LETTER TO THE EDITOR

ANCA positive propylthiouracil induced pyoderma gangrenosum

Drugs from almost every class of pharmaceutic agent have been reported to cause vasculitis.

Vasculitis among patients taking propylthiouracil (PTU) has been reported since 1950s (1) but relation of p-ANCA positive vasculitis in patients with hyperthyroidism on PTU treatment was first reported by Stankus and Johnson in 1992 (2).

In majority of the cases, approximately 80%, pyoderma gangrenosum (PG) has been associated with systematic diseases such as ulcerative colitis, Crohn's disease, rheumatoid arthritis, Behcet's syndrome, monoclonal gammapathy (especially IgA) and chronic myeloid leukemia (3). There were also rare reports about drug induced PG reported to associate with iodide, bromide, isotretinoin, granulocyte colony stimulating factor and granulocyte-macrophage colony stimulating factor (4). PTU induced p-ANCA associated PG has been first reported by Darben et al. (5) in 1999. Hong et al. (6) reported second case in 2004. Here we report another case of PG in a p-ANCA positive patient treated for years with PTU for hyperthyroidism due to Graves' disease.

A 52-yr-old female patient was admitted to an endocrinology outpatient clinic with the diagnosis of Graves' disease and ulcerated skin lesions on both her lower extremities. She had also had intermittent joint pain on wrists, elbows, knees, shoulders and spine for 3 months but there were no signs or symptoms of arthritis. She had been on PTU treatment for 2 yr and in the remission period of Graves' disease in the last 6-month period. The patient had no history or symptoms of malignancy, infectious disease or inflammatory bowel disease. On physical examination, thyroid gland was diffusely enlarged. There were spontaneously healed scar lesions and 3 to 10 cm diameter round necrotic ulcers on both legs, the surfaces of which were filled with blood, pus and granulation tissue. The patient stated that these lesions had begun as painful red-blue nodular lesions then pustulated to skin as a progressively enlarging ulcer and healed with scarring. PTU treatment was stopped and her joint pain improved in the following days. Skin biopsy from edge of ulcers showed that there were prominent neutrophilic infiltrations and evidence of leukocytoclasis in small blood vessels in papillary dermis. There was no obvious evidence of bacterial or fungal infections. The diagnosis was PG in both dermatological consultation and pathological examination. We treated our patient with 60 mg/day of prednisolone. Wound healing was observed by the end of 3 weeks and steroid treatment was tapered. The steroid treatment was stopped at the end of second month. Complete healing with scarring was achieved at the end of therapy. In 12 months follow-up period, there was no relapse in both dermal lesions and Graves' disease.

Kitahara et al. (7) reported that in 19-PTU induced P-ANCA positive vasculitis cases, females were more dominantly affected and also in most of the cases vasculitis appeared after a few years of medication. In both Darben's and Hong's reports, cases were female and treatment periods were 3 and 2 yr, respectively, similar to our case.

Darben et al. (5) reported that P-ANCA, on antigen specific ELISA showed mixed specificities to include IgM myeloperoxidase (MPO), IgG elastase and lactoferrin. Hong et al. (6) confirmed these multiple antigenic specificities. Elastase and lactoferrin specific P-ANCA have been considered as possible markers for drug-induced autoimmune disorders in the literature (8). The role of PTU in the pathogenesis of PG is still unknown. ANCA positive interstitial pneumonia lung lesions, adult respiratory distress like syndrome, pleural effusions, alveolar hemorrhage, cavitary lung lesions (9), pericarditis (10) and nephritis (11) were also reported in patients on PTU treatment. The inflammatory and immunologic effects that have been attributed to ANCA include activating primed neutrophils to degranulate to produce oxygen free radicals, increasing expression of adhesion molecules on both neutrophils and endothelial cells, stimulating the release of interleukin-8 and interfering with control of the enzyme activities of these target antigens (6). All these complications should also be accepted as indirect evidence of these mechanisms. Further studies are needed to clarify the role of PTU in conjunction with ANCA in the pathogenesis of these complications.

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