Editorial

Henoch-Schönlein purpura (IgA vasculitis): the paradox of the different incidence and clinical spectrum in children and adults

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Immunoglobulin A (IgA) vasculitis is characterised histologically by infiltration of the small blood vessels, predominantly capillaries, venules, or arterioles, with polymorphonuclear leukocytes and the presence of leukocytoclasia (1). Immunofluorescence staining usually reveals the presence of IgA1-dominant immune deposits in the walls of the small vessels and in the renal glomeruli (1). Classically, it was called Henoch-Schönlein purpura (HSP), and many clinicians still use this term to describe this type of vasculitis. Because of that, we will use it throughout this editorial.

Many epidemiological studies support the claim that HSP is the most common type of vasculitis in children and an infrequent condition in adults (2). The disease is observed predominantly in children between the ages of 2 and 10, and the median age of onset is 4 years (2, 3). The incidence is much lower in adults. A good example of this marked difference in the incidence according to the age at disease presentation was disclosed in the epidemiological studies from the Lugo region of Northwestern Spain. In that region, the overall average annual incidence rate of HSP for the period 1990-1999 was 126.4/million people aged 14 years and younger (3). In contrast, in the same area, the annual incidence rate of HSP in the period 1988-1997 was 14.3/million people aged 21 years or older (4).

This small blood vessel vasculitis typically involves skin, gut, and joints, with renal involvement constituting its more serious manifestation. Skin involvement is present in 100% of cases and it is characterised by a rash of symmetric erythematous papules of the buttocks and lower extremities, which progresses to palpable purpura (5).

The paediatric form of the disease is generally benign and self-limited (3, 6). It is more severe in adults, generally due to renal complications that include persistent haematuria and proteinuria and in some cases chronic kidney disease that may lead to end-stage kidney disease (7-11). At histopathologic level, adults often have more severe renal changes than paediatric patients (12). A recent retrospective study that included 417 patients with HSP seen at Hospital Universitario Marqués de Valdecilla, Santander (Spain) between 1975 and 2012 confirmed the differences in the clinical spectrum of HSP according to the age at presentation of the patients (13).

Therefore, HSP is more common in children but more severe in adults. One may wonder whether there is an explanation for this paradox. Unfortunately, the reasons for such a discrepancy in the clinical spectrum and outcome of HSP according to the age of onset are far from being understood.

A genetic component influences the susceptibility to HSP. A recent study confirmed a strong association of this small-vessel vasculitis with the HLA-DRB1*01 phenotype (14). This was due to the increased frequency of the HLA-DRB1*0103 allele in HSP patients compared with controls (14). However, no HLA-DRB1 phenotype differences were observed when patients were stratified according to specific features of the disease, such as disease onset before or after age 20 years or the presence of joint or gastrointestinal manifestations and nephritis (14). Smaller studies suggested the influence of gene polymorphisms, such as the IL-8 gene polymorphism, in the risk of nephritis and severe renal diseases (15). However, no association with the age of the onset of this vasculitis was found in these studies.

It is possible that certain aetiological factors associate with different

outcome of the vasculitis. Infections and drugs have been implicated in the pathogenesis of HSP (2). As previously discussed, data from the large retrospective series of Santander (Spain) unveiled marked epidemiologic differences in the development of HSP between children and adults (13). In this series the presence of potential precipitating factors was more commonly observed in children than in adults. It was especially true for infections as a whole (43% *vs*. 23%, respectively) and more specifically associated with an upper respiratory tract infection shortly before the onset of the vasculitis (39% *vs*. 14%, respectively) (13). Therefore, it is possible that higher susceptibility to upper respiratory tract infections in children may account for an increased incidence of this vasculitis in paediatric individuals.

In general, the prevalence and severity of comorbidity increases with age. Therefore, it is possible that the combined effect of comorbidity and aging may be the reason for a more severe expression of HSP. In this regard, a study aimed to assess possible differences according to the age of onset in HSP patients occurring in adulthood yielded interesting results (16). The medical records of all consecutive patients older than 20 years who had been diagnosed with HSP at a tertiary referral hospital of Korea between January 1997 and December 2014 were reviewed retrospectively. Patients were divided into early-onset (age <60 years) and late-onset (age ≥60 years) groups according to the age of disease onset (16). Only the early-onset group had the triggering factor of upper respiratory tract infections at diagnosis (14/69 *vs*. 0/31) (16). Patients with HSP older than 60 years were more likely to have renal involvement (27/31 *vs*. 43/69), and renal insufficiency (14/31 [45.2%] *vs*. 7/69 [10.1%]) at presentation (16). The later onset group also had higher frequency of diabetes and hypertension at the time of disease onset (16). Moreover, HSP patients with late-onset disease were more likely to suffer chronic renal insufficiency at follow-up and die than those with early-onset disease (16).

Although classification criteria for HSP were considered useful for paediatric patients, low concordance among different classification criteria for HSP was recently reported in adults (17). This limitation may be because in some cases classification criteria were originally developed for children. This fact highlights the need of new set of criteria to better define HSP adults.

In conclusion, current data do not explain the differences in the incidence and clinical outcome between children and adults with HSP. Further studies in this field are warranted.

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