



Neck of femur fracture: Previous history of malignancy is not an indication to send femoral head for routine histology

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Abstract

Background Neck of femur fractures is the most common fractures associated with low-velocity injury in the elderly. Some patients may require further histological examination of the femoral head due clinical suspicion of malignance as a cause of fracture.

Objectives To review whether standard screening question(s) could be used to identify patients that require histological examinations following neck of femur fracture.

Study design and methods Femoral heads sent for histological examination over a period of 5 years were identified from hospital database. All patients presenting acutely with neck of femur fracture above the age of 70 were included, and their case notes were retrospectively reviewed. Reason for histopathological examination were categorised into three screening questions: (Q1) clinical suspicion based on history alone, i.e. neck of femur fracture with no clear history of fall or trauma or preceding hip pain, (Q2) radiological evidence of suspicious abnormality on admission radiographs, (Q3) previous history of malignancy or concurrent malignancy or (Q4) combination of above.

Results In total, 119 samples of femoral head were sent and 18 patients had a positive histology. The sensitivity and specificity of these questions individually showed very poor correlation to positive histology with lowest for (Q3) previous history of malignancy (0.39 and 0.51, respectively). However, combining Q1 and Q2 the sensitivity is improved to 1.0 (95% CI 1.0–1.0) and specificity to 0.35 (95% CI 0.25–0.44) with a positive predictive value of 0.21 (95% CI 0.13–0.30) and negative predictive value of 1.00 (95% CI 1.00–1.00).

Conclusion History of previous malignancy poorly correlates with positive histology. Routine request based on these screening criteria is not cost-effective in patient management.

Level of evidence Prognostic level III.

Keywords Neck of femur fracture · Malignant · Histopathological examination · Bone tumour · Hemiarthroplasty · Femoral head · Screening questions · Sensitivity specificity · Cancer treatment · Survival

Introduction

Neck of femur fracture is one of the commonest causes for hospital admissions and is increasing with the ageing population [1, 2]. Many of these fractures are sustained due to low-energy injuries, typically falling from standing height,

secondary to osteoporosis [3]. Occasionally malignancy in the form of metastatic disease or primary bone tumour can predispose to these fractures [4, 5].

Patients who sustain neck of femur fracture without a history of trauma or have a history of hip pain preceding the fall or in some occasions admission X-rays with suspected lytic or sclerotic lesion may require further investigations. Histopathological examination of the femoral head, following hemiarthroplasty, is a means of verifying the diagnosis and could help in the early detection of bone- and bone marrow-related disorders [6–8]. However, performing such analysis is time-consuming with cost implications and it is prudent to identify which patient could benefit from further investigations.

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The aim of this project is to review whether standard screening question(s) could be used to identify patients that require histological examinations following neck of femur fracture.

Materials and methods

Using the coding system, all femoral head sent for histological analysis was identified over a 5-year period between 2012 and 2017. For the purpose of this study, only patients presenting acutely with intracapsular neck of femur fracture, undergoing hemiarthroplasty, above the age of 70 were included. Patients with extracapsular fracture or undergoing procedures other than hip arthroplasty were excluded.

Each patient's notes and radiographs were retrospectively reviewed and analysed for reasons of femoral head being sent to histopathological examination using three screening questions: (Q1) clinical suspicion based on history alone, i.e. neck of femur fracture with no clear history of fall or trauma or preceding hip pain, (Q2) radiological evidence of suspicious abnormality on admission radiographs, (Q3) previous history of malignancy or concurrent malignancy or (Q4) combination of above.

Patients' data were analysed to calculate sensitivity, specificity, positive predictive values and negative predictive values for each screening question. Results are presented as values with 95% confidence intervals (95% CI) using SPSS (version 8).

Results

During this study period, 358 femoral heads were sent for histopathological examination, for various clinical indications, over a period of 5 years. All patients' notes were individually assessed, and 119 patients had histopathological examination request for suspected malignancy causing intracapsular neck of femur fracture. There were 18 patients with positive histology of which nine cases were newly diagnosed malignancy. Fifteen patients had metastatic disease at the time of presentation. The number of specimens in each screening question is: (Q1)—47, (Q2)—3, (Q3)—32 and (Q4)—37.

The proportion of samples positive for malignancy on histology is: Q1—3 ($n=47$), Q2—3 ($n=3$) and Q3—none ($n=32$). The most common histological type of malignancy was adenocarcinoma of which nine were new cases presenting with metastasis.

All patients underwent cemented hemiarthroplasty (two with long stem for X-ray diagnosis of metastatic lesions further down the femur), and there were no immediate or late wound complications. Ten patients died within 30 days of

surgery. Average discharge time from hospital was 26 days and over 73% went to nursing home or rehabilitation.

All patients with positive histology were referred to oncological team and followed up at the time of this study. In all cases, the treatment was found to be palliative. At the time of data collection, 14 of 18 patients had died (78%) with an average survival of 12 months (range 1 day–39 months).

Screening clinical question(s)

The sensitivity of a (Q1) was 0.72 (95% CI 0.51–0.93) (Table 1). The specificity was 0.37 (95% CI 0.27–0.46), positive predictive value 0.17 (95% CI 0.09–0.25) and negative predictive value 0.88 (95% CI 0.78–0.98).

The sensitivity of (Q2) was 0.72 (95% CI 0.51–0.93) (Table 1). The specificity was 0.92 (95% CI 0.86–0.97), positive predictive value 0.62 (95% CI 0.41–0.82) and negative predictive value 0.95 (95% CI 0.91–0.99).

The sensitivity of (Q3) was 0.39 (95% CI 0.16–0.61) (Table 1). The specificity was 0.51 (95% CI 0.41–0.60), positive predictive value 0.12 (95% CI 0.04–0.21) and negative predictive value 0.82 (95% CI 0.73–0.92).

When (Q4) combination of more than one question of above, i.e. a suspicious history with abnormal radiology, was analysed, sensitivity was improved to 1.00 (95% CI 1.00–1.00), specificity was 0.35 (95% CI 0.25–0.44) (Table 1), positive predictive value was 0.21 (95% CI 0.13–0.30) and negative predictive value was 1.00 (95% CI 1.00–1.00).

Considering these screening criteria, the number of femoral head samples requiring histopathological examination would be reduced by 32 (26%) with no missed cases. Cost analysis showed histopathological examination of each femoral head costs around £150–300 and it would have saved (32×150) over a period of 5 years.

Table 1 Suspicious clinical history, radiographical abnormalities and previous or current history of malignancy

Screening question(s)		Histo-pathological result	
		+	-
(Q1) Suspicious clinical history	+	13	64
	-	5	37
(Q2) Radiographical abnormalities	+	13	8
	-	5	93
(Q3) Previous or current history of malignancy	+	7	50
	-	11	51
(Q4) Suspicious clinical history and radiographical abnormalities	+	18	66
	-	0	35

Discussion

Proximal femur is the commonest site for pathological fracture with an incidence of 40–60% of which one-third of these fractures occurring in the femoral neck [9, 10]. Patients presenting with no clear history of trauma or having radiological findings with suspicious of malignancy may require further investigation. Histological examination confirms the presence of malignancy or healthy tissue; in addition, it can provide information about the grade and type of neoplasm. This information can be very valuable to confirm the diagnosis and to then guide further management [11].

However, laboratory investigations are time-consuming and have cost implications on the health system. Typically, each sample is decalcified and mounted on slides prior to H&E staining and immunohistochemistry which takes several days to prepare and analyse these samples [12]. It is estimated cost of analysis per femoral head is around £150 to £300 lb, this amounting to £4800 to £9600 in a single orthopaedic unit catering to a population of 400,000 people. With the rising healthcare cost and constrains on existing facilities, it is prudent to rationalise which patient would most benefit from further investigations.

In this study, as shown in previous study, the majority of femoral head samples sent for histopathological examination were negative for malignancy (85%) [13, 14]. Using screening clinical questions, we found routine histological examination based only on (Q3) previous history of malignancy or concurrent malignancy, without (Q1) clinical suspicion based on history or (Q2) radiological evidence of suspicious abnormality, had the least sensitivity or specificity (Table 1). Using screening clinical questions could potentially reduce the histological investigations by 26%.

Pathological fractures are usually due to advanced malignancy. With current advances in radiotherapy and chemotherapy, the outcome and prognosis in these patients have improved [15, 16]. In this study, all patients with a positive tissue sample were referred to oncology; however, the management of all patients was only palliative and with very poor survival outcome. Patients in this cohort group have a poor outcome due to other associated comorbidities with or without malignancy [17]. Malek et al. reported similar results in a large series of 533 patients with femoral neck fracture over 2 years; 32 patients had bone specimens sent for histology. 12.5% cases had positive histology, and mortality in negative cases was 16% compared to 25% in metastatic fracture cases over an average of 3 years [8].

It is debatable whether histological examination results altered the management of these patients significantly to influence the survival of these patients. But having a

histologically confirmed diagnosis becomes a paramount prerequisite for oncologist before commencing the patient on any treatment even if it is palliative treatment. This is true in the cases where patients had no previous history of malignancy as they are most likely to benefit from oncological input [14]. 83% of our patients already had metastasis (15/18) at the time of presentation (50% new cases), and the likely survival of these patients with or without oncological treatment is unknown [18–21]. Decision for oncology treatment hence have to be judged on merit of individual patient comorbidity with consultation of the patient and relatives as any interventional has its on associated complications [21–23].

There a few limitations of the study; we are unaware of cases of malignancy that were missed by the histopathological specimens or where no sample was sent. This was outside the scope of this project which aimed to identify features associated with positive histopathological diagnosis.

Conclusion

The data from this study demonstrate that past medical history of malignancy alone is not an indication to request for histopathological examination of the femoral head. Using screening questions could potentially be a cost-effective method to identify patients likely with malignancy.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All applicable international, national and/or institutional guidelines for the care and use of animals were followed. This article does not contain any studies with human participants or animals performed by any of the authors. Data used in this study were within the approval of hospital ethical standards.

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