SAS Journal of Medicine
Abbreviated Key Title: SAS J Med
ISSN 2454-5112
Journal homepage: https://saspublishers.com

OPEN ACCESS

Rheumatology

Gougerot Sjögren Syndrome and Medular Aplasia: A Case Report and Review of the Literature

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DOI: 10.36347/sasjm.2022.v08i10.004 | **Received:** 28.08.2022 | **Accepted:** 04.10.2022 | **Published:** 07.10.2022

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Abstract **Case Report**

Introduction: Gougerot-Sjögren's syndrome (GSS) is a non-organ specific auto-immune epithelitis that affects essentially exocrine glands characterized by an inflammation of the epithelium, in particular salivary and lacrimal epithelium, leading to oral (xerostomia) and ocular (xerophthalmia) dryness, with the possibility of extra-glandular involvement, which reflects its systemic nature. Its prevalence is estimated between 0.01 and 0.09%. Its association with medullary aplasia (MA) is rare; the latter is of various origins, in particular drug-related, linked to methotrexate. ***Objective:*** To present an observation that seems to us remarkable by the exceptional association of primary Gougerot-Sjögren's syndrome (PGS) and bone marrow aplasia in an octogenarian woman (80 years old). ***Observation:*** This was an octogenarian woman followed in rheumatology since 1993 for a pGSS based on joint involvement made of persistent bilateral asymmetric dry polyarthritis without deformity associated with ocular and oral dryness, accessory salivary gland biopsy (ASGB) at Chisholm and Masson grade 4 by ACR/EULAR 2016 7-point classification criteria, she was on 15mg methotrexate/semaine, 400mg hydroxychloroquine/day for 23years. She presented at entry with fever (T° 39.5°C), the pallor of integuments and conjunctivae, ecchymosis versus hepatomegaly, splenomegaly and bone pain were absent. Biology finds: Pancytopenia made of aregenerative anemia (Hemoglobin at 7.2g/dl, reticulocyte rate at 5934/mm3), leukopenia at 270/mm3, neutropenia at 70/mm3, lymphopenia at 150/mm3 and Thrombopenia at 9000/mm3. The medullogram concluded that the patient was suffering from bone marrow aplasia with poor cellularity, even deserted, but the renal, hepatic, cardiac and infectious investigations were normal. Thus, bone marrow aplasia in a patient followed for primary GSS under methotrexate for 23 years was retained. The treatment was hospitalization, transfusion of 1200ml of platelet concentrate, tramadol 50mg x 3/d in mini-infusion, Fleming (amoxicillin + clavulanic acid) 1g x2/d and Rovamycin 3 million x 2/d, unfortunately, the continuation was marked by her death at D4 of hospitalization. ***Conclusion:*** Medullar aplasia and pGSS are an exceptional association in elderly subjects requiring early diagnosis and management to improve the vital prognosis.

Keywords: Bone marrow aplasia, pGSS, pancytopenia, medullogram, Dakar, Senegal.

INTRODUCTION

Gougerot-Sjögren's syndrome (GSS) is a non-organ specific auto-immune epithelitis that affects essentially exocrine glands characterized by an inflammation of the epithelium, in particular salivary and lacrimal epithelium, leading to oral (xerostomia) and ocular (xerophthalmia) dryness, with the possibility of extra-glandular involvement, which reflects its systemic nature [1]. It most often affects women with a female/male sex ratio of 9:1. The peak frequency of the disease is around the age of 50. Its prevalence is variable according to the data but estimated in recent studies to be between 0.01 and 0.09%, making it a rare disease [1]. It's association with bone marrow aplasia (BMA) is rare [2], the occurrence of BMA can be of various origins, in particular drug-induced related to methotrexate. We report the exceptional association of bone marrow aplasia and primary Gougerot-Sjögren's disease in an octogenarian woman (80 years).

OBSERVATION

This was an octogenarian woman followed in rheumatology since 1993 for a primary Gougerot-

Sjögren's syndrome based on joint involvement made of bilateral asymmetrical persistent non-ankylosing chronic dry polyarthritis and ocular and oral dryness, Accessory salivary gland biopsy (ASGB) at Chisholm and Masson grade 4 by the ACR/EULAR 2016 classification criteria at 7 points, she was on 15mg methotrexate/semaine, 400mg hydroxychloroquine/day for more than 23 years.

She presented at entry : Normal consciousness with a Glasgow score of 13/15 (eye opening: 5; verbal response: 3; motor skills: 5), febrile (T° 39. 5°C), heart rate at 73 beats/min, blood pressure at 100/70mnHg, normal diuresis, pallor of the integuments and conjunctivae, ecchymosis, no hepatomegaly or splenomegaly, free ganglion areas, bone pain was absent, alteration of the general condition WHO stage 3 and the rest of the somatic examination was normal.

Biological analysis finds: Pancytopenia made of aregenerative anemia (Hemoglobin at 7.2g/dl and reticulocyte count at 5934/mm3), leukopenia at 270/mm3, neutropenia at 70/mm3, lymphopenia at 15 The medullary aplasia with poor or even deserted cellularity was found based on the medullogram, but the renal, hepatic, cardiac and infectious investigations were normal. Thus, bone marrow aplasia in a patient followed for primary GSS under methotrexate for 23 years was retained. The course of action was hospitalization, transfusion of 1200ml of platelet concentrate, tramadol 50mg x 3/d in mini-infusion, Fleming (amoxicillin + clavulanic acid) 1g x2/d and Rovamycin 3 million x 2/d, unfortunately the outcome was marked by her death at D4 of hospitalization.

COMMENT

Our observation is that of a bone marrow aplasia in an octogenarian woman (80 years old) followed for primary GSS under methotrexate for 23 years which is of epidemiological, diagnostic, prognostic and therapeutic interest.

The frequency of the association of bone marrow aplasia and pGSS is poorly known, and even rare.

In Europe, in France, Liozon E *et al.*, found in Limoges 1 case of severe corticosteroid-sensitive bone marrow aplasia, revealing a Gougerot-Sjögren syndrome with monoclonal IgA in a 71-year-old female patient [3], and Quiquandon I *et al.*, described in Paris 1 case of pGSS and bone marrow aplasia in a 28-year-old patient [4].

In Asia, in China, Yu W *et al.*, reported one case of pGSS complicating pancytopenia, cerebral hemorrhage and nervous system involvement in a 49-year-old female patient [5]. In Japan, Satoh M *et al.*, described one case of pancytopenia complicating pGSS in a 78-year-old female patient [6].

In Africa, cases of bone marrow aplasia have been reported in Congo (27 cases) [7], Ivory Coast (34 cases) [8], Ethiopia (25 cases) [9], but we have not found any association with pGSS, and our observation is to our knowledge the first in sub-Saharan Africa.

Medullary aplasia is related to a quantitative insufficiency of hematopoiesis with a deficit of blood cell production responsible for an aregenerative anemia, thrombocytopenia with spontaneous cutaneous-mucosal hemorrhagic syndrome and leukoneutropenia leading to infections (peripheral pancytopenia), which implies a hypocellular bone marrow with endogenous or exogenous hematopoietic stem cell (HSC) damage [10, 11].

Our octogenarian patient with primary Gougerot Sjögren's syndrome for which she had been under immunosuppressive treatment (methotrexate) for more than two decades finally presented with the pallor of integuments and conjunctivae, fever (T° 39.5°C) and ecchymoses. These symptoms are consistent with the data in the literature that the clinical appearance is related to the severity and duration of the underlying pancytopenia.

Hemorrhagic manifestations of thrombocytopenia are early and include petechiae, ecchymosis, epistaxis and mucosal bleeding.

Neutropenia may be associated with fever, mouth ulcers and bacterial infections. But these signs are rarely present early.

Pallor, fatigue, and tachycardia are often delayed because the lifespan of erythrocytes (120 days) far exceeds that of platelets (10 days) or white blood cells (WBC) (variable, but measured in hours for granulocytes). Adenopathy, splenomegaly, and severe weight loss are rare and may suggest other underlying disorders [12,13]. The main objectives of current medical treatment of AM are to reduce complications related to cytopenias, improve quality of life and minimize adverse effects of treatment. Our octogenarian benefited from a 1200ml platelet concentrate transfusion, tramadol 50mg x 3/d in mini-infusion, Fleming (amoxicillin + clavulanic acid) 1g x2/d and Rovamycin 3m x 2/d. This is in line with the literature according to which the treatment is based on supportive care aimed at managing episodes of febrile neutropenia with appropriate antibiotic therapy, correction of anemia and thrombocytopenia with transfusions of red blood cells in case of profound or poorly tolerated anemia and platelets in case of hemorrhagic syndrome or very deep thrombocytopenia It is also based on a specific treatment which consists in the transplantation of hematopoietic stem cells in any young subject under 40 years of age with a geno-identical donor (25% in the siblings) with a survival

rate of more than 80%, and on immunosuppressive treatment with cyclosporine and anti-lymphocyte serum in any patient over 40 years of age or without a compatible donor with a survival of more than 70%, but with a risk of clonal evolution towards acute myeloid leukemia or myelodysplasia or acquisition of a paroxysmal nocturnal hemoglobinuria clone (PNH). Patients who do not respond to immunosuppressive therapy may benefit from unrelated bone marrow transplantation [14, 15].

CONCLUSION

AOS is a very serious hemopathy, its association with pGSS is rare.

Early diagnosis and management in a specialized setting improve functional and vital prognosis.

Close hematological monitoring of patients with pGSS under immunosuppressive therapy is essential, especially in elderly subjects, to meet the challenge.

Sincere Thanks

To all those who participated in the care of the patient in one way or another with a special mention to all the staff of the rheumatology department of the Dantec hospital in Dakar.

DECLARATION OF CONFLICTS OF INTEREST

No conflicts of interest.

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