Open versus needle biopsy in diagnosing neuroblastoma

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Background: Open surgical biopsy is traditionally advocated prior to initiating therapy in UKCCCLG neuroblastoma protocols. We report a single centre experience comparing the utility of open biopsy vs image guided needle biopsy in aiding the definitive diagnosis and risk stratification of neuroblastoma – (Shimada classification, MYCN expression, cytogenetics – 1p 11q, 17 q).

Methods: Medical records of all new cases of neuroblastoma presenting to a single UKCCCLG centre during January 2002–July 2013 were examined.

Results: Thirty nine patients underwent a biopsy of primary tumour for neuroblastoma during the study. Twenty one children had open biopsy and eighteen cases had a needle biopsy. Staging of neuroblastoma revealed - stage 4 (n = 26), stage 3 (n = 7), stage 2 (n = 3) and stage 4S (n = 3). Sites of primary tumour were adrenal gland (n = 20), abdomen (n = 12), thoracic (n = 4), abdomino-thoracic (n = 2) and abdomino pelvic regions (n = 1). All patients (open vs needle) had adequate tissue retrieved for histological diagnosis of neuroblastoma. One needle and one open biopsy case did not have MYCN status determined despite adequate tissue sampling. Seventeen patients (7 open and 10 needle biopsies) had 1p and 17q status reported in MLPA testing (Multiplex Ligation-dependent Probe Amplification). No single patient required a repeat tumour biopsy. Morbidity in the series was minimal with only one child – open biopsy group, requiring emergent laparotomy to control bleeding from an abdominal primary tumour. No complications were recorded with needle biopsy.

Conclusions: Open and image guided needle biopsy appear to yield adequate tissue sampling for diagnosis, risk classification and staging of neuroblastoma. Further larger co-operative studies may usefully guide national and international protocols.

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Neuroblastoma is the most common extracranial solid tumour in childhood and the most frequently diagnosed neoplasm in infancy [1]. It accounts for more than 7% of malignancies in patients younger than 15 years and around 15% of all paediatric oncology deaths [2]. Neuroblastoma tumours derive their origins from undifferentiated and/or differentiating cells emanating from neural crest-derived sympathetic precursors. Neuroblastoma is well noted for its remarkable broad spectrum of clinical behaviour. The tumour is best described as enigmatic and unpredictable due to its contrasting pattern(s) of clinical behaviour notably life threatening progression, maturation to ganglioneuroblastoma or ganglioneuroma, and the capacity for spontaneous regression. Even maturation toward, or initiation as benign ganglioneuroma may be associated unpredictably with compromise of vital structures.

In 2009, the International Neuroblastoma Risk Group (INRG) task force developed a new staging system (INRGSS) to facilitate a consensus based approach for pre-treatment risk stratification [3]. This currently widely accepted classification uses age, extent of disease and biological factors including MYCN, tumour cell DNA content and 11q23 [4] to stratify risk categories for treatment. Adequate tumour tissue sampling to permit diagnosis is thus mandatory to aid accurate risk stratification and treatment assignment. Open surgical biopsy is currently a key element in UKCCCLG and European neuroblastoma protocols. Two published studies designed to compare open and needle core biopsy techniques in neuroblastoma reported very different findings and hence recommendations regarding which technique is superior are controversial [5,6]. The aim of this study was therefore to critically evaluate evolving experience at our centre with regard to the feasibility and adequacy of tissue sampling and the risk stratification of neuroblastoma tumours with open or image-guided needle core biopsy.

1. Methods

We conducted a retrospective review of medical case records of all patients who were newly diagnosed with neuroblastoma at Alder Hey Children’s Hospital during the period January 2002–July 2013. All cases were included in the study. The International Neuroblastoma Risk Group (INRG) risk classification is a consensus based approach for pre-treatment risk stratification [3]. This currently widely accepted classification uses age, extent of disease and biological factors including MYCN, tumour cell DNA content and 11q23 [4] to stratify risk categories for treatment. Adequate tumour tissue sampling to permit diagnosis is thus mandatory to aid accurate risk stratification and treatment assignment. Open surgical biopsy is currently a key element in UKCCCLG and European neuroblastoma protocols. Two published studies designed to compare open and needle core biopsy techniques in neuroblastoma reported very different findings and hence recommendations regarding which technique is superior are controversial [5,6]. The aim of this study was therefore to critically evaluate evolving experience at our centre with regard to the feasibility and adequacy of tissue sampling and the risk stratification of neuroblastoma tumours with open or image-guided needle core biopsy.
Children’s Hospital between January 2002 – July 2013. Records were studied and the following information extracted – (i) age at diagnosis, (ii) gender, (iii) INSS stage, (iv) type of biopsy – needle vs open, (v) histology (vi) MYCN status, (vii) 1p, 11q, 17q, (viii) post biopsy complications (ix) need for blood transfusion within 48 hours of biopsy and (x) need for repeat biopsy.

Both open and needle biopsies were performed under general anaesthesia. Open surgical biopsy was performed for abdominal, pelvic and thoracic lesions using a mini laparotomy or minithoracotomy incision by the paediatric oncology service. After tumours were clearly identified a 1cm² tissue sample was excised using a scalpel blade. Haemostasis was achieved using bipolar diathermy and absorbable haemostats – SURGICEL® (ETHICON INC Johnson & Johnson Company) or TISSEEL (Baxter Healthcare UK) where necessary.

Core needle biopsies were performed under ultrasound guidance by the interventional radiology department with a BIOPINCE disposable full core biopsy instrument (18 G) – Angiotech Medical Device Technologies Inc., Gainesville, FL, USA. A minimum of 4 needle core biopsies were taken to ensure adequate tumour sampling.

2. Results

Thirty nine patients (20 female) underwent biopsy for solid tumours. Twenty one cases had open surgical biopsy and 18 had needle core biopsy. Median age at biopsy was 24 months (range 1-76 months). Twenty six patients had INSS stage 4 disease, seven had stage 3, three stage 2 and three stage 4s. Anatomical sites included – adrenal gland (n = 20), abdomen (n = 12), thorax (n = 4), thoraco-abdominal (n = 2), and abdomino-pelvic(n = 1). A single infant with an adrenal primary tumour had metastatic liver lesions biopsied.

2.1. Tissue adequacy

No single patient required a repeat biopsy. All cases had adequate tissue sampling for histology (Shimada staging). Twenty patients (95%) in the open biopsy group and 17 (94%) patients having needle biopsy group had MYCN status accurately reported. Four patients who did not have MYCN status determined had widespread metastatic disease and were subsequently treated as ‘high risk’ cases. Twenty – 8 open and 12 needle biopsy cases had 1p status recorded. Eighteen patients – 7 open and 11 needle biopsy had 17q status determined. All tumours biopsied from 2010–2013 had 100% MLPA reporting for 1p, 11q and 17q status.

2.2. Complications

A single patient (a Stage 4 adrenal primary lesion) – who underwent open biopsy of tumour required blood transfusion and an emergent laparotomy to control bleeding. Blood loss for all other patients with either biopsy technique was minimal – median fall in haemoglobin recorded was 1.3 g – range 0–4.5 g (NS). Needle biopsy patients experienced no complications.

3. Discussion

Various modalities deployed in the treatment of newly diagnosed neuroblastoma include surgery, chemotherapy, radiotherapy, differentiation therapy, immunotherapy, and in selected cases notably 4s disease careful observation only. Most clinical trials now stratify neuroblastoma patients into low, intermediate or high-risk groups based on age of the patient, INSS stage, histology according to the INPC, MYCN status, and DNA ploidy [6,7]. The biological heterogeneity of neuroblastoma tumours occurring in childhood has resulted in a dichotomization of therapeutic approaches directed at reducing intensity of treatment in tumours deemed to have favourable biology and an intensification of chemoradiotherapy in those lesions linked with an adverse prognosis [2]. It is therefore paramount that the diagnosis and risk stratification of neuroblastoma is wholly accurate.

Only a limited number of reports have examined the technical feasibility of undertaking image-guided needle core biopsy of paediatric neuroblastic tumors [8,9]. Open surgical biopsy has traditionally been the favoured time honoured approach in neuroblastoma and is currently recommended in UKCCCG guidelines. The utility of open biopsy preferred commonly by oncologists and surgeons is due to the ability to achieve an adequately sized tissue sample for the complete histological and molecular characterisation of neuroblastoma [6]. At our centre (from 2010 onwards) – after the early success of initiating needle biopsy we developed the uniform practice of performing needle biopsy for all anatomically accessible lesions. All needle biopsies were of sufficient high quality with crucial biology adequate for Shimada histological classification including data on MYCN, 1p and 11q, 17q with modern laboratory methods [10,11]. Gupta et al reported a duodenal injury and small bowel obstruction occurring in their series of thirteen children having open biopsy [5]. Six patients who had open biopsy also required blood transfusions within five days of biopsy. More recently, Hassan et al published their early experience with open and needle biopsy and found a significantly higher number of major complications in patients having open biopsy [6]. We are fortunate that open surgical biopsies at our institution did not result in a significantly greater number of complications than needle biopsy except for a single patient who required emergent re-exploration to control bleeding from a stage 4 adrenal primary.

Heterogeneity is a characteristic hallmark of neuroblastoma, and it is well known that samples taken from different regions of a primary tumour are known to vary in terms of MYCN, 1p status, neuronal components and extent of differentiation [12]. To this end needle biopsy cores taken from multiple sites within a neuroblastoma tumour has many theoretical advantages over open biopsy in accurately determining disease risk [13].

Image guided needle biopsy does though have some limitations which include the technical challenges to adequately access tumours in anatomical sites surrounded by distended bowel or large blood vessels. Clotting derangements are not a definitive contraindication as open biopsy may result in as much or more bleeding than needle biopsy. Using the biopsy core needle for example the interventional radiologist has the advantage of being able to adequately seal the needle track with Gelfoam haemostatics to minimise bleeding. The number of cores that can be taken vary between 4–8 ensuring good sampling of vital healthy tumour tissue. Additionally the versatility of multiple needle core samples can also usefully aid tumour banking and storage for future collaborative studies, research and clinical trials.

In summary, experience at this UKCCCG centre with needle biopsy indicates it yields adequate tissue sampling for the diagnosis, risk classification and staging of neuroblastoma. Larger co-operative studies may usefully support the wider practice of deploying needle biopsy in future protocols and neuroblastoma staging.

References