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Concordance Between Clinical and Histopathological Diagnoses of Corneal Specimens

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As advances in high-resolution imaging occur, the usefulness of histopathologic diagnosis in many spheres of medicine is being questioned.¹ In a large series of autopsies, a 1999 study found discrepancies between clinical and post-mortem diagnoses in 36.24% of cases.² This and other studies have led some to suggest that all human tissue undergo histologic examination. With ballooning health care costs and a growing number of tools to aid in clinical diagnosis (slit-lamp biomicroscopy, confocal microscopy, anterior segment optical coherence tomography, etc), many have begun to question whether all corneal specimens should be sent for histopathologic examination. We sought to answer this question by retrospectively comparing clinical and histopathologic diagnoses.

A retrospective cross-sectional case series of corneal specimens was assembled from 3 institutions: The University of Wisconsin Madison (2007–2014), Scheie Eye Institute of the University of Pennsylvania (2008–2014), and Wills Eye Hospital (2008–2015). Institutional review board/ethics committee approval was obtained, and patients of all ages and genders were included in this study. The patients' ages, genders, clinical diagnoses, and histopathologic diagnoses were recorded from the pathology requisition forms, clinical notes, and histopathology reports. Similar information was collected from the Shahid Beheshti University of Medical Sciences (Tehran, Iran), and is reported separately.

A total of 1804 corneal specimens from 940 men and 864 women were reviewed. The average patient age was 59.9 years, with a minimum patient age of 2 months, and maximum of 103 years. The types of specimens were as follows: 1238 penetrating keratoplasties, 354 endothelial keratoplasties, 195 corneal biopsies, and 17 lamellar keratoplasties. The diagnoses were as follows: 11 acute trauma or chemical burns, 30 epithelial and stromal dystrophies, 81 noninfectious ulcers, 89 infectious keratitis, 168 scarring, 249 pseudophakic bullous keratopathy, 263 keratoconus, 293 endothelial dystrophies, 363 postoperative complications (i.e., graft failure, rejection, ectasia, etc), and 257 other (neoplasia, pterygia, cysts, etc). Concordance between clinical and histopathologic diagnoses was 88% (1594 of 1804) for all cases, and varied depending on the diagnosis, ranging from 72% for infectious keratitis to 100% for acute trauma and burns (Fig 1). Data from Shahid Beheshti University of Medical Sciences is shown in Figure 2 (available at www.aojournal.org).

There was a wide spectrum in the rate of concordance between the different disease categories. Data from the Shahid Beheshti University of Medical Sciences were reported separately owing to the large proportion of its patients with mustard gas keratopathy secondary to chemical warfare with this lipophilic alkylating agent [bis- (2-chloroethyl) sulfide].³ The clinical diagnosis in both groups was most accurate in scenarios relying heavily on patient history, such as acute trauma and burns. A clinical diagnosis of keratoconus, which is frequently aided by personal and family histories, clinical signs, symptoms, and multiple modalities of corneal imaging, was also excellent. As expected, postoperative complications such as failed corneal grafts were also nearly always correctly diagnosed. In both groups, histopathologic examination was most useful in cases of infection. Infection was a big cause of discordance between clinical and histologic diagnosis in a similar study.⁴ Although the clinical diagnoses of corneal specimens are often correct, some cellular features such as atypia can only reliably be seen using histology. Histologic examination can often confirm fungal and acanthamoeba keratitis (Fig 3; available at www.aojournal.org) before growth on cultures, although polymerase chain reaction has become an effective, although not widely available, alternative. In summary, although there was a high level of concordance between clinical and histologic diagnoses, histopathology creates unique educational, teaching, and research value, and provides an opportunity to inform medical and surgical management, reassure the patient and clinician, and confirm heritable disease. It remains the most definitive method of diagnosis, and should be considered for all corneal specimens.

References

1. Goldman BI. Reviving the hospital autopsy. Arch Pathol Lab Med. 2016; 140:503–504. [PubMed: 27232345]
2. Ermenc B. Discrepancies between clinical and post-mortem diagnoses of causes of death. Med Sci Law. 1999; 39:287–292. [PubMed: 10581907]
3. Blodi FC. Mustard gas keratopathy. Int Ophthalmol Clin. 1971; 11:1–13.
4. Rezaei Kanavi M, Javadi A, Javadi MA, et al. Concordance between clinical and histopathologic diagnosis in recipient corneas. Eur J Ophthalmol. 2011; 21:691–694. [PubMed: 21360481]

Figure 1.
Concordance between clinical and histopathological diagnoses (percent).

Figure 2.
A, Fungal hyphae (arrow; stain: Grocott's methenamine; original magnification, $\times 20$). B, Acanthamoeba cysts (arrow; stain: periodic acid-Schiff; original magnification, $\times 20$). Diagnosed by histology in cases of keratitis with negative cultures.

Figure 3.
Concordance at Shahid Beheshti University of Medical Sciences (Percent)