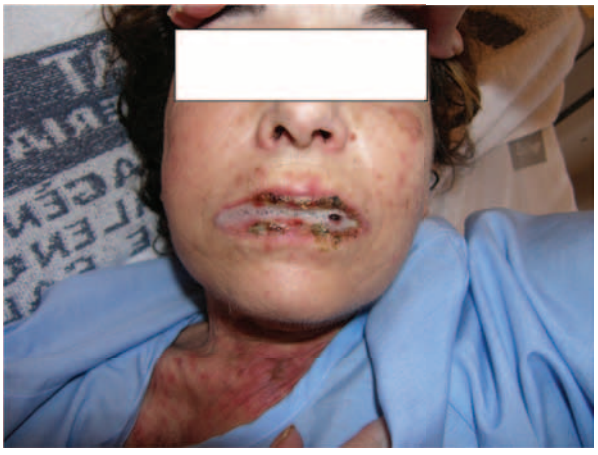
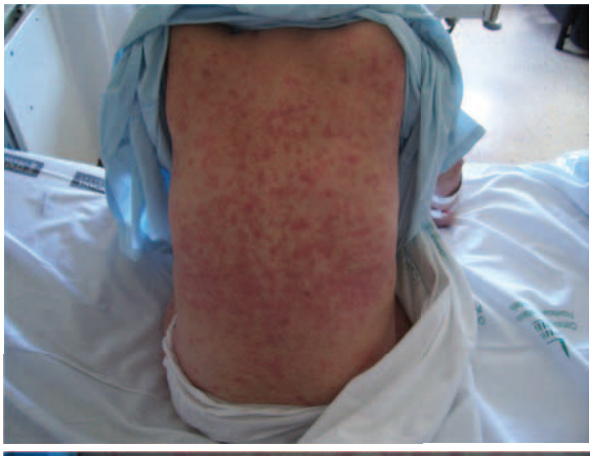
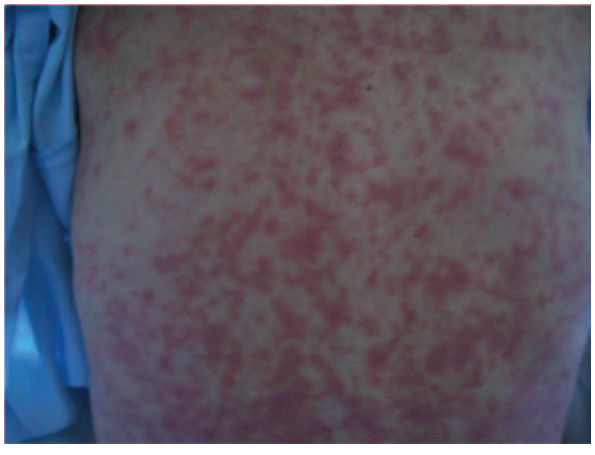


Figure 2, a and b. Papules coalescing into plaques over the trunk.



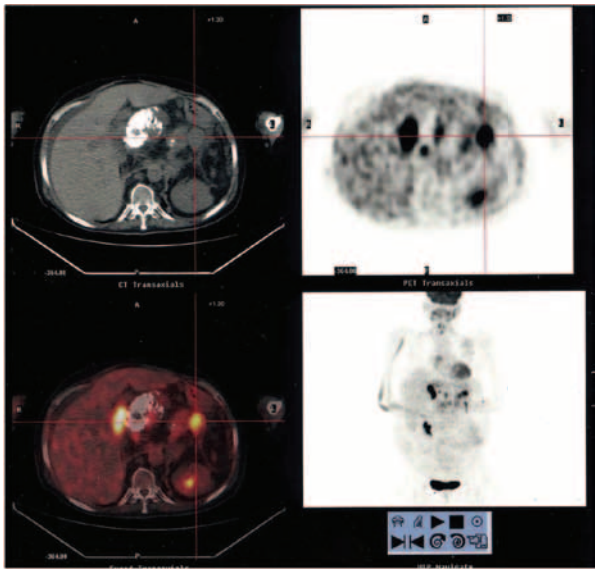


tongue, as well as papules coalescing into plaques symmetrically distributed over the trunk (Figure 2, a and b) and extremities. Her anogenital area was also partially eroded, while her conjunctiva was uninvolved.

Blood analyses showed: white blood cells 28,200 per mm^3 (with normal differentials), hemoglobin 10.2 g/dl (with normal mean corpuscular volume), platelets 650.000 per mm^3, lactic dehydrogenase (LDH) 573 IU/l, C-reactive protein 33 mg/dl, erythrocyte sedimentation rate 69 mm in the first hour, rheumatoid factor 41 ng/ml, albumin 2.65 g/dl, fibrinogen 483 mg/dl, brain natriuretic peptide 267 pg/ml, angiotensin converting enzyme 102 IU/l, interleukin-6 103 ng/l, and CA-125 270 U/ml. Serum immunoelectrophoresis revealed a small monoclonal component, which was not present in urine. Arterial blood gas analysis, while breathing room air, showed: pH 7.31, PCO2 43 mm Hg and PO2 61 mm Hg. A peripheral blood smear was normal. Autoantibodies against the plakin protein family (envoplakin, periplakin, desmoplakin I and desmoplakin II) were present in the serum. Ascitic fluid obtained at paracentesis showed: glucose 151 mg/dl, albumin 1.9 g/dl, LDH 100 IU/l, and white blood cells 50 per mm^3 (35 % polynuclears and 65 % mononuclears); gram staining and culture were negative, and cytology disclosed no malignant cells. A comprehensive serology testing, including HIV, human herpesvirus-8 and hepatotropic viruses, was negative. Cultures of blood and sputum were also negative.

Chest radiographs, an electrocardiogram, and an echocardiogram were unrevealing. An abdominal ultrasound showed moderate ascites, an epigastric partially calcified mass, and multiple lymphadenopathies in all territories. A positron emission tomography/computed tomography with F18-fluorodeoxyglucose revealed multiple lymphadenopathies throughout the neck, thorax, abdomen and pelvis (Figure 3), consistent with multicentric Castleman's disease and/or follicular dendritic cell sarcoma. A skin biopsy of one of the plaques in the

Figure 3. Positron emission tomography/computed tomography with F18-fluorodeoxyglucose revealing multiple lymphadenopathies throughout the neck, thorax, abdomen and pelvis, and a 10 cm in diameter partially calcified mass in the epigastrium and left hypochondrium.



abdomen showed suprabasal acantholysis, clefts with scattered necrotic keratinocytes, and vacuolar interface changes with lymphohistiocytic infiltration in the upper dermis; direct immunofluorescence disclosed intercellular deposits of IgG throughout the epidermis, whereas indirect immunofluorescence demonstrated IgG autoantibodies directed to the intercellular substance of stratified epithelium.

Treatment was instituted with intravenous immunoglobulin and rituximab with no response in mucocutaneous lesions. The patient also received oxygen therapy, broad spectrum antibiotics, spironolactone and prednisone 60 mg per day, but her condition progressively deteriorated, with worsening dyspnea and hypoxemia, and she finally died.

3. Discussion

Paraneoplastic pemphigus is a life-threatening autoimmune erosive and blistering mucocutaneous disease. The condition is generally associated with a variety of hematologic and neoplastic disorders, such as Castleman's disease, non-Hodgkin's lymphoma, thymoma, follicular dendritic cell sarcoma, chronic lymphocytic leukemia, Waldenstrom's macroglobulinemia, and epithelial cell carcinoma [2]. Suprabasal acantholysis and clefts with scattered necrotic keratinocytes are the typical histopathological cutaneous features. These lesions are provoked by antiepidermal antibodies produced by the cells in the associated tumors. Prognosis is grim, with death frequently occurring as a result of bronchiolitis obliterans. Removal of the associated tumor, when feasible, is the best therapeutic option, and intravenous immunoglobulins have also demonstrated some efficacy in the disease [1,3].

Dendritic cell neoplasms are rare tumors that are being increasingly recognized. The World Health Organization recommends classifying them into five groups: Langerhans' cell histiocytosis, Langerhans' cell sarcoma, interdigitating dendritic cell sarcoma/tumor, follicular dendritic cell sarcoma/tumor, and dendritic cell sarcoma, not otherwise specified [4]. Follicular dendritic cell sarcoma generally presents as an asymptomatic, slow growing well circumscribed mass, with a favorable prognosis; but in some cases it can locally invade tissues and even metastasize, most commonly to the liver and lungs, and constitutional symptoms may then be present. Recommended treatment varies from case to case, and may include surgery, radiation therapy, and chemotherapy [5].

Castleman's disease is a non-clonal lymph node hyperplasia. Pathologically it is classified as hyaline vascular, plasmacytic, or mixed cellularity types. Clinically it may adopt a unicentric or localized presentation that is usually asymptomatic, or a multicentric presentation that is frequently accompanied of systemic symptoms. An association of the disease has been found with HIV infection, Kaposi sarcoma, malignant lymphoma and a number of other diseases. Traditionally treatment has consisted of surgery, radiation therapy or chemotherapy, but new drugs, such as rituximab or tocilizumab, may also have a role [6].

A variety of associations of Castleman's disease, dendritic cell neoplasm and paraneoplastic pemphigus has been described [1,2,7]. But the simultaneous occurrence of these three rare diseases is exceptional. In a review of the literature, using the search profile "(follicular OR dendritic) AND pemphigus AND (Castleman OR Castleman's)" in Medline, we found three other cases, similar to ours, of the triple association Castleman's disease, dendritic cell neoplasm and paraneoplastic pemphigus [8-10]. In Table 1 we summarize the features of all four cases. As can be seen all four cases have many similarities among them: all patients presented the follicular dendritic cell sarcoma modality of dendritic cell neoplasm, all of them were diagnosed of the hyaline vascular type of Castleman's disease, and all died shortly after the diagnosis of paraneoplastic pemphigus was made.

Disclosures

The authors report no conflicts of interest regarding the article.

Table 1. Characteristics of the patients with the triple association Castleman's disease, dendritic cell neoplasm, and paraneoplastic pemphigus described in the literature.

Case #	Gender	Dendritic cell neoplasm[a]	Castleman's disease [b]	Paraneoplastic pemphigus [c]	Outcome[d]	Reference
1	Female	Follicular dendritic cell sarcoma, 53	Multicentric, hyaline vascular type, 53	53	Death, 54	8
2	Male	Follicular dendritic cell sarcoma, 66	Multicentric, hyaline vascular type, 66	66	Death, 66	9
3	Male	Follicular dendritic cell sarcoma, 32	Unicentric, hyaline vascular type, 32	32	Death, 32	10
4	Female	Follicular dendritic cell sarcoma, 53	Multicentric, hyaline vascular type, 59	61	Death, 62	Our case

[a] Histologic type, age at diagnosis; [b] anatomical distribution, histologic type, age at diagnosis; [c] age at diagnosis; [d] death or alive, age of death if applicable.

References

[1] Zhu X, Zhang B. Paraneoplastic pemphigus. J Dermatol 2007;34:503-511

[2] Kaplan I, Hodak E, Ackerman L, Mimouni D, Anhalt GJ, Calderon S. Neoplasms associated with paraneoplastic pemphigus: a review with emphasis on non-hematologic malignancy and oral mucosal manifestations. Oral Oncol 2004;40:553-562

[3] Mimouni D, Anhalt GJ, Lazarova Z, et al. Paraneoplastic pemphigus in children and adolescents. Br J Dermatol 2002;147:725-732

[4] Kairouz S, Hashash J, Kabbara W, McHayleh W, Tabbara IA. Dendritic cell neoplasms: an overview. Am J Hematol 2007;82:924-928

[5] Choi BS, Baek JH, Shin YM, et al. Follicular dendritic cell sarcoma: a case report and review of the literature. Cancer Res Treat 2010;42:121-124

[6] Roca B. Castleman's Disease. A Review. AIDS Rev 2009;11:3-7

[7] Meijs M, Mekkes J, van Noesel C, et al. Paraneoplastic pemphigus associated with follicular dendritic cell sarcoma without Castleman's disease; treatment with rituximab. Int J Dermatol 2008;47:632-634

[8] Marzano AV, Vezzoli P, Mariotti F, Boneschi V, Caputo R, Berti E. Paraneoplastic pemphigus associated with follicular dendritic cell sarcoma and Castleman disease. Br J Dermatol 2005;153:214-215

[9] Lee IJ, Kim SC, Kim HS, et al. Paraneoplastic pemphigus associated with follicular dendritic cell sarcoma arising from Castleman's tumor. J Am Acad Dermatol 1999;40:294-297

[10] Gironet N, De Muret A, Machet L, et al. [Paraneoplastic pemphigus revealing dendritic cell sarcoma originating from Castleman's disease of the neck]. Ann Dermatol Venereol 2005;132:41-44