



Impact of Oncologist Initiated Selective Review of Pathology Specimens in Multidisciplinary Onco-pathological Discussions on the Management of Malignancies in a University Hospital in India

Unni S. Pillai¹, Biswajit Dubashi^{1*}, Smita Kayal¹, Sunu. Cyriac¹, Debdatta Basu²,
Ranjith Kumar¹, Sajini Elizabeth Jacob² and Bhawna Badhe²

¹Department of Medical Oncology, JIPMER, Puducherry, Pin-605 006, India.

²Department of Pathology, JIPMER, Puducherry, Pin-605 006, India.

Authors' contributions

All the authors contributed equally to the article. Authors USP and BD were involved in drafting the article, revising it critically content and final approval of the version submitted to the journal. Authors USP and BD were involved in data collection management and analysis. All authors read and approved the final manuscript.

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ABSTRACT

Aim: Reported discrepancy rates after pathology review of surgical pathology specimens vary widely from 1.3% to as high as 80%. The purpose of this study was to assess the frequency of discordant diagnoses after onco – pathological discussions and to determine whether these contributed to a change in the treatment decision.

Methods: All the consecutive cases, whose diagnoses and management were discussed in the onco – pathological discussions from January 2010 to April 2015 at Jawaharlal Institute of Post Graduate Medical Education and Research, (JIPMER) India, were included in the study. Written

*Corresponding author: E-mail: drbiswajitdm@gmail.com, biswajit.d@jipmer.edu.in;

informed consent was taken from all the participants. The data was collected retrospectively from the onco- pathology register and the hospital records of the patients. The patients were considered to have a change in the diagnoses only when it resulted in a significant change in therapy or prognosis.

Results: A total of 353 cases were discussed and analyzed in the onco-pathological discussions. Among these 353 cases, 147 cases (41.75%) were haematological malignancies and 206 cases (58.25%) were solid tumors. Discussions were held on 614 pathological specimens, 354 biopsies, 64 cytology and 196 bone marrow studies. Clinically significant discordances were noted between the initial reports and the impressions after onco – pathological discussions in 33 cases (9.35%). The rate of discordance was 8.1% for heamato lymphoid malignancies and 10.12% for solid tumors. Among these 33 cases, follow-up details were available for 24 patients (72.7%) and the clinical behavior of the diseases correlated with the review diagnoses made at the onco – pathological discussions rather than the initial reports.

Conclusions: The onco – pathological discussions have a significant impact on the treatment decisions and outcomes. Onco- pathological discussions should be made as a part of all multidisciplinary boards.

Keywords: Pathology; cytopathology; immunohistochemistry.

1. INTRODUCTION

Secondary review of pathology materials is a standard practice in many institutions before choosing optimal treatment for patients with cancer in developed countries [1]. Numerous studies have addressed the role of second opinions within general surgical pathology and have reported discrepancy rates up to 9%, with around 6% having major therapeutic significance [1-8]. The discrepancies were as high as 80% in site-specific malignancy studies [9].

Considerable knowledge has been gained in this arena especially when a secondary review is mandatory as a part of large multi-centre trials [10,11]. There are organ specific and malignancy-specific guidelines for pathological reviews and it is a standard practice in many of the academic centers in developed nations [12].

Unfortunately, pathological reviews are seldom done in many of the developing nations and there are no national standardized operating procedure guidelines or national reference centers in resource-poor regions [13-16]. There are also practical difficulties in dealing with large volumes of pathological specimens with limited manpower and resources in these regions. In these situations, a selective pathological review of cases may be a way forward, especially in challenging cases [17].

We analyze the impact of combined review of clinical, pathological and laboratory parameters in onco –pathological discussions in an academic university center in India. Studies on the impact

of such onco - pathological discussions on diagnosis and further on treatment are rare. The purpose of this study was to assess the rate of discordant diagnoses and to determine whether these contributed to a change in the treatment.

2. MATERIALS AND METHODS

The onco- pathological review in our study is defined as a review of pathological specimens by a group of pathologists and oncologist, initiated at the request of treating oncologist, in a multidisciplinary case conference process. This is different from the routine mandatory review by a second pathologist of all the malignancies which is the standard of care at many developed nations and academic institutions since the process of review was initiated after a comprehensive pathology report from the side of treating oncologist. All the cases discussed in the onco -pathological discussions between, January 2010 to April 2015 and treated at JIPMER hospital for malignancy were included in our study. Consultation or review at the request of the primary pathologist or prior to finalization of the primary pathologist's report is not included in this study. The cases for onco -pathological discussions were selected by the treating oncologist at the department of medical oncology whenever there were discordances between clinical behaviour of tumor (eg- a sensitive tumor did not respond to standard chemotherapy), radiological or biological behaviour (eg-unusual site of metastasis) of the tumour and pathological diagnoses, want of detailed pathology report, to find out primary in cases of occult primary with

metastasis and academic discussion of rare tumors.

Discussions were held on the clinical details, and all the available imaging, laboratory and pathological findings including cytochemistry, immunohistochemistry, molecular and the genetic tests were reviewed by a panel of expert pathologists from the respective field, and clinicians to arrive at a possible consensus diagnosis. The material reviewed encompassed the full spectrum of all the available pathology specimens for individual patients. Additional pathological, radiological and genetic tests were carried out to reach diagnosis after discussion as directed by the panel.

Cases were considered to have discordance only when the change in diagnosis resulted in a significant change in therapy or prognosis. Changes that have only modified the histologic grade were not taken into consideration because it could be argued that assignment of a grade often is subjective and the consequences of a changed grade on therapy are frequently ambiguous. Using a TNM staging framework, changes in T classification were considered significant because it is possible to determine the accurate pathological T, N, and M classification from the gross specimens, pathological and cytological slides and radiological findings which have been submitted.

The descriptive data was collected for concordance or discordance and represented as frequencies and percentages. A chi-square test or fishers exact t test was performed using SPSS version19 to determine which organ systems were more likely to have a significant change in pathologic diagnosis. An attempt was made to obtain follow-up information on all cases with a discrepant diagnosis. All statistical analysis was carried out at 5% level of significance and a p value less than 0.05 was considered as significant.

3. RESULTS

We have analyzed 353 cases which were discussed in onco-pathological discussions from January 2010 to April 2015 in our hospital. The mean age of the patients was 45.4 years (range 6 months to 73 years). Among the 353 cases, 58.5% were females.

Among these 353cases, 147 cases (41.75%) were haematological malignancies and 206

cases (58.25%) were solid tumors. There was 9.35% discordance between the initial report by the pathologist and secondary review by the multi-disciplinary onco-pathology board (33 of 353 patients) resulting in the change in the management of the patient. The discordance rate was 8.1% for heamato lymphoid malignancies and 10.12% for solid tumors. (Table 1) There was statistically no significant difference in discordance between solid tumor and hematolymphoid malignancies in our study (p-0.52).

Table 1. Overall discrepancies in the findings after the onco pathological meeting

Change	Heamato lymphoid	Solid tumour
Primary histological type	7	13
Malignant to benign	1	2
Benign to malignant	1	2
Upstaged	2	0
Down staged	1	2
Margin status changed	0	2
Total	12	21

The total number of specimens retrieved and reviewed were 614(354 biopsies, 64 cytology, and 196 bone marrow studies) during the study period. The discordance rate was 2% for bone marrow samples, 3.2% for cytology and 7.6% for histopathology samples. The discordance was significantly higher among the histopathology specimen compared to cytology or bone marrow samples (p-0.007) (Table 2).

Table 2. Discordance rate among pathology specimen type

Specimen	Number	Change	Discordance %
Cytology	64	2	3.2
Bone marrow	196	4	2%
Histopathology	354	27	7.6%

Among the hematolymphoid malignancies majority of the cases were acute leukemia and NHL (32.65% each) (Table 3). A comprehensive Immuno histochemistry panel along with cytogenetic analysis and molecular test were employed to confirm the discordance among hematolymphoid malignancies. There was significantly higher discordance in NHL after onco-pathology discussions (p-0.012). The discordance among other hematolymphoid malignancies was statistically not significant.

Among solid tumors, the most common were breast cancer (27.18%) followed by gastrointestinal carcinomas (21.85%). There were 6 cases in which primary tumors were unknown constituting 2.9% of all cases among solid tumors there was significantly higher discordance in ovarian malignancy (p-0.004) and carcinoma of unknown primary (p-0.015).

The changes made in the diagnoses of carcinoma ovary and germ cell tumors were on the pre-operative diagnosis, made on cytology or biopsy specimen. Availability of large specimens after surgery resulted in the comprehensive evaluation and contributed to correct diagnosis in these cases. The majority of the changes in the diagnosis and treatment of gastrointestinal malignancies can be attributed to the identification of more lymph nodes after careful examination of the specimen (Table 4).

There were changes in the treatment of 21 patients (63.6%) of cases after onco-pathological discussions. The changes in the 12 cases (36.4%) had an impact on prognostication of the disease but there was no change in treatment. These changes include subtype changes in acute lymphoblastic leukaemia (we use multicentre protocol 841 for all pediatric leukemia irrespective of lineage or risk during the study period), changes in NHL subtypes (all the NHL patients were offered CHOP during the study period) and identification of primary tumour in unknown primary (There were uniform

chemotherapy protocol for all the unknown primary tumours).

4. DISCUSSION

Second opinion studies in oncology typically are comprised of single organ system or disease reviewed by expert pathologists [1-9]. In the present retrospective study, we analyzed the work of a multi-disciplinary onco-pathology meeting in a teaching university hospital, JIPMER in India, thus gaining useful insight into the capture of cases to be discussed and the impact of discussion on clinical decision making.

The cases discussed in the meeting were only a fraction of the total number of cases treated at the center since only selected cases were discussed. The pathological diagnostic discordance of 9.35% in our study. The discrepancies in pathological diagnosis were uniform for both haematological and solid tumors in our study. There were significantly more discrepancies in NHL, ovarian neoplasm and carcinoma of unknown primary.

Ganesan et al from South India published the role of clinicopathological meeting in ovarian cancer and reported a discrepancy of 52.5% [17]. This was consistent with the high level of discordance found in the present study. The reported discrepancies in the present study were less compared to the available published literature (Table 5).

Table 3. Discordance in hematolymphoid malignancies

Site	Number	Change	Discordance %	Treatment change %
Acute leukemia	48	3	6.25	2
NHL	48	8	16.7	4.2
Myeloma	25	0	0	0
Chronic leukemia	10	0	0	0
Hodgkins lymphoma	11	0	0	0
LCH	5	1	20	20

Table 4. Discordance in solid malignancies

Site	Number	Change	Discordance %	Treatment change %
Breast	56	2	3.6	3.6
GIT	45	5	11.1	8.8
Sarcoma	25	2	8	8
Lung	22	1	4.5	0
Ovary	18	6	30	30
PNET	10	1	10	10
Germ cell tumor	8	1	12.5	12.5
Cups	6	3	50	17
Others	16	0	0	0

Table 5. Reported rates of discordance in other studies

Study	Year of study	Number of patients	Site of malignancy	Discrepancy (%)
Chafe S et al. [11]	2000	514	Female genital tract	12%
Ganesan P et al. [17]	2008	91	Ovary	52.7%
Rao et al. [18]	2014	107	Urogenital tract	26.7%
Murthy V et al. [19]	2014	242	Breast	42%

The significant achievement of the onco-pathological discussion was identification of a possible lineage of the tumor in half of the cases with unknown primary. These high rates may be due to small samples of individual cases, but we believe that onco - pathological discussions have an important role to play when the primary is unknown. A comprehensive panel of IHC along with robust clinical and imaging information may provide confidence to the pathologist to commit on the possible origin of primary malignancy.

Among hematolymphoid malignancies, there was a discrepancy rate of 16.7% for Non-Hodgkin's Lymphoma. A comprehensive immunohistochemistry panel alone helped to identify 12.5% of the discrepancies. But these discrepancies did not translate into a change in treatment since the treatment for majority of B NHLs are chemoimmunotherapy. The significance of this fact may increase as we embrace on specific subtype specific treatment intensification or de-escalation in future.

There were uniform concurrences on the diagnosis of Hodgkin's lymphoma, myeloma and chronic leukemia on initial histopathology and immunohistochemistry done at the first instance. The flow cytometry helped to identify 4.2% discrepancies in leukemia lineage mostly in pediatric acute lymphoblastic leukemia, but treatment was not changed since the institutional policy was to treat them on MCP 841 protocol which does not risk stratify based on the lineage. There was a significant change in the treatment plan in a child with suspected relapse with LCH, wherein an image finding prompted for repeat biopsy study which in turn confirmed the relapse.

We recommend oncologist initiated selective review of pathology specimens in multidisciplinary onco-pathological meeting especially for carcinoma of ovary, non hodgkin's lymphoma and carcinoma of unknown primary. The selective review is suitable for the resource poor regions since the pathologist and the oncologist are not burdened with reviewing and discussing the whole malignancies and can save time and cost.

5. CONCLUSION

The onco- pathological discussions have a definite impact on the treatment decisions in selected situations in resource-poor regions and help in predicting the outcome of the disease and delivering better treatment.

ETHICAL APPROVAL

All authors hereby declare that the data was collected retrospectively from the onco pathology register and patients files and all the analysis been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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