

Rosai Dorfman Destombes's Disease about 5 Cases

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Abstract

Rosai Dorfman's Disease (RDD) Destombes also called sinus histiocytosis with massive lymphadenopathy is a lymphoproliferative pathology usually benign, of unknown etiology, and of low incidence. It is a rare, but well-defined clinicopathological entity, which predominantly affects children and adolescents without distinction of gender or race. It manifests itself generally by bulky cervical lymphadenopathies, most often bilateral, painless, of benign but persistent evolution and a long-term fever associated with a non-specific biological inflammatory syndrome. Extra lymph node locations are described in association with lymph node involvement or isolation. The definitive diagnosis of Rosai Dorfman's disease is histological, characterized by histiocytic infiltration with emperipolesis essentially of lymphocytes. The etiopathogenesis of the condition remains unclear, based on infectious and immunological hypotheses without clear evidence. The management is not well codified, it combines depending on the case, surgery; corticosteroids; antimetabolites and interferon alpha. Studies devoted to this condition in tropical Africa are rare. We report the clinical and progressive features of 5 observations of Rosai Dorfman's disease.

Keywords

Rosai Dorfman, Histiocytosis, Dakar

1. Introduction

Rosai Dorfman's Disease (RDD) Destombes also called sinus histiocytosis with massive lymphadenopathy is a pathology usually benign, of unknown etiology

and of low incidence [1]. It is a clinico-pathological entity which mostly affects children and adolescents. It manifests itself generally by bulky cervical lymphadenopathies, most often bilateral, non-painful. Extra lymph node sites such as skin, upper respiratory track and bone are described in association with lymph node involvement or in isolation. In tropical Africa, Rosai Dorfman's disease poses a problem of differential diagnosis with lymph node tuberculosis, Hodgkin's and non-Hodgkin's lymphoma; because of their clinical similarity and often leads to diagnostic errors. Lymph node histology shows massive sinus infiltration of histiocyto-macrophagic cells presenting typical immunohistochemical features [2] like positive staining for S-100, for the CD1a and CD68 antigens. The aim of our study is to report the clinical and progressive features of 5 observations of Rosai Dorfman's disease, with consents of the 5 patients.

2. Clinical Observations

2.1. Observation 1

This is a 20-year-old Senegalese female patient admitted to the internal medicine department of Aristide Le Dantec Hospital (ALDH) on 12/01/2016 for chronic left submaxillary macro-adenopathy and bilateral latero-cervical polymicroadenopathies (Figure 1).

The onset of symptoms would date back to 02/10/2016 marked by the appearance of a painless swelling under the left maxilla, progressively increasing in volume and latero-cervical polymicroadenopathies associated with a fatty cough with mucopurulent sputum without chest pain, diffuse headaches and dizziness, all evolving in a context of apyrexia and a conservation of the general condition. The patient had no medical, surgical or specific history, there was no primary tuberculosis infection, nor any notion of tuberculous contagion.

The physical examination at the entrance showed:

- An asymmetric macro-adenopathy under the left maxilla measuring approximately 5 cm, firm, mobile, non-inflammatory, without tendency to fistulization.



Figure 1. Bilateral cervical macroadenopathies with a left maxillary keloid post biopsy of a left maxillary macroadenopathy.

- Bilateral cervical polymicroadenopathies, non-inflammatory, without tendency to fistulization, firm, mobile.
- A keloid of 4 cm under left maxilla.
- A febricule at 37.8°C.

Biology has reported hypochromic microcytic anemia, with a hemoglobin level of 10.9 g/dl, hyperplaquetosis at 656,000 elements/mm³, neutrophils at 75,400 elements/mm³; sedimentation rate (SR) at the 1st hour: 81 mm; C-reactive protein (CRP): 48 mg/l. The serum protein electrophoresis demonstrated hypoalbuminemia and polyclonal hyperglobulinemia. Retroviral serology, HBs antigen (HbsAg) and acid-fast bacilli (AFB) in the sputum were negative. The chest X-ray as well as the abdominal ultrasound was unremarkable.

The anatomopathological examination shows a ganglion surrounded by a thickened fibrous capsule (**Figure 2**). This ganglion is marked by distended sinuses and obstructed by a population of large histiocytes with clear cytoplasm. These cells contain lymphocytes mixed with plasma cells in their cytoplasm, sometimes producing images of emperipolesis.

The treatment consisted of oral corticosteroid therapy made of prednisone 1 mg/kg/day with adjuvant measures. The evolution was marked by the decrease in the volume of lymphadenopathy, the submaxillary keloid being persistent.

2.2. Observation 2

He was a 27-year-old guinean, admitted to the internal medicine department of Aristide Le Dantec hospital on 04/04/2014 for 2 ulcero-budding swellings, under the right chin and under the left parotid with latero-cervical polyadenopathies (**Figure 3**). The onset of symptoms dates back to February 2011, marked by the appearance of an unencrypted fever, mostly nocturnal, without chills or sweats, accompanied by vomiting streaked with blood. This had motivated a consultation at the Conakry hospital where an antibiotic was prescribed but without clinical improvement. Right and left painless axillary nodular lesions, gradually increasing in size, appeared three months later. The clinical picture raising the

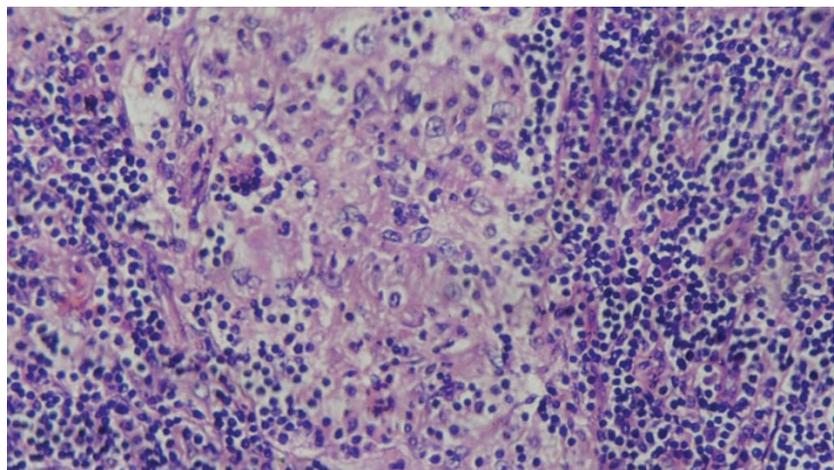


Figure 2. A ganglion surrounded by a thickened fibrous capsule.

suspicion of tuberculosis, an anti-tuberculosis treatment (protocol not specified) was established, then stopped before the negativity of the tuberculin tests. New cervical nodular lesions, right and then left, and endo-nasal nodular lesion gradually appeared, causing an obstruction of the nasal cavity with episodes of epistaxis not quantified; as well as purple red papular lesions, nodular in some sites, gradually increasing in size, changing color and becoming yellowish, non-pruritic, painless, located in the trunk, back (**Figure 4**), pubis and face.

The clinical examination at the entrance showed:

- Two swellings measuring approximately 4 to 6 cm in diameter, budding, rounded, not bleeding on contact, sitting at the level of the left submandibular and right parotid region.
- Papular-nodular lesions, multiple, purple red and yellowish, of soft consistency, measuring 0.5 to 2 cm in diameter, randomly dispersed, on the back, trunk, pubic region and face.
- Papular-nodular, yellowish lesions on the endo-nasal site.
- Nodules, elastic, painless, four in number, located in the occipital region of the scalp.
- Polyadenopathies fixed relative to the deep plane, of firm and elastic consistency, painless, located at the cervical, supra-clavicular, axillary, inguinal level.



Figure 3. Bilateral cervical lymphadenopathies with budding swelling in the right parotid region.



Figure 4. Papulonodular lesions, purplish red, on the back.

This clinical picture evolves in a context of fever and deterioration of the general condition with weight loss estimated at 8 kg in 1 year, associated with non-selective anorexia and physical asthenia.

In biology, we have hypochromic microcytic anemia, with a hemoglobin level of 8.3 g/dl, and a hyperplaquetosis at 474,000 elements/mm³. A CRP: 48 mg/l. The serum protein electrophoresis demonstrated hypoalbuminemia (34.69 g/l) and polyclonal hyperglobulinemia. Retroviral serology, HBsAg and AFB in the sputum were negative. The chest and face radiography were unremarkable. The abdomino-pelvic ultrasound showed hilar, hepatic, splenic, and lumbar-aortic polyadenopathies. Kidney and liver function returned to normal. The lymph node and cutaneous histologies respectively objectified a significant enlargement of the sinuses, infiltrated by large histiocytes with the presence of an image of emperipolesis; exclusive involvement of the dermis with polymorphic infiltrate of neutrophils, lymphocytes and eosinophils, clearer histiocytic islets composed of large cells with a clear cytoplasm. Treatment consisted of oral corticosteroid therapy (prednisone) at a dose of 1 mg/kg/day with adjuvant measures. Nasal corticosteroid therapy at the rate of two sprays per day had been prescribed. The evolution was marked by the decrease in the volume of lymphadenopathy, an involution of the two tumor masses (**Figure 5**) and the healing of skin lesions (**Figure 6**).

2.3. Observation 3

This is a 21-year-old female patient, followed for 6 years for recurrent lymphocytic polyseritis with pericardial, pleural and peritoneal involvement in the cardiology department of Aristide Le Dantec hospital and then in the internal medicine department of Abass Ndao hospital. The explorations carried out for etiological aim were negative: AFB in the sputum, the adenosine desaminase assay, the search for malignant cells in effusion fluids, HIV1 and HIV2 serologies, HBsAg, native anti-DNA antibodies, anti-ECT. The thoraco-abdomino-pelvic



Figure 5. Image showing small cervical lymphadenopathies with involution of the tumor mass in the right parotid region.



Figure 6. Atrophic skin lesions.

CT scan returned to normal.

The evolution was marked by the occurrence of four episodes of pericardial tamponade requiring pericardocentesis and the creation of a pleuro-pericardial window in May 2017 as well as the installation of a pleural drain, bringing back a daily production of 200 ml. The clinical examination revealed, in addition to pleural effusions, free ascites of low abundance and pericardial friction, firm bilateral non-inflammatory and non-fistulised axillary micro-adenopathies. The other lymph node areas, in particular the cervical glands, were free. The rest of the exam was normal.

Biology had found a hypochromic, microcytic anemia with a hemoglobin level at 11.6 g/l, leukopenia at $2700/\text{mm}^3$, an accelerated sedimentation rate at 47 mm at the 1st hour and a positive C-reactive protein at 11 mg/l. Doppler echocardiography concluded that there was significant dilation of the two atria with no sign of pericardial constriction with normal valve structures. The bi-ventricular function was preserved. Lymph node biopsy had shown sinus histiocytosis with no evidence of histological malignancy, with CD68 positive and CD1a negative immunohistochemistry in favor of Rosai-Dorfman's disease.

Corticotherapy has therefore been instituted with prednisone at a rate of 1 mg/kg/day in addition to the adjuvant treatment. The evolution was favorable after two months of treatment with a complete regression of the effusions (pericardial, peritoneal and pleural). On the biological level there is a good evolution of the parameters with a disappearance of leukopenia at the hemogram and also of the inflammatory syndrome.

2.4. Observation 4

This is an 18-year-old female patient with no specific medical history; hospitalized at the ALDH internal medicine department for chronic and diffuse macropolyadenopathy. Symptoms had started in June 2011, marked by the appearance of a painless, right latero-cervical and axillary swelling, gradually increasing in volume; this motivated a consultation where a biopsy was indicated, showing

a non-specific reaction adenitis. The whole evolving in a context of apyrexia and conservation of the general condition.

The clinical examination at the entrance showed: a macropolyadenopathy, diffuse, bilateral and asymmetrical, of firm consistency, fixed relative to the deep plane, painless, non-compressive, without tendency to fistulization with healthy looking skin.

In biology, we have an SR accelerated to 80 mm at the first hour. The electrophoresis of serum proteins showed polyclonal hypergammaglobulinemia. Tuberculin skin test (TST), AFB in the sputum and retroviral serology were negative. The chest X-ray and abdominal ultrasound were unremarkable. Lymph node histology showed histiocytic proliferation, sinus dilation and lymphophagocytosis.

A corticosteroid treatment was started, at a dose of 0.5 mg/kg/day, with the adjuvant measures. The evolution has been favorable to date.

2.5. Observations 5

She is a 40-year-old Senegalese woman who consulted in 2006 at the Internal Medicine Service of Aristide Le Dantec Hospital. The picture was marked by the installation of a permanent, mild fever, worsening evening, without chills, accompanied by sweating, physical weakness and unencrypted weight loss. A month later, the patient noticed a swelling on the left supraclavicular level that increased rapidly in volume. It will be followed by another one at the level of the right inguinal fold. This table motivated a consultation at the hospital of her locality or a tuberculosis treatment was started after 15 days of hospitalization. After three months of anti-tuberculosis treatment, her general condition worsened, the swellings increased in volume, the fever persisted, and the weight loss increased, which had motivated her transfer to the internal medicine department of Aristide Le Dantec hospital.

The clinical examination at the entrance showed:

- A left supraclavicular lymphadenopathy, measuring approximately 3 to 4 cm in diameter, painless, of elastic consistency, not fistulized, mobile, and without periadenitis.
- Left axillary and inguinal lymphadenopathies which had the same characteristics as those which were left supraclavicular.
- A febricule at 37.8°C.

Biological examinations showed hypochromic microcytic anemia with a hemoglobin level of 7.9 g/dl. The platelet count was 578,000 cells/ml, the white blood cell count was 7500 cells/ml. SR: accelerated to 125 mm at the first hour.

The blood ionogram, renal, hepatic and metabolic balance (glycemia, uricemia, lipidogram) were normal. Tuberculin skin test and retroviral serology were negative.

The lymph node biopsy revealed a homogenization of the follicular architecture with numerous histiocytes in layers. The lymphoid cells had no nuclear aty-

pia. The abdominal ultrasound showed large left mesenteric and latero-aortic lymphadenopathy. The chest radiograph showed homogeneous opacities deforming the contours of the mediastinum suggestive of mediastinal lymphadenopathy.

The patient was put on corticosteroid therapy at a dose of 1 mg/kg/day. The evolution was favorable with partial regression of cervical lymphadenopathy and disappearance of those located at the inguinal level.

The clinical and paraclinical profile of the observations is summarized in **Table 1**.

3. Discussion

We have reported 5 observations of Rosai Dorfman's disease. This disease mainly affects children or adults: 80% of patients are under 20 years of age at diagnosis. However, the diagnosis can be made much later in life up to 60 years of age [3]. The average age in our study is 28.3 years, higher than that reported in the literature [4], it could be linked to a diagnostic delay. This could be explained, on the one hand, by the diagnostic similarities with infectious causes, such as lymph node tuberculosis and lymphomas and, on the other hand, to the delay in consultation noted in our patients.

The pathophysiology of RDD is unknown. The immunohistochemical characteristics of histiocytes are in favor of macrophagic pathology. No infectious

Table 1. Clinico-biological profiles of our patients.

Clinical and biological signs	Patients				
	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Adenopathies	Macro-adenopathy under left maxilla, bilateral latero-cervical polymicroadenopathies	Cervical, supra-clavicular, axillary, inguinal, hilar, hepatic, splenic, lumbo-aortic	Bilateral axillary micro-adenopathies	Diffuse, bilateral macro-poly-adenopathies	Left supraclavicular, left axillary and inguinal, mesenteric, left latero-aortic, mediastinal
Extra-lymph node involvement	Absence	Skin and endo-nasal papulo-nodular lesions. Left submandibular budding swelling and right parotid swelling.	Pericardial, pleural, peritoneal effusions	Absence	Absence
Hb (g/dl)	10.9	8.3	11.6		7.9
MCV (fL)	76.9	65.5	75		
MCHC (pg)	24	18.6			
Platelets (elts/mm ³)	656,000	474,000			578,000
Leucocytes (elts/mm ³)	75400		2700		7500
CRP (mg/L)	48	48	11		
SR 1 st hour (mm)	81		47	80	125

cause has so far been formally identified. The disease is sporadic in the vast majority of cases [3].

The most frequent clinical sign is the presence of bulky cervical lymphadenopathies (90% of cases), typically bilateral and not painful, of hard consistency and sometimes bulky. Lymphadenopathy is also often found at other sites, particularly axillary or mediastinal [3].

Clinically, cervical lymphadenopathy was noted in four patients. They were large, painless, non-compressive, of elastic consistency and with healthy looking skin. Other extra-cervical localizations have been reported, notably axillary and inguinal. Two of our patients presented a deep lymph node involvement (lumbo-aortic, splenic, hepatic and mediastinal). Only one patient presented with recurrent lymphocytic polyseritis with pericardial, pleural and peritoneal involvement.

Extra-lymph node involvement is present in approximately 50% of cases. The most frequently affected extra-ganglionic sites (10% - 30%) are the eyes, soft tissues including intrathoracic, skin and sinuses or other otolaryngological (ENT) lesions. More rarely (<10%) can affect the central nervous system, bones, salivary glands, reins and urinary tract and testes. Exceptionally, cardiac, mammary or digestive locations have been recognized. It is possible, although rare, to find isolated extraganglionic localizations, this being particularly frequent in neurological and bone disorders [3].

Cutaneous involvement, one of the most frequent of the extra ganglionic localizations of RDD [5], was noted in one of our patients, in the form of papules and nodules, red-purplish and yellowish, dispersed in the back, trunk, the face and the suprapubic region; as well as voluminous swellings, budding, rounded, not bleeding on contact, sitting in the region of the left submandibular and right parotid.

ENT (Ear-Nose-Throat) involvement was noted in the only patient with the cutaneous form, in the form of bilateral epistaxis secondary to the existence of nodular endo-nasal lesions. In the literature, ENT involvement is frequent, it mainly concerns the upper aero-digestive tract and salivary glands [4]; we can even find thyroid damage such as goiter or thyroid nodules [6].

Cardiac involvement has been described in the form of valve or sub-valve involvement. One of our patients presented with a very aggressive pericardial attack without valve involvement which was integrated into a context of polyseritis.

An inflammatory syndrome is common, sometimes accompanied by inflammatory anemia. The lymphocyte count is variable. In the original description, a leukocytosis was noted, but it is inconsistent. Polyclonal hypergammaglobulinemia is frequently found (70% of cases), including in non-Afro-Caribbean patients [3]. These data from the literature can be superimposed on the data found in our observations.

The diagnosis of Rosai Dorfman's disease is confirmed by the results of histological analysis in front of a compatible clinical and radiological picture. It is posed in front of an accumulation of histiocytes with large round nuclei and

strongly nucleated, and large eosinophilic or sometimes xanthomized cytoplasm (the “cells of Destombes”) which are constantly CD68 (+), CD1a (–) and most often PS100 (+). One of the characteristics of the disease is the presence of emperipolesis lesions corresponding to the presence of lymphocytes, plasma cells or polynuclear cells within the cytoplasm of histiocytes, a translation of the wrapping of the cytoplasm of these around other leukocytes. This phenomenon is different from phagocytosis [3].

Nodal and/or cutaneous histology allows us to make the diagnosis of RDD, showing a histiocytic proliferation with an image of emperipolesis, corresponding to the active penetration of lymphocytes into the histiocytic or macrophage cell, without phagocytosis; thus agreeing with the histological aspects described in the literature [5]. Lymph node biopsy had shown sinus histiocytosis with no evidence of histological malignancy, with CD68 positive and CD1a negative in the third patient.

RDD usually has a spontaneously favorable development. The treatments are indicated in the event of a disabling clinical manifestation. Surgical treatment or radiotherapy can be undertaken in the event of compressive localization, in particular neurological or ENT. Skin damage is particularly resistant to treatment with a response in only 29% of cases. In this location, local treatments (surgical excision, laser treatment) are more effective than corticosteroids, including generally. Various treatments have been tried and described: steroids, mercaptopurine, thalidomide in cutaneous forms, cladribine, azathioprine, vincristine, methotrexate, rituximab, vinblastine or even interferon alpha. Anti-TNF-alpha drugs have been tried without efficacy [3].

Indeed, several therapeutic protocols have been proposed, the most classic of which is prolonged corticosteroid therapy [7]. The latter was introduced in our patients at a dose of 0.5 to 1 mg/kg/day, in addition to adjuvant measures. The evolution was favorable in our patients, affirming the benign and resolving nature of this disease.

4. Conclusion

Rosai Dorfman’s disease is a histiocytosis which is one of the non-Langerhans histiocytoses. The etiopathogenesis of the affection remains unclear, based on infectious and immunological hypotheses without clear evidence. All the diagnostic difficulty lies in the evocation of this rare affection in front of atypical clinical pictures. As the management is not well codified, it combines surgery and/or corticosteroids depending on the case.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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