Urinary Neopterin and Kynurenine in Herpes gestationis

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Sir

Neopterin is a degradation product of dihydroneopterin triphosphate, the first intermediate in the biosynthesis of tetrahydrobiopterin [1]. In vitro human monocytes/macrophages produce neopterin when stimulated by interferon-γ (IFN-γ) released from activated T cells. Other cell types do not produce measurable amounts of neopterin following various stimuli. Therefore, neopterin production appears to be closely associated with monocyte/macrophage activation. Neopterin monitoring has consequently been proposed for the follow-up of patients with HIV infection, malignant and auto-immune diseases [2]. Furthermore, it has recently been reported that IFN-γ induces tryptophan degradation in vitro by the activation of indoleamino-2,3-dioxygenase [3], a key enzyme in the complex kynurenine pathway; this appears to contribute to the antimicrobial effects of IFN-γ [4]. In vitro, the cleavage of tryptophan by indoleamino-2,3-dioxygenase is parallel to neopterin release by monocytes/macrophages [5].

High levels of IFN-γ have been found in the bullous fluid of bullous pemphigoid, being higher than those observed in the sera of the same patients [6]. We have analysed urinary neopterin and kynurenine in a patient with herpes gestationis (HG) that is considered as a form of bullous pemphigoid of pregnancy, in order to detect signs of IFN-γ-induced monocyte/macrophage activation in HG.

The patient was a 32 year-old female in the 7th month of her first pregnancy: HG was diagnosed on the basis of a typical pruritic bullous eruption on the abdomen and lower limbs with linear C3 and IgG deposits detected by direct immunofluorescence.

Urinary neopterin excretion was determined on the first urine of the morning by high-performance liquid chromatography as described elsewhere [7]. Results were expressed as micromoles neopterin per moles creatinine excretion. As control group we studied 10 healthy pregnant women ranging from the 4th to the 8th month of pregnancy. The values of neopterin in our control group were in accordance with previous evaluations in pregnant women [8].
Urinary kynurenine was detected by ultraviolet wavelengths adjusted to optimal values by the computerized data system Varian Vista 402 controlled time program. Wavelengths used for kynurenine were: ultraviolet 260 (detection limit 500 nmol/l). Kynurenine from Table 1. Urinary excretion (µmol/mol) of neopterin and kynurenine (means ± SD)

HG (n = 1) Healthy pregnant women (n = 10)
Neopterin 739 ± 22 226 ± 33
Kynurenine 568 ± 138 84 ± 27
Sigma was used as internal standard [9], and values related to the urinary creatinine during the same chromatographic run of the urinary neopterin.

Table 1 shows that urinary excretions of both neopterin and kynurenine were elevated in the patient with HG. The values in our patient correspond to a 3-weeks evaluation (from the 7th to the 8th month of pregnancy) and were observed before starting corticosteroid therapy. These findings indicate that IFN-γ activated monocytes/macrophages are present in patients with HG and that the consequent increase in kynurenine pathway metabolites could contribute to the fetal damage [10]; whether this is particular to our patient or will appear to be a novel biological sign of HG should await further studies.

References