Microchimerism: Fears and Hopes

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For those who are not used yet to this rather recent concept, microchimerism refers to the presence of very low numbers of allogeneic cells in an individual. Most interest in this phenomenon has been raised after the demonstration by the group of Diana Bianchi, a researcher working previously on prenatal diagnosis, that fetal cells – present in the peripheral blood of women during pregnancy – may persist decades after delivery [1]. Fetal semi-allogeneic cells were indeed largely known to be tolerated during pregnancy, through various pathways. However, the cause of such an escape of foreign cells from the maternal immune surveillance for a very long time remains an unanswered intriguing question. Some have hypothesized that such an escape could be due to a leakage of paternal antigens from fetal cells, while others evoked a homology in the major histocompatibility complex leading to a ‘compatibility from the mother’s view’ [2]. Nevertheless, whatever the mechanism of this tolerance, the evidence that such foreign cells could persist has been the rationale for many authors to evaluate a possible implication of chimeric cells in deleterious consequences for the host. Why these investigators focused on such a harmful role is easy to understand: several diseases classified as auto-immune predominate in females, the gender in whom persisting fetal circulation from a previous pregnancy may occur, and in addition several of these ‘auto-immune diseases’ looked like ‘allo-immune diseases’, namely graft-versus-host reaction (GvHD). Based on this, several groups have shown an association between fetal cell persistence and systemic sclerosis (SSc) [3–6]. In addition, such fetal cells were also found in involved tissues such as the skin [4]. At that point, a fascinating perspective appeared possible: spontaneous SSc could be an anti-maternal reaction of the fetus, similar to posttransfusional GvHD. However, many points were quickly raised against this pathway. First, nearly all studies found a significant level of normal females with chimerism. Second, sclerodermoid GvHD displays several clinical, pathological and immunological differences to SSc [7]. Third, no increase in SSc appeared to be reported after red blood cell transfusion [8]. Finally, other studies failed to find more chimerism in females with SSc as compared with controls [9, 10]. Therefore, a real controversy about the implication of chimerism in SSc is still to be debated. Some consider that the presence of chimeric cells would act as one step in a multistep phenomenon in the pathogenesis of SSc, either by direct T cell antihost reactivity or by inhibition of host T regulatory cells with consecutive auto-immunity. Other authors believe by contrast that these fetal cells are recruited into damaged tissue in order to participate in tissue repair as well see below.

Quickly, after investigating SSc, several auto-immune diseases were evaluated. Interestingly, using different techniques, 2 groups showed in 2000 that juvenile dermatomyositis was associated with the presence of maternal cells in the blood and the muscle of affected sons, while controls with non-inflammatory myopathies had no such cells [11, 12]. We were therefore in the same scenario as in SSc: allogeneic cells, coming from the reverse traf-
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References


