LEVEL OF ERRORS, CHANGE IN DIAGNOSIS AND THEIR IMPACT ON MANAGEMENT IN CASES REFERRED FOR SECOND OPINION

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ABSTRACT

Objective: To determine the frequency of change in diagnosis and level of errors in cases referred to Armed Forces Institute of Pathology for second opinion and their impact on modifications of treatment and prognosis.

Study Design: Cross sectional study.

Place and Duration of Study: Department of Histopathology, Armed Forces Institute of Pathology, Rawalpindi, form Mar to Oct 2017

Methodology: All the cases referred for review diagnosis were tested by applying panel of immunohistochemical markers and special stains on formalin fixed paraffin embedded tissue sections as decided on morphology. Level of errors were defined as level I error: minor discrepancy with no impact on management, level II: minor discrepancy with impact on management, level III: main category remains same but there was change/confirmation of specific diagnostic entity with an impact on management and level IV: gross changes in diagnosis with significant impact on management. Level IV was further subdivided into IV a: benign misdiagnosed as malignant, IV b: malignant misdiagnosed as benign and IV c: changes in tumor subtype.

Results: A total of 100 cases, where review diagnosis was changed were included. Minor discrepancies (level I and level II) were observed in only 7% cases with little or no impact on the management. Most frequent discrepancy observed as Level III in 75% cases. Major discrepancy (Level IV errors) was noted in 18% cases.

Conclusion: There were high discrepancy rates between previous diagnosis and review diagnosis. The higher use of extended panels of immunohistochemistry markers were the most likely explanations.

Keywords: Discrepancy in diagnosis, Immunohistochemistry, Review diagnosis, Second opinion.

INTRODUCTION

Several studies reported the advantages of obtaining second opinion for more accurate diagnosis[1,2]. Second opinion after initial histopathological diagnosis is required in different situations[3-6]. The criteria when to get the second opinion vary considerably[3]. It may be needed for the patient/relatives satisfaction and if clinical impression of treating clinician does not tally with histological diagnosis. Sometimes second opinion is required when the patient is not responding to the treatment being given after initial diagnosis[4]. Such second opinions help to expose diagnostic errors and helps in proper management of patient[5]. Jamal *et al*, reported in their study that in 50.7% of the total cases, diagnosis was changed on review, out of which majority were malignant[3]. Hamdani *et al*, reported 72% discrepancy between initial and review diagnosis[6]. In the same study, different categories of discrepancies have also been discussed. In Pakistan, surgical pathology is still evolving as a science and clinicians are becoming increasingly aware of the importance of an accurate surgical pathology diagnosis for the treatment of their patients. While the basic aim of the practice of surgical pathology is to provide accurate diagnosis, it is equally essential to prevent an erroneous diagnosis, which can result in serious errors in the treatment and prognosis of the patient[7]. In a developing country like Pakistan most of the centers lack the facility of immunohistochemistry and special stains, which is thought to be essential for the diagnosis in many cases, and this further necessitates the importance of second opinion from more specialized referral centers. The section of Histopathology at Armed Forces Institute of Pathology (AFIP) Rawalpindi is serving as the major referral center for diagnostic surgical pathology. With the aid of extended immunohistochemical panel and special stains, accurate diagnosis has been made possible and subsequent change in the diagnosis of referred cases for review has a huge impact on the modification of management of patients.

The purpose of this study was to review the cases sent to AFIP for second opinion and to determine the changes in the diagnosis and to ascertain level of errors in the diagnosis. The results would help to establish the significance of acquiring second opinion and use of extended panel of immunohistochemistry for accurate diagnosis and subsequent benefit for the patient and

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also to ascertain various level of errors in the diagnosis of histopathological cases.

METHODOLOGY

This descriptive cross-sectional study was carried out at the AFIP, Rawalpindi, after taking approval from Institutional Review Board (certificate reference no: FC-HSP16-17/READ-IRB/17/416). A total of 100 cases, referred for second opinion to the department of Histopathology, from March to October 2017 were enrolled for the study. Cases for second opinion were received as paraffin blocks or slides and assigned new departmental number. Tissue was cut into sections by tissue microtome so that each section is not >5 microns thick. Slides were stained with Haematoxylin & Eosin (H&E) staining. The Immunohistochemical markers and special stains were applied as per differential diagnosis made on H&E slide and according to the manufacturer's guidelines. Immunohistochemistry results were interpreted on high power field objective. Nuclear, cytoplasmic and membranous staining pattern were used to determine positivity and negativity. With the baseline guidance from categories of diagnostic errors, mentioned in the study by Hamdani *et al*[10], various level of errors have been defined as level I error: minor discrepancy with no impact on management, level II error: minor discrepancy with impact on management, level III error: main category remains same but there is change/confirmation of specific diagnostic entity with an impact on management and level IV error: gross changes in diagnosis with significant impact on management. Level IV was further subdivided into IV a: benign misdiagnosed as malignant, IV b: malignant misdiagnosed as benign and IVc: changes in tumor subtype. Statistical software SPSS 21 was used for description and analysis of result.

RESULTS

A total of one hundred (n=100) review cases with subsequent change in the diagnosis were analyzed for various diagnostic errors. Minor discrepancies (level I and level II) and major discrepancy (Level IV errors with significant impact on management) were observed less frequently. Whereas, bulk of the cases were found to be falling in the category of Level III errors. The detailed distribution of these errors is shown in figure. Level III and Level IV errors are further elaborated in table-I & II respectively.

Table-I: Details of level-III errors.

Previous Diagnosis	Review Diagnosis	Number of Cases	Percentage
Malignant neoplasm	Specific diagnosis of carcinoma	45	60
Metastatic carcinoma	Identification of primary of tumor	9	12
Lymphoproliferative disorder	Specific diagnosis of lymphoma	12	16
Spindle cell neoplasm	Specific diagnosis of soft tissue tumor	9	12

Table-II: Detail of level-IV errors.

Previous Diagnosis	Review diagnosis	Category
Low grade sarcoma	Giant cell rich lesion	IV-A
Non Hodgkin's lymphoma most likely small lymphocytic lymphoma	Chronic caseating granulomatous inflammation-lymph node	
Malignant neoplasm	Reactive lymphoid hyperplasia	
Neurofibroma	Leiomyosarcoma	IV-B
Extensively autolyzed biopsy	Small round blue cell tumor Ewing's sarcoma	
Intradermal nevus	Malignant melanoma	
Adenomatous hyperplasia	Adenocarcinoma prostate	
Liposarcoma	Fat necrosis	
Thymoma (B2)	Thymic carcinoma	
Invasive ductal carcinoma	Squamous cell carcinoma	IV-C
Langerhans cell histiocytosis	T-cell lymphoblastic lymphoma	
Papillary urothelial carcinoma	Small cell neuroendocrine carcinoma	
Adenocarcinoma	Follicular carcinoma	
Adenocarcinoma	Pleural mesothelioma	
Follicular lymphoma	Extra nodal marginal zone lymphoma (MALT)	
Malignant serous carcinoma	Mucinous carcinoma	
Mixed papillary ependymoma (WHO grade I)	Non Hodgkin's lymphoma (DLBCL)	
Anaplastic astrocytoma (WHO Grade III)	Glioblastoma multiforme (WHO Grade IV)	

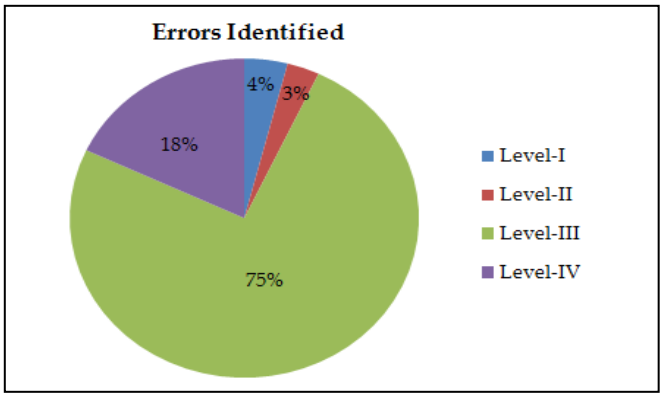

Figure: Errors identified during second opinion.

DISCUSSION

Most frequent discrepancy observed as Level III (main category remains same but there was change/ confirmation of specific diagnostic entity with an impact on management) in 75% cases. Major discrepancy (Level IV errors) was noted in 18% cases. In study previously conducted at the same department in 2006-7, reported concurrence rate between initial and review diagnosis was 53%. There were 23.5% of cases where major discrepancy was found resulting in the change in management. They applied immunohistochemistry markers in 64% of cases while we applied in all cases[8]. In another similar study at our department conducted in 2012, diagnostic agreement was reported as 49.3%, where there was no change in the review diagnosis and in 50.7% of cases discrepancies were found and the review diagnosis was changed[2]. In the present study diagnostic agreement was observed in only 7% cases where only minor discrepancies were observed with no/negligible impact on the management. During this time we have made extended panel of immunohistochemistry markers available at AFIP, which were helpful in making exact diagnosis and subtyping of tumor. Moreover, in the previous study immunohistochemistry markers were applied in 74% of cases while we applied those markers in all (100%) cases. These could be the possible explanations of higher discrepancy rates in the present study. In a similar study, Somcutian *et al*, evaluated the degree of concordance among histological diagnosis of sarcomas between non-specialized pathology center and highly specialized pathology center in Europe. They reported that complete diagnostic agreement was achieved in 62.5% of cases. Partial disagreement was achieved in 26.1% and major disagreement was observed in 11.4% of cases. They concluded that immunohistochemistry was the major responsible factor followed by difficulties in the interpretation of the morphology[9]. Diagnostic agreement rate was much lower in our study, likely due to difference in defining the discrepancy, however, major discrepancy rate (18%) in our study are comparable with their study. Al-Ibraheemi *et al*, reported 71% diagnostic agreement with a major discrepancy rate of 8%[10]. Thway *et al*, in their study found diagnostic agreement in 250 cases (71.8%), with 57 (16.4%) major discrepancies[11]. In a multicentral study from Europe, referral for second opinion showed a complete diag-nostic agreement in 56%, partial agreement in 35% and complete disagreement in 8% of cases[12]. The high variation in diagnostic agreements and discrepancy rates across the studies might be in part due to different definitions used for labeling discrepancy levels, variation in the panel of immunohistochemistry markers used in these studies and the impact of using molecular diagnostics and other ancillary tests in aid to the final diagnosis[13]. All these factors can contribute to the variation in discrepancy rates observed across various studies. In our setup we do not use molecular diagnostic techniques.

Although, in routine clinical practice, the idea of getting second opinion in every case seems quite daunting, yet the higher rates of disagreements reported in several studies is of grave concern. This variability in pathological diagnosis eventually results in high financial burden and also includes consequences of incorrect treatment in the form of higher morbidity and mortality rates[14]. It has also been hypothesized that poor inter-professional collaborations and coordination may have an adverse impact on delivery of services and care of patients. Case reviews and discussions at multidisciplinary team meetings have been evolved into standard practice with an aim to provide evidence-based management recommendations. The major advantages observed from such multidisciplinary meetings were competence development and patient support[15]. In a recent study, main barriers to a joint treatment recommendation were reported to be need for supplementary investigations and insufficient pathology reports[16]. Pillay *et al*, conducted a systematic review to evaluate the empirical benefits of such multidisciplinary team meetings and reported that between 4% and 45% of patients discussed at such meetings experienced changes in diagnostic reports after the meeting, which were likely more accurate. However, there was little evidence about improvement in clinical outcomes[17]. Several strategies have been assessed for improving delivery of healthcare services in low income countries. It has been reported that lack of coordination of care and lack of research addressing

coordination of care are the main areas need to be focused in these countries[18]. We suggest future research at our settings aiming towards number of interventions that can improve inter-professional collaborations.

We suggest establishing regular multidisciplinary meetings with other surgical pathology departments referring their cases for second opinion. We argue that the quality of decision making process in multidisciplinary meetings largely depend upon the quality of information being presented. Hahlweg *et al*, in their recent study demonstrated that there were great differences in quality of different aspects of information presented at these meetings. Final recommendations varied significantly and time constraints were found to play a major role[19]. Furthermore, healthcare professionals encounter various problems when collaborating in clinical practice and conducting regular multidisciplinary team meetings needs considerable investment of time and finances. In recent times, health informatics have been developed as an integrating factor for academic professionals to work as inter-professional healthcare teams for better practices and overall management of patients[20]. We also suggest implying modern health informatics system at our settings to tackle these problems. Modern day telemedicine techniques could be used to achieve these outcomes. This will help in presenting the quality information to the panel of experts sitting at a distance and also will reduce investment of time and finances. More accurate diagnosis concluded from these telemedicine sessions would also help to reduce the financial burden incurred to the patients and could also reduce the consequences of incorrect treatment based in inaccurate diagnosis. We also encourage seeking benefit from ancillary molecular diagnostic tools for achieving diagnostic accuracy.

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CONCLUSION

High discrepancy rates for Level-III and Level-IV errors. The use of extended panels of immunohistochemistry markers were the most likely explanations. Based on our study results we encourage getting second opinion for difficult cases, whether this opinion is in the form of intradepartmental meeting or getting review from another advanced lab. We suggest implying modern day telemedicine techniques to reduce the burden on our healthcare system due to referral for second opinion in substantial number of cases. This will help in presenting the quality information to the panel of experts sitting at a distance and also will reduce investment of time and finances.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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