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Abstract

Aim—To complete an audit of bone marrow trephine biopsy adequacy in children *Material*—605 specimens from children with neuroblastoma submitted by 25 centres were reviewed centrally. This reassessment ran between January 1995 and August 1998.

Results-25% of specimens (95% confidence interval (CI) 21% to 29%) were inadequate compared with 17% (95% CI 14% to 20%) in a previous study. Variation between individual centres' performance remains high (5-54% of specimens inadequate). Had five centres performed as well as previously, the inadequate biopsy rate would have been unchanged from that found in the previous study. There was no important improvement in any centre's performance. Earlier suggestions about change in practice have had no discernible impact on centres' ability to obtain adequate bone marrow trephine biopsies from children.

Conclusions—The responsibility for improving the rate of adequate biopsies lies with individual centres. Reporting pathologists might help by making even more positive attempts to influence operators within their own centres. (J Clin Pathol 1999;52:851–852)

Keywords: bone marrow trephine biopsy; children; neuroblastoma

We previously reported a 17% average rate of inadequate bone marrow trephine biopsies from children in a retrospective, multicentre study.¹ We privately alerted individual centres to their own results before the anonymised results were published and made suggestions in that publication that any all or a combination of the following steps might be taken to reduce this rate: increasing the proportion of biopsies taken by haematologists; retraining unsuccessful operators; concentrating on successful operators (of whatever specialty); and increasing the feedback about quality of specimens from those reporting the biopsies to the operators. We have reassessed the performance of a large number of centres who submitted trephine biopsy specimens from children with neuroblastoma for central review with the aim of discovering whether any improvement had occurred.

Methods

This reassessment covered the period between January 1995 and August 1998 and includes all bone marrow biopsies taken, submitted, and

reviewed during that period. Criteria for adequacy were as previously described.1 Briefly, cores were considered inadequate unless the sections contained at least 0.5 cm of well preserved bone marrow, as opposed to cortical bone/cartilage, or obvious tumour was detectable. No attempt was made to repeat the exercise of determining the specialty of the usual operators; it seemed unlikely that individual centres would have implemented alterations in practice at the same time as each other, and it remains possible that some centres did not attempt to modify their practice until after the results of our earlier study were published. In addition no cores from two centres from the previous study have been reviewed during the course of this reassessment and two other centres in the current study did not participate in the earlier one. Confidence intervals were obtained from standard tables (Documenta Geigy, Scientific Tables).

Results

In total, sections from 605 bone marrow trephine biopsies from 150 children with neuroblastoma submitted by 25 centres were reviewed for this reassessment. Of these, 154 (25%; 95% confidence interval (CI) 21% to 29%) were considered inadequate, compared with 139 of 822 (17%; 95% CI 14% to 20%) from the previous study.1 The confidence intervals do not overlap. This probably represents a true deterioration in performance. Table 1 compares the performance of those 13 centres in the present study which each submitted at least 20 cores with their earlier results. No centre had a convincingly improved performance. Inadequate biopsy rates varied widely among these 13, from 5% to more than 50%. Two centres, numbers 3 and 8, had previously submitted so few cores (reflected in the wide confidence intervals) that it is inappropriate to compare their current with past performance. No striking differences were noted between current and past rates of inadequate biopsies from centres 1, 2, 4, 6, 7, and 9. There may have been a deterioration in the performance of centres 5 and 10, and in 11-13 there is a strong suggestion that they may not be doing as well as previously; the confidence intervals of current and past performance in these three do not overlap. Much of the overall deterioration in results can be accounted for by the increased rates of inadequate biopsies from these five centres; had they performed at their previous level we might reasonably have expected 52 fewer inadequate cores. This would have reduced the overall inadequacy rate to 17%, the figure observed in our earlier study.¹

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Table 1 Inadequate biopsy rates in 13 centres submitting 20 or more cores, ranked according to % of inadequate cores in the present study, compared with rates found in the previous study¹

Centre	Total cores	Inadequate, current study		Inadequate, previous study	
		n (%)	95% CI	(%)	95% CI
1	40	2 (5.0)	0.6 to 16.9	(5.0)	1.5 to 13.4
2	36	2 (5.0)	0.7 to 18.7	(5.4)	1.1 to 14.9
3	28	3 (10.7)	2.3 to 28.2	(33.3)	4.3 to 77.7*
ł	33	4 (12.1)	3.4 to 28.2	(18.4)	7.7 to 34.3
;	69	10 (14.5)	7.1 to 25.0	(2.6)	0.3 to 9.1
,	44	8 (18.2)	8.2 to 32.7	(16.7)	4.7 to 37.4
	30	8 (26.7)	12.3 to 45.9	(16.0)	4.5 to 36.1
3	35	9 (25.7)	12.5 to 43.3	(33.3)	9.9 to 65.1*
1	23	6 (26.1)	10.2 to 48.4	(18.3)	10.6 to 28.4
0	73	21 (28.8)	18.8 to 40.6	(18.8)	10.1 to 30.5
1	24	13 (54.2)	32.8 to 74.5	(15.5)	8.5 to 25.0
2	57	31 (54.4)	40.7 to 67.6	(16.9)	9.0 to 27.7
3	33	18 (54.6)	36.4 to 71.9	(13.2)	14.6 to 33.8

*These two centres submitted fewer than 20 biopsy cores in the previous study. CI, confidence interval.

Discussion

This reassessment completes one audit cycle. Its chief finding is of a disappointing overall deterioration in the proportion of adequate biopsies. The study is deficient as an audit in at least one respect; we recommended a range of options which centres might adopt in order to improve their performance but, because of the number of centres involved and the potential complexities of timing and detail of any modifications in practice that each centre might have adopted, we did not attempt to identify or categorise those modifications. At one extreme no changes in practice may have occurred; at the other, the full range of suggested options may have had no effect on performance.

No formal statistical analysis of individual centres' performance has been carried out. The "controls" for this study are historical. Although we believe we have not become more demanding in our criteria of adequacy it remains possible that our qualitative assessment of features other than the length of cores could have changed over the years. It is also possible that some centres have submitted for review cores which in the past might have been discarded locally as being worthless. Other uncontrolled influences may also have affected the results. For example, because our adequacy criteria allowed some small cores to be included if obvious tumour was present, the proportion of cases with tumour

infiltrating the bone marrow might affect the results; there may have been some artificial increase in the inadequate biopsy rate owing to greater numbers of children with limited stage disease. However, it is unlikely that such influences alone can account for the bulk of the deterioration. We may have inappropriately apportioned the burden of the overall deterioration in performance. In only three centres was there no overlap in confidence intervals; our decision to include centres 5 and 10 in the calculation of "excess" inadequate biopsies was taken merely to illustrate the way in which nonsignificant differences from individual centres can accumulate if the trend in each is in the same direction.

In any event, it now seems unlikely that further published comments from the central reviewers of these biopsy specimens will have much direct impact on individual centres' performance. It is now even more important than before that local initiatives, in particular active and direct feedback from reporting pathologists, are employed to influence the operators. Each centre must bear a responsibility for maintaining or improving the quality of bone marrow biopsy cores from children, whatever disease they may have. The ability of several centres to maintain high success rates underlines our view that inadequate biopsy rates of > 30% should not routinely be tolerated by any centre; nor is there any good reason for being complacent about rates of even 20%.

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 Reid MM, Roald B. Adequacy of bone marrow biopsy specimens in children. J Clin Pathol 1996;49:226-9.