LETTERS TO THE EDITOR

Differential diagnosis of iridocorneal endothelial syndrome and posterior polymorphous endothelial dystrophy

EDITOR,—In the paper by Laganowski et al the point is made strongly that endothelial specular photomicroscopy (ESP) by revealing ICE cells and distinguishing between ICE- and PPD-like cells, will allow a definitive diagnosis even in uncertain cases and thus promote accurate management of patients and their families. Their own cases reflect the consistent unilaterality of iridocorneal endothelial (ICE) syndrome and the frequent bilaterality of posterior polymorphous dystrophy (PPD). The authors describe unilaterality in four out of 19 vesicular types, none out of two of the diffuse, and 14 out of 23 of the band type. Taken at face value this might suggest that there could be a large percentage of people with unilateral PPD disease that could be mistaken for the consistently unilateral ICE syndrome. On the other hand, the band type of PPD is so characteristic in its pattern that it does not share a similar slit-lamp picture with any ICE syndrome patient. Once these patients have been taken from the unilateral cases, then there is only one strictly unilateral case out of the 44 patients in whom a possible confusion could exist. Examination of this patient’s relatives would almost certainly show typical PPD findings which would confirm the diagnosis without the need for expensive instrumentation such as specular microscopy.

In addition, Laganowski et al assert that subtotal ICE plus syndrome has a characteristic circumscribed nest of abnormal endothelial cells which is pathognomonic of ICE and not seen in PPD. Figure 11 in the paper by Hirst and Waring,1 bears a remarkable resemblance to Figure 2 of Laganowski et al.2 The patient described by Hirst and Waring came from a family of patients with posterior polymorphous endothelial dystrophy in which histology confirmed the diagnosis in one of the family members. As Laganowski et al contend ‘while the two conditions may conceivably co-exist in the same eye or in different members of the same family, the ICE syndrome and PPD are distinct entities, the only explanation for our case would be that the two diseases are co-existing in the same family, or perhaps it is more likely that the findings of Laganowski et al are not pathognomonic of the subtotal ICE plus syndrome. Similar findings to these seen in Figure 2 were seen in a further 11 patients with the geographic and type of posterior polymorphous endothelial dystrophy in the original study by Hirst and Waring.1 Since that time, examination of further patients has confirmed these abnormal cells occurring in typical, familial, posterior polymorphous endothelial dystrophy.

In the first line of the discussion, it is suggested that Hirst and Waring reported the simultaneous occurrence of ICE syndrome and PPD in an individual or separately in different members of a family.2 We have not reported this. Perhaps the confusion was in the similar cell findings in some of our patients with geographic PPD and their patients with sub-total ICE plus. This finding is not ours alone as the similarity of cells as seen in Figure 2 of Laganowski et al is also illustrated in Figure 2 in our original paper.1 He highlights the difficulty in differentiating between these two conditions if the family history is negative and examination of family members provides no additional patient involvement.

Contrary to the statement that histopathological studies are based only on decompen-sated cornea and that they reveal differences in Descemet’s membrane which makes a relationship between ICE and PPD highly unlikely, there are some similarities histopathologically in the conditions particularly relating to intermediate filament staining as described by Rodrigues et al3 and Hirst et al.4 This is not to suggest that these are one and the same disease, or that they even occur in the same patient population: rather, as discussed in Hirst, it is possible that in the progressive geographic PPD, and the ICE syndrome a final common pathway of epithelialisation of the anterior segment takes place. The pathology bears an uncanny resemblance to iatrogenically produced epithelial downgrowth.

I would caution readers against assuming that the present histological study of PPD and ICE syndrome can necessarily be differentiated by specular microscopy. There is much still to be understood about these two diseases, and perhaps the future may show that they are actually variants of one disease which might explain the confusing picture resulting from different researchers’ findings.

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Reply

EDITOR,—We thank Dr Hirst for his comments on our paper.1 The purpose of our study was to determine whether the specular microscopic features of the ICE syndrome and PPD were unique and could be used to establish a definitive diagnosis in cases which apparently have features of both. We, therefore, chose patients with features of unequivocal ICE or PPD on slit-lamp examination.

We acknowledge that the majority of ICE and PPD cases can be distinguished clinically at the slit-lamp. In some cases, however, confusion and misdiagnosis occur and our paper confirms that such errors in diagnosis and classification can be overcome by examining the corneas by the expanded field contact specular microscopy, a non-invasive, painless outpatient technique.

We assert that ‘ICE cells’, which give rise to the hammered silver appearance on slit-lamp examination and appear as a negative of normal endothelial cells with the specular microscope, are pathognomonic of the ICE syndrome. In some cases of ‘subtotal ICE plus’ these cells may appear as an isolated feature in the remaining endothelium. We agree that Figure 11 in the paper by Hirst and Waring,1 resembles our Figure 2 of ‘subtotal ICE plus’.2 We contend that their Figure 11 shows classic ICE cells well demarcated from endothelium and is therefore of the relatives ‘ICE plus’. That this patient’s relatives have posterior polymorphous dystrophy (PPD) would not lead us to change our diagnosis since we believe that the diagnosis of ICE or PPD can only be based on the clinical signs of the corneas (providing, as this study has demonstrated, the condition has distinguishing features) and that ICE and PPD can coexist in different members of the same family in the same eye.

Dr Hirst’s historical report is from a relative of the case shown in his Figure 11. To extrapolate histological data from one family member with PPD to explain different physical signs in another member is scientifically unacceptable. Furthermore, this corneal button was not examined preoperatively by specular microscopy. The only currently practical means of deriving unequivocal evidence to distinguish ICE and PPD is to examine the endothelium from an affected eye with precise cell to cell correlation of specular micrographs with light and electron micrographs.

With regard to PPD, we disagree that examination of the corneal endothelium is the ‘criterion of diagnosis’. Moreover, in Hirst and Waring’s paper,2 the majority of relatives of patients with PPD showed no abnormality.

We do disagree with Hirst and Waring that ICE is ‘consistently unilateral’; six of our 80 patients with ICE syndrome have typical ICE cells bilaterally. We do agree, however, given the advanced pathology of corneal buttons removed at keratoplasty, that the histopathology may well represent a common pathway of cellular response and therefore be a poor discriminator of the primary diagnosis.

We are sure that Dr Hirst would agree that the present enigma of ICE/PPD will only be resolved by close collaboration between clinician and pathologist, and preferably by building detailed correlative databases as a multicentre activity.

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