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Circulating microfilariae in haematological malignancies: do they have a role in pathogenesis?

L.S. Kerketta and K. Ghosh*†

National Institute of Immunohaematology, 13th Floor, KEM Hospital, Parel, Mumbai 400012, India

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Abstract

Filariasis is very common in tropical countries. It is endemic in the coastal areas of India. We report four cases of haematological malignancy where peripheral blood and bone marrow smears did not show any microfilariae but conventional cytogenetic preparations from all the four cases showed the presence of parasites. Their morphology confirmed the diagnosis of all cases as bancroftian filariasis. Therefore all types of cytogenetic preparations should be screened carefully in the endemic areas along the coastal zones of India for the presence of this parasite.

Introduction

Filarial infection is an important cause of morbidity in many coastal areas of India. It presents as fever, lymphatic obstruction, tropical pulmonary eosinophilia and sometimes asymptomatic microfilaraemia. Many reports are available describing microfilariae in tissue preparations, biopsies and bone marrow preparations in many diseases, including haematological malignancies (S. Gupta *et al.*, 2001; K, Gupta *et al.*, 2002; Singh *et al.*, 2010; Arundhati *et al.*, 2011). In laboratory diagnosis (Cheesbrough, 2006), microfilariae are commonly demonstrated in peripheral blood and cytological smears or in histological preparations. This is the first report of the detection of microfilariae in conventional cytogenetic preparations.

Case reports

Case 1

A 40-year-old man presented with low-grade pyrexia, dry cough and bronchospasm of 2 weeks' duration. Complete blood counts (CBC) showed haemoglobin (Hb) 9.8 g/dl, a white blood cell count of 8.4×10^3/µl and platelets 106×10^3/µl. A peripheral blood smear showed a normal differential count with normocytic, normochromic red blood cells and hyperglobulinaemia. His serum protein electrophoresis showed an M (monoclonal) band. Bone marrow aspirate showed hypercellular marrow with 42% plasma cells. There was a relative suppression of erythroid and myeloid elements. Erythropoesis was normocytic and normochromic. Microfilariae were detected in the cytogenetic preparation and the final diagnosis was multiple myeloma with filariasis.

Case 2

A 65-year-old man was diagnosed with repeated left ventricular failure. Investigations showed Hb 10 g/dl, white blood cell counts of 10×10^3/µl, platelets 140×10^3/µl with a normal differential count. The patient showed biventricular hypertrophy with restrictive cardiomyopathy. Bone marrow aspirate showed 15% plasma cells with hypercellular marrow. Plasma protein electrophoresis showed a monoclonal band, and Bence Jones protein was found in the urine. Bone marrow karyotype preparation showed microfilariae and abdominal fat biopsy showed amyloidosis. A diagnosis of multiple myeloma with cardiac amyloidosis and circulating microfilariae was made.

Case 3

A 21-year-old man presented with fever, pallor, general weakness and generalized pigmentation. Bleeding manifestations, such as petechiae and gum bleeding, were also seen. On examination a generalized lymphadenopathy, splenomegaly and hepatomegaly were

*E-mail: kanjakshaghosh@hotmail.com
†Present address: Surat Raktadan Kendra & Research Centre, Udhna Magdalla Road, Surat 395002, Gujrat, India.

observed. Investigations showed Hb 4.1 g/dl, total white blood cell count 56×10^3/µl, lymphoblasts 72%, polymorphs 8%, lymphocytes 20% and platelets 20×10^3/µl. Immunophenotyping revealed that marrow haematopoietic cells were positive for CD10, CD19, CD20, CD22 and HLA-DR and a diagnosis of B-cell acute lymphoblastic leukaemia was made. The bone marrow of this patient was processed for cytogenetic evaluation and microfilariae were detected in the cytogenetic preparation (fig. 1).

Case 4

A 35-year-old man presented with a dry cough, generalized body ache and anorexia of 2 months' duration. He had abdominal fullness and generalized weakness for 15 days. CBC revealed Hb 9.2 g/dl, total white blood cell count 263×10^3/µl, neutrophils 67%, myelocytes 13%, basophils 2%, eosinophils 1%, myelocytes 9% and platelets 376×10^3/µl. Bone marrow aspiration smear showed hypercellular marrow, erythroid cells 6%, promyelocytes 1%, myelocytes and metamyelocytes 30%, bands and neutrophils 56%, basophils 2%, lymphocytes 1% and myeloblasts 4%. The erythroid series was relatively reduced and showed megaloblastic maturation. The myeloid series presented marked hyperplasia and sequential maturation was seen up to the neutrophilic stage with demonstrable giant precursors. The megakaryocyte series showed micromegakaryocytes, and the case was diagnosed as chronic myeloid leukaemia. Cytogenetic investigation revealed a Ph +ve karyotype, and microfilariae were also detected in this preparation. Hence a diagnosis of chronic myeloid leukaemia, in the chronic phase, with filariasis was made.

Discussion

Filariasis is a common global problem (Cheesbrough, 2006). There are eight species of filarial parasites that are specific to humans. In India bancroftian filariasis is widely distributed, comprising 98% of the total filarial infections. Brugian filariasis (*Brugia malayi*) is found 2% of cases, and is localized in the central part of Kerala state along the coast, small pockets of Andhra Pradesh, Tamilnadu, Assam, Orissa and Madhya Pradesh (Russel *et al.*, 1980).

Detection of microfilariae from peripheral blood, bone marrow and other tissues is achieved by screening pathological smears. However, in our cases, microfilariae were not detected in blood/bone marrow smears which were prepared to rule out leukaemia. Patients were also asymptomatic for filariasis. Microfilariae were only detected in cytogenetic preparations when sent to us for cytogenetic investigation. This could be due to the low concentration of parasites in the blood and bone marrow, and the cytogenetic method acted as a microfilaria concentration technique (Kerketta *et al.*, 2012). There are many reports of the co-existence of microfilariae in many cancers, which raises the question whether they are merely accidental passengers in the tissues or if these patients are more prone to filarial infection due to their immunocompromised status, or whether microfilariae could have a role in the pathogenesis of these disorders, as chronic parasitic infections are associated with lower immunosurveillance, and chronic antigenic stimulation due to parasites may sustain

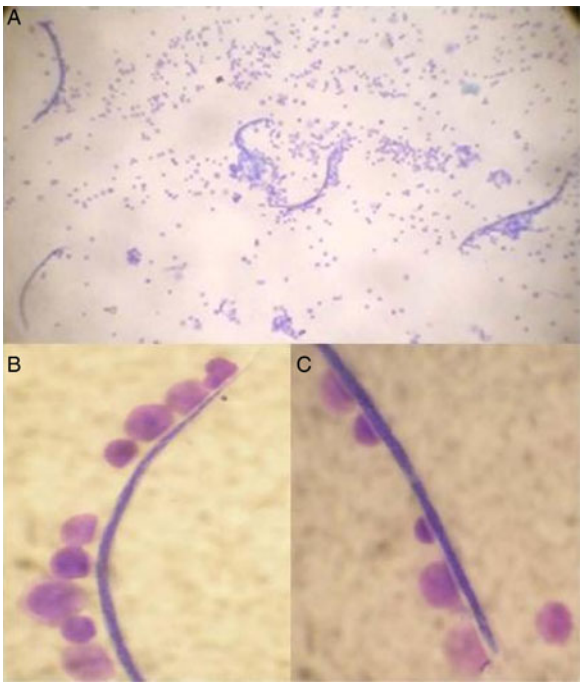

Fig. 1. (A) Microfilariae of *Wuchereria bancrofti* (Giemsa, ×10). (B) Distal and (C) proximal end of microfilariae with hyaline sheath and somatic granules with palisading leucocytes (Giemsa, ×100).

the proliferation of immunoeffector cells (Tajima *et al.*, 1981; Hoerauf *et al.*, 2005; Emmanuel *et al.*, 2011). This angle needs to be studied further in detail. Moreover, the Indian Cancer Registry shows a higher prevalence of lymphoproliferative disorders in areas of endemic filariasis (Nandkumar, 2001; Sabesan *et al.*, 2010).

In our present observation of a small series of patients, a significant number had microfilariae (4/209; 2%) compared to none in the similarly processed equivalent number of marrow smears with non-malignant disorders (Chi square test, $P < 0.05$). Hence, there is a persuasive argument for confirming this finding through a large-scale, well-defined epidemiological study in filaria-endemic areas, using a sensitive technique, such as the circulating filarial antigen test for bancroftian filariasis (Weil *et al.*, 1997), to prove or disprove such an association convincingly.

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Conflict of interest

None.

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