Chronic Urticaria and IgA Myeloma

Sir,

Paraproteins that result from a monoclonal proliferation of immunoglobulin-secreting B lymphocytes are associated with a wide variety of skin disorders (1, 2). Urticaria is, in some cases, associated with the presence of a monoclonal component. The association of a monoclonal IgM gammopathy with chronic urticaria is well known, and is a defining feature of Schnitzler's syndrome (3). Recently, Nashan et al. (4) reported a patient who developed chronic urticaria, arthralgia, a raised erythrocyte sedimentation rate and IgG paraproteinaemia. They believed their patient to have an IgG variant of Schnitzler's syndrome. We report a patient who developed chronic urticaria in the setting of an IgA myeloma. The two events were closely linked on the basis of chronology and evolution, therefore reinforcing the possible link between monoclonal gammopathies and some cases of chronic urticaria.

CASE REPORT

A 46-year-old male patient was referred to the dermatology department with a 5-year history of intermittent, antihistamine-resistant urticaria. When urticaria was diagnosed, laboratory investigations showed a normal blood count and a slightly increased erythrocyte sedimentation rate (ESR) of 25 mm/h. As urticaria persisted, his attending physician repeated those investigations every year, showing a steady increase in the ESR. When he was referred to us, the ESR was 100 mm/h. He was in good general condition and had erythematous, oedematous, and sometimes annular plaques, mainly on his arms, buttocks and trunk. Individual weals were pruriginous and resolved within 12 h. Purpura was never observed. He related 2 episodes of angio-oedema. Otherwise, his examination was unremarkable.

Laboratory investigations. C-reactive protein and complement levels (CH50, C3 and C4 fractions) were within normal range. Serum protein immunoelectrophoresis showed an IgAλ monoclonal spike. The serum IgA level was 33.7 g/l (normal range: 1.04 – 3.32), the IgG level 4.6 g/l (normal range: 6 – 12) and the IgM level 0.13 g/l (normal range: 0.57 – 1.63). Bence-Jones proteinuria was present (1.6 g/24 h). Bone marrow examination revealed important plasmocytosis (31.6%). An extensive work-up excluded autoimmune or infectious diseases as causative agents for the urticaria. Total blood count, serum calcium, renal, hepatic and thyroid function and skeletal X-rays were normal.

The patient was then referred to the Haematology department where he was treated with intense chemotherapy (high-dose methylprednisolone, high-dose cyclophosphamide and 3 cycles of vincristin, adriamycine and methylprednisolone) and then conditioned with etoposide, cyclophosphamide and alkeran for autologous stem cell bone marrow transplantation after total body irradiation. His urticaria resolved after the first cycle of high-dose cyclophosphamide, when his monoclonal IgA gammopathy was below 12 g/l. It did not reappear one year after bone marrow transplantation, in the absence of any treatment, and the patient remains in complete remission.

DISCUSSION

In this case report, chronic urticaria seems to have appeared simultaneously with an IgAλ myeloma. The treatment of the myeloma was also effective for the urticaria. Although this finding can be related to effects of immunosuppressive treatment other than suppression of paraproteinaemia, urticaria did not reappear within one year of follow-up in the absence of any treatment. These findings suggest a link between the IgA myeloma and the urticaria.

Chronic urticaria has already been associated with monoclonal gammopathies, mainly of the IgM isotype, defining Schnitzler's syndrome (3). In this situation, evolution is usually long-term and benign, although in some cases true lymphoma has developed (5). Pathogenesis of the urticaria is unclear, but seems to be related at least in part to the skin deposition of the monoclonal component, as attested by direct immunofluorescence findings (6). We found only one case report suggesting a link between IgA myeloma and urticaria (7). In this case report, the histology was said to represent "acute vasculitis", and this patient had a reduction in total haemolytic complement, which was not the case in our patient. Unfortunately, no skin biopsy was performed in our patient.

We think that in certain circumstances, monoclonal gammopathies can be associated with chronic urticaria, independent of the immunoglobulin isotype. Whether this link is purely epidemiological or causative, as suggested by some direct immunofluorescence studies (6), remains yet to be established. Nevertheless, the exploration of chronic urticaria should include serum immunoelectrophoresis, especially when fever, bone pain, arthralgia or elevated ESR are present.

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