CORRESPONDENCE

Futility of Performing Bone Marrow Cultures in Pyrexia of Unknown Origin

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To The Editor,

Pyrexia of unknown origin (PUO) is a common clinical problem. PUO has been defined by Petersdorf and Beeson as duration of illness of more than 3 weeks before diagnosis and repeatedly documented increased body temperature of more 38.3 °C [1]. This has now been modified to include patients who are diagnosed after two outpatient visits or 3 days in hospital. Additional categories have now been added which including HIV-associated PUO includes HIV-positive patients with fever as above for 4 weeks as outpatients or 3 days as inpatients, with an uncertain diagnosis after 3 days of investigation, where at least 2 days have been allowed for cultures to incubate [2]. Many times a four stage clinical protocol is used to investigate PUO which includes infections, collagen vascular diseases, malignancies and miscellaneous [3]. The etiology of PUO varies with age, sex and geographical location. Bone marrow examination is often performed when other investigation have been non-contributory [4]. Present study was designed to evaluate the clinical utility of performing bone marrow culture in patients with undiagnosed PUO.

Retrospective data of patients in whom bone marrow examination was performed for PUO was analysed. Study period was over 3 years from 1st January 2013 to 31st December 2015. Diagnostic work-up included a history, physical examination, complete blood count, liver and kidney function tests, antinuclear antibody, viral markers,

urinalysis, blood and urine cultures, chest radiography, and diagnostic contrast-enhanced chest, abdominal, and pelvic CT scans. Blood, urine, cerebrospinal fluid (when indicated), sputum, tracheal secretions, bronchoalveolar lavage and stool analysis were performed for diagnosis as and when indicated. If these were inconclusive then bone marrow aspirate and biopsy were performed by trained physicians/haematologist under sterile aseptic conditions and immediately inoculated into BacT/ALERT FA plus bottle for adults (5–10 ml)—manufactured by Bioréieux and BacT/ALERT PF for paediatrics (3–5 ml)—manufactured by Bioréieux. All Cultures were performed in an automated blood culture system BacT/ALERT 3D (Bioréieux).

Blood culture was sent in 28 patients and was positive in 1 (3.5 %). The organism isolated in blood culture was *E. faecalis*. Urine culture was sent in 31 patients and was positive in 8 (25 %). The organisms isolated were *E. faecium*, followed by *E. coli* and others which included *Pseudomonas aeruginosa*, *Chryseobacterium indologenes* and *Providencia kettgiri*.

Bone marrow examination and biopsy was performed in 39 cases of PUO. A bone marrow culture was sent in 23 (59 %) cases. Out of 39 patients of PUO in the study group 20 (51 %) were males and 19 (49 %) were females. Median age was 49 years (3–92 years). Bone marrow examination helped in reaching a diagnosis of 7 (17 %) cases with granuloma in 5 cases, metastasis in 1 case and chronic lymphoproliferative disorder in 1 case.

Bone Marrow Culture was sterile in all 23 (100 %) cases sent and was non contributory.

Bone marrow aspiration and biopsy have traditionally been performed to rule out underlying hematological malignancies as a cause of fever. Many centers routinely perform bone marrow cultures in these situations. Data

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on the utility of bone marrow culture examination in PUO has been very sparse with very few studies being conducted on it especially in immunocompetent patients. Jha et al. [5] demonstrated that bone marrow cultures were more useful than blood cultures in evaluation of patients with PUO especially in patients of salmonella infection who have taken antibiotics. Another study found that bone marrow cultures were not justified for routine clinical evaluation of PUO but may be valuable after culture results for blood and easily obtainable tissues have been negative [6]. India being a tropical country, most prolonged fever is empirically treated with broad spectrum antibiotics which cover salmonella typhi. This could possibly explain why we did not isolate salmonella in our bone marrow cultures.

In the present study bone marrow evaluation yielded a diagnosis in 7 (17 %) cases. This is in line with current literature [7, 8]. Tuberculosis is a common infection found in India. Accordingly, it was the most common infectious etiology of PUO found in our study (n = 5).

None of the bacterial bone marrow cultures revealed a diagnosis in our study population. Hence, in our opinion doing a bone marrow culture does not add over and above a conventional blood culture. We suggest that by preventing unnecessary bone marrow cultures we can conserve hospital resources, reduce patient's expenses and avoid repeated aspirations to collect a sample for culture in difficult cases.

We conclude that bone marrow evaluation is a useful modality in evaluation of pyrexia of unknown origin. However, bone marrow cultures are futile.

Compliance with Ethical Standards

Conflict of interest Anupama Arya and Rahul Naithani declare that they have no conflict of interest.

Ethical Approval This article does not contain any studies with human participants performed by any of the authors.

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