was negative.The patient was treated with hydroxyurea, which decreased the size of his spleen and the number of peripheral eosinophils.A few months later he underwent an unrelated bone marrow transplantation and was in remission a year later.

The diagnosis of CEL does not fit exactly the criteria proposed by Brito-Babapulle, since our patient has marked myelodysplasia. However the presence of fibrosis, hypercellularity in bone marrow, hepatosplenomegaly and the good response to hydroxyurea make diagnoses other than myeloproliferative disorder difficult.

The clonality of eosinophils, one of the key criteria could not be established directly since the detected cytogenetic alteration turned out to be constitutional. He fulfills other criteria proposed by Brito-Babapulle: major (medullary fibrosis, trilineage dysplasia, presence of ALIP) and minor (splenomegaly, normal levels of Ig, marked morphologic abnormalities of eosinophils). In resemblance of AML M4 Eo, in which the clonality of the eosinophils is well established, the cytochemical abnormalities of these cells are the same as in our case.[4]

Finally, the presence of a constitutional cytogenetic alteration not previously described associated with any hematological disease raises two questions: does an uncommon traslocation have a possible pathogenic role in an also uncommon disease; and any undescribed cytogenetic alteration must be discarded as constitutional.[7]

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Key words

Chronic eosinophilic leukemia, constitutional cytogenetic alteration, unrelated bone marrow transplantation.

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Childhood Hemophagocytic Syndrome Associated with Kikuchi's Disease

We reported the cases of two children with Kikuchi's disease who developed hemophagocytic syndrome (HS) and responded well to intravenous immunoglobulin and corticosteroid therapy. Childhood HS may be associated with Kikuchi's disease and seems to have a less aggressive clinical course and better prognosis. Chemotherapy could be reserved for those who fail to respond to such a regimen.

Sir,

Hemophagocytic syndrome (HS) is a histiocytic reactive process frequently associated with infection[1,2] or malignancy.[3] An etoposide-containing regimen has produced satisfactory results in non-familial childhood HS,[4] but the patients' long-term survival is still uncertain.[5] In contrast, subacute histiocytic necrotizing lymphadenitis or Kikuchi's disease is a well-defined and distinct clinicopathologic entity and usually follows a benign self-limited clinical course.

There are only two reports of HS simultaneously associated with Kikuchi's disease in the literature,[6,7] but the prognosis and treatment strategy for HS in Kikuchi's disease is still unknown. We here report the cases of two children with simultaneous Kikuchi's disease and HS.

Case #1. A 14-year old boy had a two-week history of fever, fatigue, poor appetite and progressive cervical lymph node swelling. On examination, he had a temperature of 39°C and cervical lymphadenopathy (6 to 4 cm in diameter). The liver was palpable 6 cm below the right costal margin. The initial blood profiles were within normal limits. Elevation of acute C-reactive protein (CRP) level to 38.8 mg/L was noted. Despite the supportive and empirical antibiotic treatment, intermittent spiking fever and constitutional symptoms remained. Biopsy of lymph nodes revealed paracortical necrotizing lesions with typical features of Kikuchi's disease (Figure 1). *In situ* hybridization for Epstein-Barr virus (EBV) genome using the EBER-1 probe was negative. Progressive leukopenia, thrombocytopenia, coagulopathy and increasingly deranged liver function occurred in the subsequent days (Table 1). A bone marrow aspiration showed

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Table 1 Presenting laboratory features in the two cases.

	Case #1	*Case #2*
Peripheral blood		
RBC (10^6/mm^3)	4.13	3.23
Hb (g/dL)	12.0	9.7
Plt (10^3/mm^3)	98	219
WBC (/mm^3)	1.45	1.4
ANC	1102	560
APTT (sec)	56.3/32	38.1/24.3
Fibrinogen (mg/dL)	ND	413
FDP(D-dimer)(μg/mL)	ND	<0.5
Blood Chemistry		
ALT (U/L)	650	219
AST (U/L)	295	223
Bilirubin (total) (mg/dL)	0.8	0.4
Alkaline phosphatase (U/L)	153	176
LDH (U/L)	1238	852
Cholesterol (mg/dL)	121	147
Triglyceride (mg/dL)	146	207
Ferritin (ng/mL)	128	1083
Serology		
CRP (mg/L)	116	24.5
ANA	1:40(-)	1:40(-)
C3 (mg/dL)	122	134
C4 (mg/dL)	29.4	42.1
CMV IgG	(+)	(+)
CMV IgM	(-)	(-)
EBVCA IgG	1:16(+)	1:80(+)
EBVCA IgM	(-)	1:10(-)
HBsAg	(-)	(-)
HCV	(-)	(-)
Toxoplasma	Neg.	Neg.

ND: not done; Neg.: negative.

significant hemophagocytosis. Intravenous immunoglobulin (IVIG, 1 g/kg/day x 2 days) and oral prednisolone (2 mg/kg/day) were administered with dramatic response. There was no evidence of disease recurrence in the following three and half years.

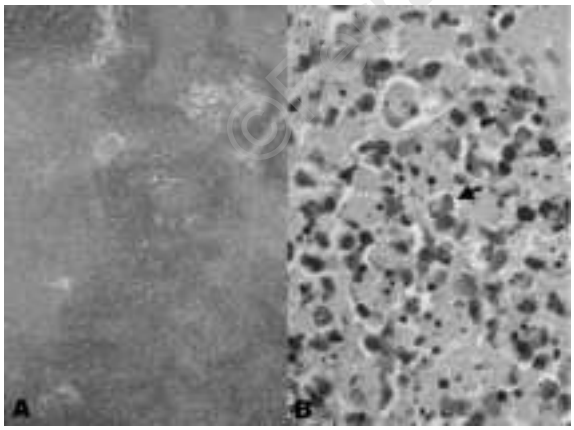

Figure 1. (A) Histologic picture of a lymph node biopsy specimen from patient #1 revealed patchy areas of necrotic lesions (hematoxylin-eosin, x100). (B) Higher magnification of the patchy lesions revealed karyorrhectic debris, a mixture of crescent histiocytes, transformed lymphocytes, and plasmacytoid monocytes (arrow) with absence of neutrophils, eosinophils and plasma cells (hematoxylin-eosin, x400).

Case #2. A 10-year old girl had bilateral neck masses for one month and fever up to 38.5°C for two weeks before admission. Elevation of acute CRP to 35.4 mg/L and an erythrocyte sedimentation rate of 88 mm/h were noted. Intermittent spiking fever persisted despite supportive treatment. In the subsequent days, progressive leukopenia, anemia, deteriorating liver function and hypertriglyceridemia developed. Coagulopathy with a prolonged activated partial thromboplastin time and elevated fibrin-derived products were later observed (Table 1). Bone marrow examination showed obvious hemophagocytosis. Right cervical lymph node biopsy revealed features of Kikuchi's disease. IVIG (1 g/kg/day x 2 days) was administered with only a partial response. The clinical symptoms and signs improved gradually after administration of prednisolone (2 mg/kg/day). There was no evidence of disease recurrence afterward.

Non-familial childhood HS, frequently associated with EBV infection runs an aggressive and potentially fatal course,[5,8] while Kikuchi's disease is usually self-limited and supportive treatment alone is sufficient. The association of HS with Kikuchi's disease is only rarely seen.[6,7] The prognosis and therapeutic strategy for this entity remains unclear. In a retrospective review of childhood Kikuchi's disease in our institution in the past 12 years, 2 of 8 cases, in contrast to none of the 43 adult cases, were associated with HS. This suggests that our childhood Kikuchi's disease has a higher incidence of being associated with HS. Although the majority of cases of childhood HS are aggressive and potentially fatal, the heterogeneous outcome of childhood HS in our previous reports reflects the diversity of this disease spectrum.5 The recognition of its association with Kikuchi's disease is therefore very important with regards to the better clinical course and therapeutic strategy.

Our current case reports indicate that childhood HS may be associated with Kikuchi's disease and assume a relatively benign course. Combination therapy with IVIG and steroids may be the treatment of choice and may provide effective control of this disease; while etoposide-containing regimens such as those adopted in EBV-associated HS could be reserved for those who fail to respond to IVIG and steroids.[5]

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Key words

Hemophagocytic syndrome, histiocytic necrotizing lymphadenitis, Kikuchi's disease.

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Technetium-99m sestamibi scintigraphy in monitoring patients with multiple myeloma

Technetium-99m-Sestamibi (^{99m}Tc-sestamibi) scintigraphy has been shown to be capable of differentiating patients with multiple myeloma (MM) in remission from those with active disease.[1-10] We studied 5 patients with MM (2 females and 3 males, age 53±17 years) before and after treatment. 99mTc-sestamibi scintigraphic results were concordant with clinical status.

^{99m}Tc-sestamibi scintigraphy was performed as previously described.[8,9] The patients were clinically and biochemically evaluated at the time of both ^{99m}Tc-sestamibi scans to determine their clinical status.

Case #1. A 72-year old man with MM. X-ray skeletal survey was negative, while ^{99m}Tc-sestamibi scan showed intense and diffuse bone marrow uptake (spine, pelvis, ribs, proximal part of both humeri and femora) with no focal increased uptake (Figure 1A). ^{99m}Tc-sestamibi scan performed after treatment with melphalan and prednisone was normal (Figure 1B). At this time the patient was considered in complete remission (plasma cell infiltration 2.5%, Hb 13.4 g/dL, monoclonal component undetectable).

Case #2. A 42-year old woman with low secretive MM. The first ^{99m}Tc-sestamibi scintigraphy showed intense and diffuse bone marrow uptake (pelvis, sternum, proximal part of both humeri and femora) and

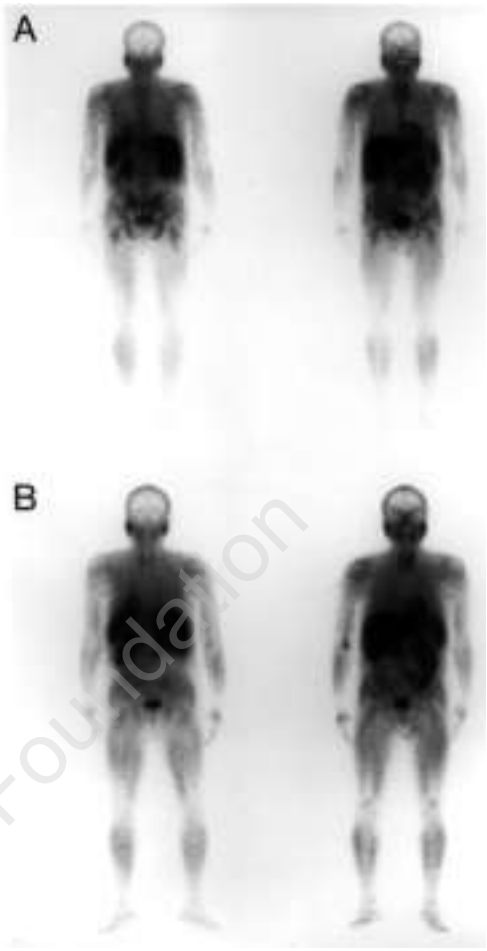

Figure 1. Posterior (left) and anterior (right) whole body scintigraphy acquired 10 minutes after i.v. injection of 99mTc-sestamibi before (A) and after (B) therapy. Before therapy (A) diffuse radiotracer uptake is visible in the spine, pelvis, ribs and proximal parts of both humeri and femura. No abnormalities are observed after therapy (B).

focal increased uptake in thoracic vertebrae (T5, T9). After 2 courses of VAD chemotherapy, increased plasma cell infiltration (72%) was found in the bone marrow, monoclonal component was 0.6 g/dL, and Hb was 10.6 g/dL. A second ^{99m}Tc-sestamibi scintigraphy showed intense and diffuse uptake in the spine and focal abnormalities in T5 and T9 as well as in the skull (fronto-parietal region).

Case #3. A 66-year old woman with micromolecular MM. Baseline ^{99m}Tc-sestamibi scintigraphy showed intense and diffuse uptake in the bone marrow (pelvis, ribs, proximal part of humeri, femora and spine) without focal increased uptake. After receiving 12 courses of melphalan and prednisone, the patient's bone marrow was normal and ^{99m}Tc-sestamibi scintigraphy did not show abnormal bone marrow uptake of the radiotracer.

Case #4. A 30-year old man with juvenile micromolecular MM. ^{99m}Tc-sestamibi scintigraphy showed several focal areas of increased radiotracer uptake.

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