Sweet’s syndrome with pulmonary involvement: Case report and literature review

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A B S T R A C T

A 74 year old female presented with fever, associated with papules and plaque in her upper and lower extremities. Exams revealed blood leukocytosis and a positive urine culture. Antibiotic therapy was initiated with no clinical response. After 1 week, chest X-ray showed right upper lobe alveolar infiltrate. A skin biopsy of the lesion showed infiltration by neutrophils, consistent with Sweet’s Syndrome. Patient’s condition progressively worsened, requiring oxygen therapy. Bronchoscopy and bronchoalveolar lavage were normal, transbronchial biopsies suggested lung involvement of Sweet’s syndrome. Anti-biotic therapy was stopped. Corticosteroid were started. Therapy resulted in rapid clinical and radiological improvement.

We report the case of a female with myelodisplastic syndrome with SS associated with pulmonary manifestations. Skin and lung biopsies revealed neutrophilic infiltrates without vasculitic changes. Respiratory involvement responded to corticosteroid therapy. A search of the literature was carried out in the Medline and Lilacs Database, using the keywords: “Sweet Syndrome”, alone and in conjunction with various terms such as “pulmonary inflammation”, “lung”. Further hand-searches were made based on the reference list of key papers. A total of 34 cases of SS with pulmonary involvement were found.

1. Introduction

Sweet’s Syndrome (SS) or acute febrile neutrophilic dermatosis is a systemic inflammatory disorder characterized by high fever, leukocytosis, and tender erythematous skin lesion. Histologically, dense dermal infiltrations of mature neutrophilic plaques with nuclear fragmentation and absences of signs of vasculitis are characteristic. Although recent reports suggest that vasculitis do not exclude SS.1-3

This syndrome typically occurs in middle-aged females. The etiology can be idiopathic (±70% of cases), parainflammatory (infection, autoimmune disorder and vaccination), paraneoplastic (hematopoietic disorders like myeloproliferative disorder, leukemia, etc).4-5

This disorder typically involves multiple organ system; pulmonary involvement in SS is quite rare. The classic pulmonary manifestations of SS described in the literature consist of bilateral infiltrates, pleural effusion and bronchiolitis obliterans – organizing pneumonia (BOOP).4-11

Systemic corticosteroid therapy is the treatment of choice for SS, achieving prompt improvement. Colchicine, indomethacin, cyclosporine and other immunosuppression therapies have been used for treatment.

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Dermatological evaluation and a skin biopsy was performed and revealed edema and dense neutrophilic infiltrates in the dermis without vasculitis. No mucosal involvement was founded. The result was consistent with SS. (Fig. 2.)

Patient’s condition progressively worsened, requiring oxygen-therapy. A videobronchoscopy with bronchoalveolar lavage (BAL) was performed, cytological and microbiological studies were negative. Antibiotic therapy was modified to imipenem, without any improvement. Amphotericin B administration was initiates as well.

Pulmonary signs did not improve on treatment with antifungal. A new chest-CT scan revealed increased alveolar infiltrates in the right upper lung with bilateral pleural effusion. A thoracocentesis was performed, consistent with a transudate.

A second videobronchoscopy with BAL and transbronchial biopsies were performed. Cytological study revealed a total cell count of 3.600 cell/ml, 72% neutrophils, 20% macrophages and 8% lymphocytes, new cultures were negative. Histopathological examination of the lung biopsy revealed extensive neutrophils infiltration with fibrin at the alveolar level, edema and focal acute and organizing pneumonia. (Fig. 3). This histological findings were similar to the one performed in the skin.

Antifungal therapy was stopped. The patient was treated with methylprednisolone (500 mg IV for 3 days) followed by oral prednisone. Steroid therapy produced a rapid improvement of cutaneous and pulmonary involvement. Patient had rapid clinical and radiographic resolution. After 2 weeks of therapy, erythematous plaques and skin lesions decreased. No recurrence was observed and chest CT scan showed a substantial improvement.

3. Discussion

The SS was described by Robert Douglas Sweet in 1964, typical manifestations are cutaneous lesion and clinical symptoms improve after treatment with systemic steroids. Extra cutaneous symptoms associated with SS are commons, occurs in ±40% of clinical presentations. Fever, arthritis, musculoskeletal and ocular involvements such as conjunctivitis, uveitis, episcleritis have been reported frequently in literature.1,2

Pulmonary involvement is very rare, in our review of 34 cases, the ratio man: female was 1:1, the age average is 57 years – old (±14 years old, range 25–82 years old). In 18 cases hematological disorders such as myelodisplastic syndrome, myeloproliferative disorder, agnogenic myeloid metaplasia, refractory anemia with excess blasts and idiopathic thrombocytopenia were present. Eight cases of SS with pulmonary involvement were in previously healthy people.3,10,12,14,16,17,23,27 Summary of demographic, clinical, diagnosis, treatment and outcome of cases reported in literature are shown in Table 1.2–30

Skin involvement was the first manifestation in 16 of 34 cases. Typical symptoms are erythematous plaques and nodules, which may be recurrent and painful. Typical skin biopsy showed a dense infiltrate of neutrophils, primarily in dermis, associated to edema without vasculitis. In 12 of 34 cases, skin lesions and pulmonary involvements are simultaneous. If there is pulmonary involvement, it usually manifests with dry cough and dyspnea.11

Chest X-ray may reveal diffuse pulmonary infiltrated or pleural effusion, chest-CT usually confirms pulmonary involvement. Videobronchoscopy usually is normal. Bronchoalveolar lavage reveals high neutrophil (> 50%) without organism in 14 cases. We did not find data of bronchoalveolar lavage in 20 cases, specially, cases reported before 1996.2–7,9–14 Transbronchial biopsy frequently shows intraalveolar dense infiltration by neutrophils, similar to skin biopsies. In 15 of 24 cases, lung biopsies revealed interstitial inflammation, edema and alveolar infiltration by large number of neutrophils. In 10 cases the diagnosis was performed without biopsy, and in 9 cases by skin biopsy only.2,9,13,19,25–28,30

Systemic corticosteroid therapy is the treatment of choice for SS with pulmonary involvement, high doses of oral or intravenous
corticosteroids decrease symptoms with prompt improvement. Immunosuppression with colchicine, cyclosporine and other drugs have been used for therapy. In our review, 32 cases were treated with prednisone; the combination with other immunosuppressive therapy was reported in 6 cases, typically with dapsone or colchicine.

The outcome of SS with pulmonary disease is good, only 5 patients died (with ARDS) and 2 patients had a recurrence of the disease. The most common outcome in SS with pulmonary disease is clinical and radiographic resolution.

Our patient presented an SS with pulmonary involvement with a medical history of myelodysplastic syndrome, an association

**Table 1**

| Reference | Year | Sex | Age | Comorbidities | Presentation | Bal | Radiology | Biopsy | Treatment | Outcome |
|-----------|------|-----|-----|---------------|--------------|-----|-----------|--------|-----------|---------|
| Soderstrom RM | 1981 | F   | 50  | AML           | S → P        | ND  | Unilateral infiltrate + effusion | Extensive PMN infiltrate | S        | 1       |
| Gibson LE | 1985 | F   | 66  | AMM           | S → P        | ND  | Bilateral infiltrate              | S                   |         | 1       |
| Rodriguez de la Serna A | 1985 | F   | 68  | Dresser's Syndrome | B         | ND  | Unilateral infiltrate + effusion | S + Dapsone           |         | 1       |
| Lazarus AA | 1986 | M   | 60  | AML           | B            | ND  | Unilateral infiltrate              | Chronic interstitial pneumonitis + neutrophilic infiltrate | S        | 1       |
| Keefe M | 1988 | F   | 67  | PP            | B            | ND  | Unilateral infiltrate              | Extensive PMN infiltrate + pleural and perivascular fibrosis | S        | 1       |
| Hatch ME | 1989 | M   | 45  | CML           | S → P        | ND  | Bilateral infiltrate              | S                   |         | 1       |
| Cohen PR | 1989 | F   | 61  | CML           | B            | ND  | Bilateral infiltrate              | S                   |         | 1       |
| Bourke SJ | 1991 | F   | 72  | None          | S → P        | 91% neutrophils | Bilateral infiltrate | Interstitial infiltrate + neutrophilic infiltrate | S        | 1       |
| Takimoto CH | 1991 | M   | 54  | MDS           | B            | ND  | Unilateral infiltrate              | Extensive PMN infiltrate + neutrophilic infiltrate | S        | 1       |
| Chien SM | 1991 | M   | 58  | None          | P → S        | ND  | Unilateral infiltrate              | Extensive PMN infiltrate + neutrophilic infiltrate | S        | 1       |
| Komiyaji | 1991 | M   | 54  | RAEB          | B            | ND  | Unilateral infiltrate              | Extensive PMN infiltrate + neutrophilic infiltrate | S        | 1       |
| Fett DL | 1995 | M   | 35  | ITP           | B            | ND  | Bilateral infiltrate + effusion   | Mixed interstitial pneumonitis | S        | 1       |
| Fett DL | 1995 | M   | 46  | DM            | B            | ND  | Bilateral infiltrate + effusion   | Mixed interstitial pneumonitis | S        | 1       |
| Fett DL | 1995 | M   | 61  | MPD           | B            | ND  | Bilateral infiltrate + effusion   | S                   |         | 1       |
| Fett DL | 1995 | M   | 74  | RAEB          | B            | ND  | Bilateral infiltrate + effusion   | S                   |         | 1       |
| Reid PT | 1996 | M   | 34  | None          | P → S        | ND  | Unilateral infiltrate              | Intestinal pneumonitis, cryptogenic organizing pneumonia | S        | 1       |
| Rodot S | 1996 | F   | 63  | AML           | S → P        | 78% neutrophils | Bilateral infiltrate | Neutrophilic infiltrate in skin biopsy | S        | 1       |
| Thurnheer R | 1997 | F   | 62  | None          | S → P        | ND  | Bilateral infiltrate              | Neutrophilic infiltrate in skin biopsy | S        | D       |
| Peters FJP | 1998 | F   | 48  | RAEB          | P → S        | ND  | Unilateral infiltrate              | Interstitial pneumonitis | S + Chemo | 1       |
| Katsura H | 1999 | F   | 70  | Sjogren       | P → S        | ND  | Unilateral infiltrate              | Neutrophilic infiltrate in skin biopsy | S + Chemo | 1       |
| Alberts | 2000 | F   | 72  | MDS           | B            | 90% neutrophils | Unilateral infiltrate | Neutrophilic infiltrate in skin biopsy | S + Chemo | 1       |
| Imanaga T | 2000 | M   | 55  | None          | S → P        | Neutrophils | Bilateral infiltrate | Chronic interstitial infiltrate + neutrophilic infiltrate | S + Cyclo | 1       |
| Longo MI et al | 2001 | M   | 51  | None          | S → P        | Neutrophils | Unilateral infiltrate | Intestinal pneumonitis, cryptogenic organizing pneumonia | S + Cyclo | 1       |
| Astudillo L et al | 2006 | M   | 62  | MDS           | S → P        | 30% neutrophils | Interlobular septal thickening | S                   |         | 1       |
| Gard R et al | 2006 | F   | 25  | MPD           | B            | Neutrophils | Unilateral infiltrate + effusion | Bronchiolitis obliterans organizing pneumonia | S + Dapsone | 1       |
| Petrig C | 2007 | M   | 67  | CML           | P → S        | Neutrophils | Bilateral infiltrate | Neutrophilic infiltrate in skin biopsy | S + Dapsone | 1       |
| Fulton JC | 2007 | M   | 25  | None          | S → P        | Neutrophils | Bilateral pulmonary nodules | S                   |         | 1       |
| Kushima H et al | 2007 | F   | 73  | Previous SS   | S → P        | Neutrophils | Unilateral infiltrate | Chronic interstitial infiltrate with alveolar wall thickening and neutrophils | S + Dapsone | 1       |
| Aydemir | 2008 | M   | 32  | CLD           | S → P        | 60% neutrophils | Bilateral infiltrate | Neutrophilic infiltrate in skin biopsy + vasculitis | S + Dapsone | 1       |
| Lawrence K | 2008 | M   | 54  | Hypertention  | S → P        | ND  | Unilateral infiltrate              | Neutrophilic infiltrate in skin biopsy | S        | 1       |
| Gaspar C | 2008 | F   | 76  | IgA Myeloma   | S → P        | ND  | Neutrophilic infiltrate in skin biopsy | S                   |         | 1       |
| Robbins C et al | 2009 | F   | 26  | S → P        | Neutrophils | Interstitial + nodule | Neutrophilic infiltrate in skin biopsy | S + Colchicine | 1       |
| Aparicio V. et al | 2010 | M   | 67  | Hypertention  | S → P        | Neutrophils | Unilateral infiltrate | Neutrophilic infiltrate in skin biopsy | S + Dapsone | 1       |
| Our case | 2011 | F   | 74  | MDS           | S → P        | 72% neutrophils | Unilateral infiltrate + effusion | Neutrophilic infiltrate in skin and lung biopsy | S       | 1       |

AMM: Agnogenic myeloid metaplasia; AML: Acute myeloid leukemia; B: Both; CML: Chronic myeloid leukemia; CLD: Chronic liver disease; Chemo: Chemotherapy; Cyclo: Cyclophosphamide; D: Death; DM: Dermatomyositis; F: Female; I: Improvement; ITP: Idiopathic thrombocytopenia; M: Male; MDS: Myelodysplastic syndrome; MPD: Myeloproliferative disorder; PP: Plantar pustulosis; P → S: Skin after pulmonary; RAEB: Refractory anemia with excess blasts; S: Steroids; S → P: Pulmonary after skin.
commonly seen. Poor response to antibiotic and clinical compro-
mised was characteristic. BAL result and lung transbronchial biopsy
revealed extensive neutrophil infiltrates. Prompt improvement of
symptoms and pulmonary involvement with corticosteroid therapy
in combination with skin and lung biopsies confirmed the diagnosis.

In conclusion, SS with pulmonary involvement is rare. Recog-
nition of Sweet’s Syndrome with lung involvement is important to
prevent severe respiratory compromise.

Conflict of interest

None.

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