Case 23.1

A 23-year-old Thai female from Suratthani

Chief complaint: Atypical target lesions turning to erythroderma with mucocutaneous erosions for 6 weeks

Fig.23.1-1

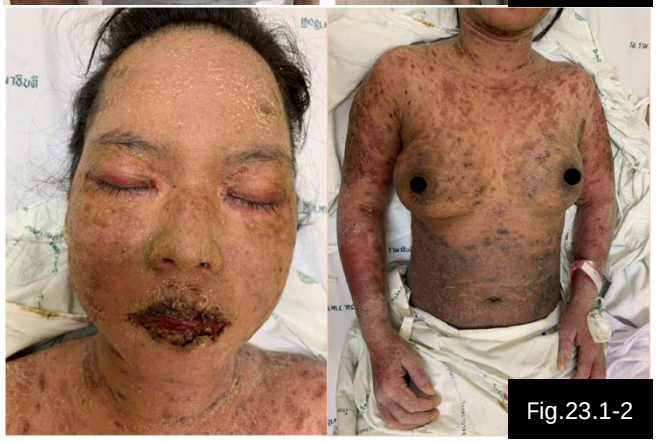

Fig.23.1-2

Present illness:

She developed atypical target lesions on her face, trunk, and upper extremities together with oral erosions (Fig. 23.1-1), a low-grade fever, and dry cough for 4 weeks. She was admitted to a provincial hospital and the skin biopsy was performed on the left thigh. The provisional diagnosis was erythema multiforme. Intravenous acyclovir and oral azithromycin were prescribed without improvement. In addition, intravenous dexamethasone 20 mg daily for 5 days, and later converted to oral prednisolone (15 mg/day) was administered. Two weeks later, the lesions transformed into generalized scaly erythroderma (Fig. 23.1-2) with severe oral and genital erosions. She was subsequently transferred to Ramathbodi hospital and the 2nd skin biopsy was performed on the chest.

Past history: No underlying disease

Family history: No family history of malignancy

Physical examination:

- V/S: BT 37.3°C, BP 130/70 mmHg, PR 90/min, RR 20/min
- HEENT: Bilateral conjunctival injection, no icteric sclerae
- Heart: Normal S1 S2, no murmur
- Lung: Normal breath sound
- Abdomen: Soft, no hepatosplenomegaly
- Lymph nodes: Impalpable

Dermatological examination:

- Scaly hemorrhagic crusted erosions on both upper and lower lips, mild erosion on bilateral buccal mucosa
- Generalized erythema with widespread scale-crusts on the trunk and all extremities, together with mild erosions on the genital site

Histopathology (S18-041197, chest):

- Interface dermatitis with lymphocytes, melanophages and necrotic keratinocytes
- Foci of suprabasal cleft and acantholytic keratinocytes (Fig. 23.1-3)

Direct immunofluorescence (DIF):

- Intercellular staining of IgG and C3
- Mixed linear and granular deposition along dermoepidermal junction of C3 (Fig. 23.1-4)

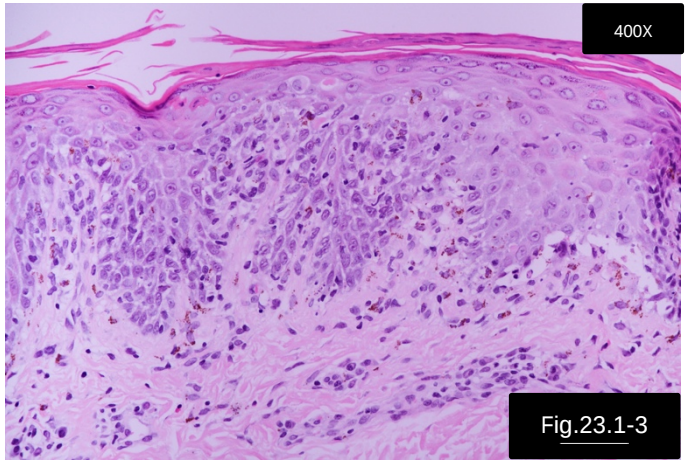

Fig.23.1-3

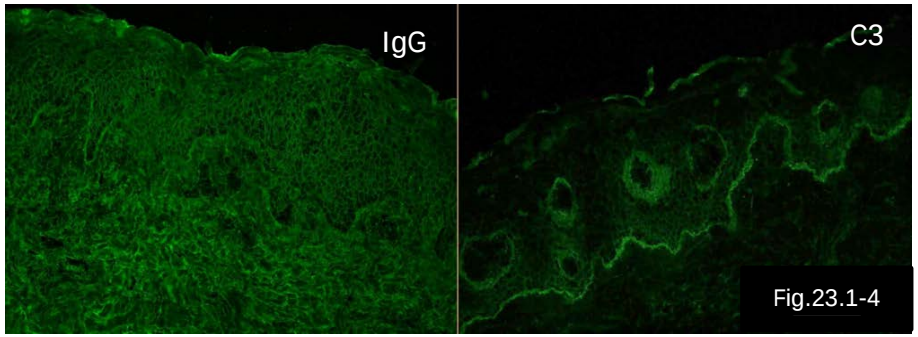

Fig.23.1-4

Laboratory investigations:

- CBC: Hb 12 g/dL, Hct 37%, Plt 507,000 /mm^3, WBC 10,600 /mm^3 (N 77%, L 11%, M 7%)
- AST/ALT: 18/14 U/L
- BUN/Cr: 10/0.5 mg/dl
- Blood samples for HSV type 1 and 2 DNA, VDRL, TPHA, and *Mycoplasma* titer: all negative
- **Anti-desmoglein 1: 47.97 U/mL and anti-desmoglein 3: >200 U/mL, (0-20 U/mL)**
- **Anti-BP180: >200 RU/mL** and Anti-BP230: 10.9 RU/mL, (0-22 RU/mL)
- **Indirect immunofluorescence study: positive circulating IgG anti-transitional epithelia**

CT with contrast of the chest and abdomen: A 6.7 x 5.5 cm, markedly enhancing oval-shaped structure at the left para-aortic region surrounded by dilated vessels with mild left hydronephrosis and mild hepatosplenomegaly

Intervention/Pathological result: She underwent the exploratory laparotomy with a tumor removal. The pathological findings were compatible with hyaline-vascular type Castleman's disease.

Diagnosis: Paraneoplastic pemphigus (PNP) with Castleman's disease (CD)

Treatment:

- Prednisolone 15 mg/day
- Intravenous immunoglobulin (IVIG) with a dose of 2 g/kg was infused every 4 weeks (3 cycles)
- Infection control
- Dressing wound with hydrocolloid dressing with silver sulfadiazine

Case 23.2
A 58-year-old Thai female from Nonthaburi
Chief complaint: Severe multiple mucocutaneous erosions for 3 weeks


Fig.23.2-1

Present illness:
She initially had itchy rash on scalp, chest and extremities. Later on, the rash progressed became desquamation especially on her trunk. She also had newly developed painful bilateral conjuntivitis, orogenital erosions, and multiple erosions on buccal mucosa for 3 weeks. She was diagnosed with toxic epidermal necrolysis and admitted to a provincial hospital. Dexamethasone and ceftriaxone were given without improvement Therefore; she was transferred to Ramathbodi hospital.

Past history:
- Underlying diseases include hypothyroid, hypertension, and dyslipidemia
- 6 months ago, she found retroperitoneal mass suspected lymphoma or sarcoma and had a surgical planning for tumor excision

Family history: No family history of malignancy
Current medications: Atenolol, simvastatin, losartan, levothyroxine
Physical examination:
- V/S: BT 38°C, BP 130/60 mmHg, PR 70/min, RR 20/min
- HEENT: Mild pale conjunctivae, anicteric sclerae, multiple erosions with hemorrhagic crust on both upper and lower lips, buccal mucosa and hard palate
- Heart: Normal S1 S2, no murmur
- Lung: Normal breath sound
- Abdomen: Soft, palpated mass at left upper abdomen
- Lymph nodes: Impalpable

Dermatological examination:
- Widespread erosions with bleeding on the scalp, trunk and all extremities
- Multiple erosions with hemorrhagic crust involving vermillion border of lips, buccal mucosa, hard palate and genital mucosa (Fig.23.2-1)

Histopathology (S18-37921, left leg):
- Suprabasal separation and intraepidermal vesicle with acantholytic cells (Fig.23.2-2)

Direct immunofluorescence (DIF): Intercellular staining of IgG and C3. Mixed linear deposition along dermoepidermal junction of C3 (Fig.23.2-3)

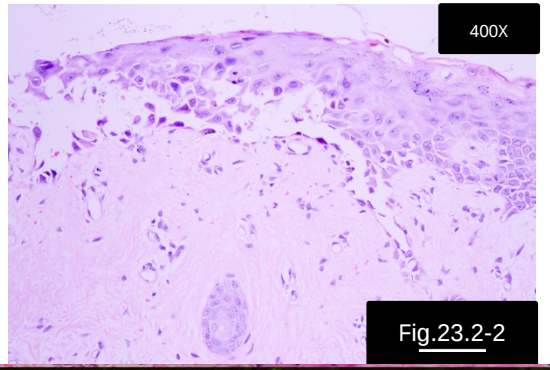

Fig.23.2-2

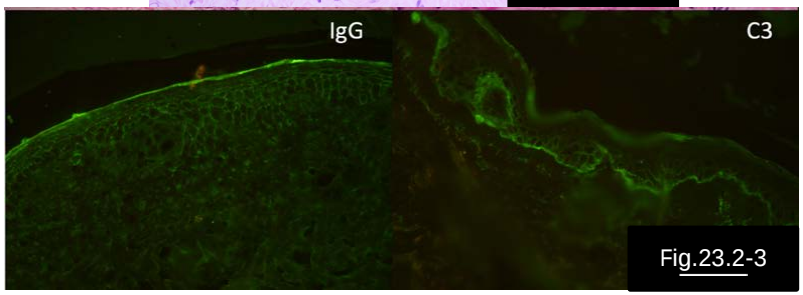

Fig.23.2-3

Laboratory investigations:

- CBC: Hb 11 g/dL, Hct 36.5%, Plt 96,000 /mm^3, WBC 3,600 /mm^3 (N 68%, L 18%, M 7%, E 7%)
- AST/ALT: 37/5 U/L
- BUN/Cr: 11/0.4 mg/dl
- **Anti-desmoglein 1: 149 U/mL and anti-desmoglein 3: >200 U/mL, (0-20 U/mL)**
- Anti-BP230: 4 RU/mL (0-22)

Computed tomography (CT) whole abdomen: Homogeneous infiltrative retroperitoneal lesion and fibrosis encircling along aorta, inferior vena cava and bilateral ureters, resulting in bilateral hydronephrosis

Diagnosis: Paraneoplastic pemphigus (PNP) with retroperitoneal mass

Treatment:

- Prednisolone 15 mg/day
- Intravenous immunoglobulin (IVIG) with a dose of 2 g/kg
- Infection control
- Dressing wound with hydrocolloid dressing with silver sulfadiazine

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Discussion:

Paraneoplastic pemphigus (PNP) is a life-threatening autoimmune blistering disorder which can be associated with hematologic and to a lesser extent solid-organ malignancies; including non-Hodgkin's lymphoma (38.6%), chronic lymphocytic leukemia (18.4%), Castleman's disease (CD) (18.4%), thymoma (5.5%), carcinomas (8.6%), and sarcomas (6.2%).[1,2] In adult patients, CD is the third most common neoplasm associated with PNP followed by non-Hodgkin's lymphoma and chronic lymphocytic leukemia.[3] Moreover, one-third of patients have an occult malignancy concomitantly with the presence of skin lesions.

The pathogenesis of PNP has not been fully understood. It could be that lymphoid neoplasms cause immune dysregulation leading to autoantibody production and immune cross-reaction against tumor within the epidermal cell surface antigens such as envoplakin, periplakin, desmoplakin1, desmoplakin2, desmoglein3.[4] Also interferon (IFN)-gamma, IFN-omega, interleukin (IL)-6, and IL-12 were demonstrated as playing crucial roles in the pathogenesis.[5,6]

Various cutaneous manifestations of PNP can be presented including erythematous macules and blisters, pemphigus-like, bullous pemphigoid-like, erythema multiforme-like lesions, and lichenoid eruptions, as well as graft-versus-host-like eruptions.[7] Interestingly, painful intractable hemorrhagic stomatitis is a hallmark feature of this disorder. Furthermore, the erosions can involve the conjunctivae and anogenital regions.[8]

Establishing the diagnosis for PNP can be difficult, often requiring several biopsies. Histopathological features vary but correspond well to the type of skin lesions presented such as epidermal acantholysis, suprabasal cleft formation, dyskeratotic keratinocytes, vacuolar changes in the basal epidermis, and epidermal exocytosis of inflammatory cells.[1] In addition, direct immunofluorescence study on a perilesional skin is useful for the diagnosis. It not only shows IgG and C3 deposition in the epithelial intercellular spaces but also reveals granular-linear complement along the basement membrane zone.[9] Indirect immunofluorescence study from rat bladder epithelium exhibits intercellular IgG staining at transitional epithelium.

Total tumor removal is a mandatory management to achieve the remission of PNP. The first line treatments are systemic corticosteroids (prednisolone 0.5-1 mg/kg/day) and rituximab.[10] The second line treatments are mycophenolate mofetil, cyclosporin A, cyclophosphamide, plasmapheresis and immunoglobulin (IVIG). However, the overall prognosis of PNP is poor. The major causes of death include bronchiolitis obliterans followed by sepsis and gastrointestinal bleeding.[11]

In summary, we present two cases of PNP with CD and with retroperitoneal mass suspected for lymphoma or sarcoma. The former was presented with atypical target lesions turning to erythroderma and the latter demonstrated a TEN-like presentation. Both patients showed severe mucocutaneous erosions. They received systemic corticosteroids and IVIG, however, nevertheless they died from sepsis complications

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