Systemic juvenile idiopathic arthritis, Kikuchi’s disease and haemophagocytic lymphohistiocytosis

SIR, I read with interest the case report of a 1-yr-old girl with systemic juvenile idiopathic arthritis and Kikuchi’s disease, who later developed haemophagocytic lymphohistiocytosis (HLH), and its successful management [1]. Diagnostic criteria for HLH were published in 1991 [2]. The diagnosis of HLH requires the presence of all five criteria (fever >38.5°C for 7 or more days, palpable splenomegaly, cytopenia involving two or more cell lines, hypertriglyceridaemia or hypofibrinogenaeemia and haemophagocytosis). The case reported by Ramanan et al. [1] satisfies the diagnostic criteria.

In a recent study of 122 children with HLH enrolled from 11 countries, the rate of parental consanguinity was 24% and there was a positive family history in 49% of cases [3]. Ramanan et al. have not commented on the parental consanguinity and the family history of their patient.

The prognosis of HLH has improved significantly since the advent of the HLH-94 protocol from the Histiocyte Society [3]. The protocol includes induction with dexamethasone and etoposide for 1 yr. However, haematopoietic cell transplantation appears to provide the best cure rate, of about 60% [4]. The 40-page HLH-94 protocol can be obtained from the Histiocyte Society of America through their website (http://www.histio.org/society/protocols/trials-protocols.shtml). However, treating physicians and potential patients must be registered before the protocol can be released.

Epstein-Barr virus and parvovirus B19 infections can be associated with both HLH and Kikuchi’s disease [5–7]. Ramanan et al. do not mention whether their patient was tested for these infections.

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Reply

SIR, We thank Dr Jawad for his comments and his interest in our paper [1]. To address the issues raised by the author, there was no family history of haemophagocytic lymphohistiocytosis (HLH) or consanguinity. We did do serology for Epstein–Barr virus (EBV) and parvovirus, both of which were negative (we mentioned in our paper that the viral serology was negative, although we did not specify the viruses checked).

As for his comments on the diagnostic criteria, these are beset with problems. The criteria were designed primarily for the diagnosis of primary HLH, but many clinicians in practice use the criteria for secondary HLH and for HLH associated with rheumatic disease. Henter et al. [2], in their criteria, acknowledge the fact that not all patients will fulfil the criteria and that clinical decisions regarding therapy need to be made even when patients do not satisfy the diagnostic criteria.

There are certain problems with the existing criteria. Low haemoglobin concentration, raised white cell count and raised platelet count are characteristic of active systemic disease in systemic onset juvenile idiopathic arthritis (SoJIA). Hence, relative cytopenia may enable earlier diagnosis of HLH compared with the absolute cytopenia in the present criteria.

One of the major problems with the existing criteria for HLH is the need for tissue demonstration of haemophagocytosis. It is well recognized that bone marrow aspirate or biopsy may not always show haemophagocytosis; furthermore, haemophagocytosis is not always demonstrable at onset [3, 4]. In one series of 27 children with primary HLH, autopsy studies revealed haemophagocytosis in the bone marrow in only 39% (9/23). On the contrary, 71 and 74% showed haemophagocytosis in the spleen and lymph nodes respectively [4]. Whilst this demonstrates that biopsies of the spleen and lymph nodes have higher yields, they constitute a much greater risk in the face of active coagulopathy. There is a need for criteria that take these difficulties into account, yet provide a robust framework for early diagnosis and treatment.

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