Pyoderma gangrenosum, acne, hidradenitis suppurativa and arthralgia: PASH or PAPA syndrome?

Auto-inflammatory diseases (AIDs) are a group of disorders characterized by the dysregulation of innate immune system and the absence of circulating autoantibodies and autoreactive T-cells. The AIDs characterized by neutrophilic dermatoses includes PAPA (pyogenic arthritis, pyoderma gangrenosum (PG) and acne), PASH (PG, acne and hidradenitis suppurativa), PAPASH (pyogenic arthritis, acne, PG and hidradenitis suppurativa), PASS (pyoderma gangrenosum, acne and sterile spondyloarthritis), PsAPASH (psoriatic arthritis, PG, acne, and hidradenitis suppurativa) and PAC (PG, acne, and ulcerative colitis).

PASH syndrome is an autoinflammatory syndrome distinct from PAPA syndrome due to lack of intensive joint inflammation. At present, there have been only 14 cases reported worldwide. According to the Philippine Dermatologic Society (PDS) central registry from 2011-2016, this is the only recorded case of PASH syndrome.

As a dermatologist, it is important that we be able to distinguish between the different auto inflammatory syndromes. Early diagnosis and management of these patients can prevent morbidity and improve the quality of life of patients. We report a rare case of PASH syndrome who dramatically improved with oral corticosteroids and dapsone.

We present a case of a 20-year-old woman of Filipino descent born in a non-consanguineous parents with a three-month history of non-healing crusted ulcers. It started as a solitary pustule located at the right arm that progressed to a plaque, which eventually ulcerated. It was noted to be pruritic and tender. It was associated with fever and symmetric polyarthralgia involving the wrists, elbows and ankles. No other family members presented with similar manifestations. Patient applied herbal liniment and self medicated with amoxicillin 500 mg/tab one tablet thrice a day with no relief. She was also seen by several physicians, given oral and topical antibiotics that didn’t seem to seem to improve her condition.

Examination revealed multiple erythematous papules, plaques, nodules, pustules, with open and closed comedones on the face (Figure 1A); hyperpigmented nodules and ulcers on the buttocks and posterior thigh (Figure 1B); erythematous, nodules and ulcers with rolled violaceous borders topped with thick yellow crusts located on the shoulders, upper and lower extremities (Figure 2A). Pathergy test was done on the volar surface of the right forearm, which revealed a pustular formation on the site after 48 hours.

Hematologic test showed elevated white blood cell of 17.55 x 10^9/uL (normal: 5-10 x 10^9/uL), predominantly neutrophilia at 82%. Erythrocyte sedimentation rate and c-reactive protein were also elevated. The hepatic and renal function test were within normal limits. Urinalysis and chest radiograph were unremarkable. Blood and wound cultures and KOH showed no growth. Purified protein derivative (PPD) tests done on 48th and 72nd hour was also negative. Antinuclear antibody (ANA) was negative.

Histopathology revealed dense inflammatory infiltrates containing predominantly neutrophils in the dermis and subcutaneous layer, which was consistent of neutrophilic dermatosis (Figure 3).

Among the different auto inflammatory syndromes, the closest differential was PAPA syndrome. Since we could not establish the presence of pyogenic sterile arthritis, we
managed the patient as a case of PASH syndrome.

Patient was started with prednisone at 20 mg/day (0.5 mg/kg/day) which was the lowest effective dose, for five months and it was gradually tapered. In addition, benzoyl peroxide 5% gel, adapalene 0.1% gel and doxycycline 200 mg/day for four months which showed resolution of acne lesions. There was improvement in the ulcers however joint pains persisted. Dapsone 50 mg/day was added after five months of prednisone as steroid-sparing, after a normal G6PD test. The dosage of dapsone was slowly increased to 200 mg daily while tapering prednisone at 5 mg daily for 1 month (Figure 2B). The skin and joint manifestations showed significant improvement after 6 months of treatment, with no recurrence after 1 year of follow-up.

PASH syndrome was first reported in 2012 and it was differentiated from PAPA syndrome because of the absence of pyogenic arthritis and absence of mutation in the PSTPIP1 gene. However, recently there was 1 reported case of PASH that has a PSTPIP1 gene mutation.5

Mutation on the PSTPIP1 gene leads to the increased binding affinity to pyrin therefore causing overproduction of IL-1ß. There will be uncontrolled release of pro-inflammatory cytokines such as IL-17, causing recruitment and activation of neutrophils.6 The diagnosis of PASH syndrome is based on its clinical features. Similar findings with PAPA syndrome, includes biopsy result showing neutrophilic infiltration and negative wound cultures.1

Corticosteroid may play an important role in the early treatment of AIDs.7 However, if treatment with a single agent is unsuccessful, another treatment option is to use combination treatment with TNF inhibitors and dapsone and/or cyclosporine.8 Other managements of PASH syndrome includes the combination of surgery and antibiotic therapy.9

Ideally, this case would be more interesting if we were able to perform a gene mutation study since PASH syndrome can also present with a heterozygous missense mutation in the PSTPIP1 gene, same with PAPA syndrome. In conclusion, we present a rare case of PASH syndrome, that presented with the typical clinical triad. We successfully treated the patient with prednisone and dapsone.

**REFERENCES**


