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SHORT REPORT

# Bone marrow biopsy morbidity and mortality

BARBARA J. BAIN *Department of Haematology, St Mary's Hospital Campus, Faculty of Medicine, Imperial College of Science, Technology and Medicine, London, UK*

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**Summary.** A postal survey of adverse events associated with bone marrow biopsy (aspiration biopsy with or without trephine biopsy) was carried out among British Society of Haematology members, between 1995 and 2001. A total of 26 adverse events, including one death directly attributable to the procedure, were reported among an estimated 54 890 biopsies. The most frequent and most serious adverse event was haemorrhage, reported in 14 patients, necessitating blood transfusion in six patients and leading to the single death. The potential risk factors most often associated with haemorrhage were a diagnosis of a myeloproliferative disorder, aspirin therapy or both. Other potential risk factors were warfarin therapy, disseminated intravascular coagulation and obesity.

**Keywords:** bone marrow aspiration, bone marrow biopsy, morbidity, mortality.

The bone marrow may be examined in life either by an aspiration biopsy or by a trephine biopsy, the latter also known as a core biopsy. Although there are a number of reports in the medical literature of morbidity and even mortality as a result of these procedures (Bain *et al,* 2001), little is known of the incidence of biopsy-related misadventure. The death of a patient in the UK in 2000 led to this survey being undertaken, in order that the frequency and nature of adverse events could be established. The study was made possible by the co-operation of the British Society for Haematology (BSH) and its members, with the results being presented at the Annual Scientific Meeting of the Society in 2002. The survey covered only diagnostic procedures, with aspiration for the purposes of bone marrow transplantation being excluded. The survey showed infrequent, but nevertheless clinically significant, biopsy-related morbidity and mortality, particularly in patients with demonstrated or suspected abnormalities of platelet function.

## MATERIALS AND METHODS

All members of the BSH were circularized twice. On the first occasion, they were asked to record retrospectively, on a proforma provided, any misadventures associated with bone marrow biopsy procedures between 1 January 1995 and the 31 December 2000. At the same time, they were alerted to the plan to circularize all members on a second occasion so that prospective information could be gathered. The second proforma was circulated at the end of the survey period, 1 January to 31 December 2001, requesting data that had been recorded during that period. All BSH members working in the UK were requested to return relevant information.

Correspondence: Dr B. J. Bain, Department of Haematology, St Mary's Hospital, Praed Street, London, W2 1NY, UK. E-mail: b.bain@ic.ac.uk

## RESULTS

Haematologists from 60 hospitals responded to the survey covering 2001. A total of 19 332 procedures were reported, with the number of procedures per hospital per year varying from 57 to 875 (mean 260, median 200). Of these procedures, 62% represented an aspirate and a trephine biopsy, 35% represented an aspirate alone, and for 3% information as to whether or not a trephine biopsy had been performed was not available. The percentage of patients having a trephine biopsy in addition to an aspirate varied very widely from 8% to virtually 100% (mean 64%, median 71%). Four hospitals reported a total of four adverse events during the 12-month period.

For the 6-year period from 1995 to 2000 inclusive, data were necessarily much less complete. Haematologists from a total of 34 hospitals reported 39 264 procedures, these being aspiration and trephine biopsy in 54%, aspiration only in 39%, and unknown in 7%. The number of procedures per hospital per year varied from 26 to 612 (mean 210, median 188). The number of patients having a trephine biopsy in addition to an aspirate varied from 22% to virtually 100% (mean 58%, median 67%). A total of 22 adverse events were reported by 17 hospitals.

**Table I.**
(A) Nature of the adverse events reported in the 7-year period surveyed.

| | |
|---|---|
| Haemorrhage | 14 |
| Needle-related incidents | 7 |
| Infection | 3 |
| Miscellaneous | 2 |

(B) Diagnoses in patients who suffered haemorrhage.

| | |
|---|---|
| Essential thrombocythaemia | 5 |
| Transformed myeloproliferative disorder | 2 |
| Myelodysplastic syndrome | 2 |
| Polycythaemia vera | 1 |
| Chronic myeloid leukaemia | 1 |
| Disseminated carcinoma | 1 |
| Anaemia of chronic disease | 1 |
| Not recorded | 1 |

The nature of the adverse events reported in the total survey period is summarized in Table IA.

The most frequent and generally most serious adverse event was haemorrhage, reported on 14 occasions. Six patients required blood transfusion, supplemented in one patient with fresh-frozen plasma, cryoprecipitate, platelets and tranexamic acid; a further patient required platelet transfusion alone. In one patient, haemorrhage was fatal despite blood transfusion and surgery, this being the index patient whose death led to the survey being performed. In another 11 patients, hospitalization was prolonged, by a period varying from 1 d to 6 weeks. Two patients developed nerve compression. The diagnoses in the patients who suffered haemorrhage showed a notable prevalence of myeloproliferative disorders (Table IB). Other risk factors identified included aspirin therapy, warfarin therapy, previously unsuspected disseminated intravascular coagulation and obesity (Table II). Only three of the 14 patients were thrombocytopenic. Probable platelet dysfunction, attributable to a myeloproliferative or myelodysplastic syndrome, aspirin therapy or interference with platelet function by fibrin-degradation products, appeared to be a more common risk factor than thrombocytopenia. Risk factors were identified in all but one of the patients who bled, and for this patient few clinical details were available. The occurrence of haemorrhage did not show any close relationship to the grade or length of experience of the operator. In nine instances, the procedure was performed by a consultant with 10–33 years experience, in one instance by a staff grade haematologist with 10 years experience, in three instances by a registrar with 2–4 years experience and in one instance by a combination of a senior house officer and consultant with, respectively, 3 months and 10 years experience.

The needle-related incidents all related to a needle breaking off in the patient, two brands of disposable needle being specifically identified. In three patients, surgical removal was required and each of these patients spent an extra 2 d in hospital. In two instances, removal was effected with pliers or similar implements, and in two instances part of the needle was left *in situ*.

The three instances of infection were: (i) minor superficial infection requiring antibiotics; (ii) an abscess requiring drainage, antibiotics and 6 d of hospitalization, and result-

**Table II.** Possible risk factors for haemorrhage in the patients in whom this occurred.

| Diagnosis | Possibility of defective platelet function | Aspirin therapy | Warfarin therapy | Disseminated intravascular coagulation | Thrombocytopenia (platelet count $\times 10^{-9}$/l in parentheses) | Obesity |
|---|---|---|---|---|---|---|
| ET | Yes | Yes | – | – | – | – |
| ET | Yes | Yes | – | – | – | – |
| ET | Yes | Yes | – | – | – | – |
| ET | Yes | – | – | – | – | – |
| ET | Yes | – | – | – | – | – |
| PRV | Yes | – | – | – | – | – |
| PRV | Yes | – | – | – | – | – |
| CML | Yes | – | – | – | – | Yes |
| BC | Yes | – | – | Yes | – | – |
| MDS | Yes | – | – | – | Yes (25) | Yes |
| MDS | Yes | – | – | – | Yes (68) | – |
| Carcinoma | Yes | – | – | Yes | Yes (50) | – |
| Anaemia of chronic disease | – | – | Yes* | – | – | – |
| Unknown | – | – | – | – | – | – |

*With an international normalized ratio of 4·2.

ET, essential thrombocythaemia; PRV, polycythaemia rubra vera; CML, chronic myeloid leukaemia; BC, blast crisis of CML; MDS, myelodysplastic syndrome.

ing in 2–3 months severe pain at the site; (iii) cellulitis in a neutropenic child undergoing treatment for acute lymphoblastic leukaemia, leading to septicaemia, hypotension, admission to an intensive care ward, 36 h of artificial ventilation, 6 weeks of hospitalization and permanent hearing loss attributable to gentamycin.

The miscellaneous adverse events were: (i) one instance of vomiting followed by loss of consciousness, and (ii) one instance of pyoderma gangrenosum in a patient with multiple myeloma, occurring initially at the biopsy site (pathergy) and subsequently at other sites; in the latter patient, treatment of the pyoderma gangrenosum led to sepsis and subsequent death.

In addition to the adverse incidents observed during the survey period, a small number of serious adverse events were reported from earlier periods of time. Although these are anecdotal in nature, they are reported here as they have not previously been recorded in the medical literature. One death from pericardial tamponade was reported following a sternal aspiration in a young woman with thrombocytopenia. One pneumothorax occurred when a needle passed through a lytic area in the sternum. One patient who was fully warfarinized because of prosthetic cardiac valves, necessitated by cardiac damage from an idiopathic hypereosinophilic syndrome, suffered a massive thigh and buttock haematoma. In addition, the author is aware of one other death occurring in the UK 35–40 years ago, as a result of cardiac puncture during an attempted sternal aspiration.

## DISCUSSION

It is clear that bone marrow aspiration and trephine biopsy are generally safe procedures but they are not completely free of risk. Despite the retrospective nature of part of the survey, it is unlikely that there has been any significant under-reporting of the more serious events as these are distressing to all concerned and usually fix themselves indelibly in the memory. In support of this view, the two UK deaths from bone marrow biopsy in the last 30 years that were already known to the author were reported in this survey, even though one was outside the study period. With regard to less serious adverse events, it is clearly likely that there has been some under-reporting, resulting, at least in part, from imperfect recall.

Nevertheless, this survey represents the first attempt to systematically record the adverse effect of bone marrow biopsy and as such it provides valuable information. The most important risk identified was of haemorrhage. This appeared to be more often related to probable impairment of platelet function than to thrombocytopenia or a coagulation factor defect. However, it should be noted that the small number of reports of bleeding related to warfarin therapy or disseminated intravascular coagulation may be largely attributable to the reluctance of haematologists to perform trephine biopsies in such patients.

Among an estimated 54 890 procedures, there was one death from haemorrhage directly attributable to the procedure, one death from sepsis that may have been indirectly attributable to the procedure, one instance of permanent disability (gentamycin toxicity) indirectly attributable to the procedure and three instances of prolonged, but not permanent, disability attributable to infection (one patient) or haemorrhage and nerve compression (two patients). Serious adverse events were reported in less than 0·05% of procedures and can, therefore, be regarded as rare occurrences.

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## REFERENCE

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