Cutaneous polyarteritis nodosa and common variable immunodeficiency: a previously unreported association

Sirs,

Cutaneous polyarteritis nodosa (c-PAN) is a necrotising inflammation of small and medium-sized vessels limited to the skin. It is characterised by subcutaneous painful nodules on the lower extremities, with no systemic involvement except for fever, myalgia, arthralgia (1). Skin biopsy shows necrotising non-granulomatous vasculitis. The cause of c-PAN is unknown. Infectious agents have been associated with the disease (2).

While vasculitis has been related to immunodeficiencies in adults, paediatric reports in this regard are scant. We describe a child with c-PAN and common variable immunodeficiency (CVID), followed in our Unit.

A 2-year-old Caucasian girl, after three weeks of intermittent fever and cutaneous erythematous, painful nodular lesions on feet, ankles and pretibial regions, was admitted to a community hospital. Her family and personal history were negative. No severe infections were noted in past medical history; vaccinations had been performed against diphtheria, tetanus, pertussis, and Hepatitis B; growth and development were within normal limits for age. Laboratory test showed anaemia (Hb=9.9 g/dl), increased ESR (86 mm/h) and CRP (4.10 mg/l), while ANA, ENA, RF, AST, ALT, IgG, IgM, IgA, complement fractions, cANCA, pANCA, and general biochemical profile were normal or negative. Infectious diseases were ruled out. For the persistence of clinical features a skin biopsy was performed and showed a necrotising non-granulomatous vasculitis. The diagnosis of c-PAN was made and treatment with methotrexate (MTX, 15 mg/m^2/week subcutaneously), and prednisone (2 mg/kg/day) was started. After about one year of well-being she was referred to our Unit for daily fevers and a persistent vasculitic rash at lower extremities despite treatment with MTX and prednisone. MTX was switched to azathioprine (AZA, 3 mg/kg/d), with good clinical control in 4 months, so that steroids were discontinued. Eight months later, laboratory test showed hypogammaglobulinaemia (IgA 29.4 mg/dl, normal values for age ± SD 93±27 mg/dl; IgM 28 mg/dl, normal values 56±18 mg/dl; IgG 571 mg/dl, normal values 929±228 mg/dl). A poor humoral response to vaccines (hepatitis B, tetanus, dyphtheria) was shown. Nevertheless, immunosuppressive therapy made it difficult to evaluate whether the hypogammaglobulinemia was related to the current therapy, or if this was the onset of a CVID. Due to the persistent remission of c-PAN on therapy, AZA was progressively stopped. The girl remained in good clinical conditions, with laboratory tests in the normal range except for a partial only improvement of immunoglobulin values (IgG low-normal, with persistence of IgA, and IgM deficiency). After several months, hypogammaglobulinaemia persisted, thus excluding a potential side effect related to AZA treatment. Other well known causes of hypogammaglobulinemia were excluded (3), and the diagnosis of CVID was made. Six months later, she presented again with myalgia, arthalgia, livedo reticularis, vasculitic lesions on feet, and some nodular lesions on the right leg. Therefore, AZA was restarted in addition to intravenous immunoglobulins (IVIG) every 4 weeks (2 gr/kg) for disease control (4). At last follow-up, after 6 years, her c-PAN is in clinical and laboratory remission on AZA only. IVIG treatment is still needed as replacement therapy (400 mg/kg monthly), due to her CVID. Of note, during her long-term follow-up at our Unit, she never developed any major infection.

About half of the individuals with CVID exhibit one or more forms of autoimmune phenomena. In the literature, some cases of vasculitis and immunodeficiency have been described, mostly in adults, but in paediatric age reports are scant (5). To our knowledge, the association of c-PAN with CVID has not been described before in the English literature. In conclusion, although the association of c-PAN and CVID can be fortuitous, both are due to immune system dysregulation, and could be related by yet unknown mechanisms.

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