Comparative aspects and aetiology

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DISCUSSION

Over the first day and a half of this meeting on comparative dysautonomias, we have heard about clinical signs, epidemiology, and some very elegant pathology, electronmicroscopic and neuropeptide studies. All of this has increased our understanding of what is going on, but leaves us with basic questions to answer. I would like to address myself to two of these questions: firstly, is the comparison we have made between grass sickness and Feline Dysautonomia valid, and is the information from dysautonomia in man of direct relevance? And secondly what, if anything, does this and the other information we have gathered tell us about aetiology?

To take the first point and answer it, the comparison between grass sickness and Feline Dysautonomia would appear to be valid. The pathology and neuropeptide studies offer similarities which are convincing. Any differences in the clinical picture can be attributed to inter-species differences, and while they may be important in those species, are probably not of over-riding significance in this discussion. Their similarity raises another interesting point for those of us in veterinary medicine who are used to making comparisons; should we not be looking in other species for comparable conditions? There has been one case report in the dog of what looks to be a very similar condition; perhaps we should be more aware of the possibility in some of our other species, e.g. the cow. The numbers of cases of pure human dysautonomia are very small, and information on underlying pathology in particular, is limited. While we can learn from many of the more sophisticated investigations of the condition in vivo in man, any comparisons we make have to be preliminary, purely because of numbers.

Turning then to the second point, what helpful information have we heard in terms of aetiology? We have been talking about pathogenesis, clinical signs and pathology, but we have not really extrapolated from these in any formal way. It may be that as a clinician I am obsessed with aetiology, but it is only by understanding
aetiology that we are going to be able to offer any degree of specific treatment and ultimately prevention. As somebody who has to actually talk to the client about prognosis and what we can or cannot do about the condition, it would seem that establishing the aetiology is of paramount importance. So I shall offer some thoughts on aetiology, referring specifically to Feline Dysautonomia but implying both FD and Grass Sickness.

It is perhaps valid to consider at the outset whether one is right to look for a single cause. Could it be that FD is multi-aetiological, the clinical signs a manifestation of a variety of insults to the autonomic nervous system alone or in conjunction with other parts of the body? The pathological changes, however, have been described as specific and different, suggesting that while FD may be multifactorial, in that there may be a number of factors influencing the condition and its development, it is likely to be the result of one underlying aetiology.

Could that aetiology be an infectious agent? There are certain features in the cat that might suggest such cause, and yet there are others which do not quite fit. One factor of note is that FD does seem to have occurred suddenly, which might be compatible with the appearance of a new infectious agent, or an infectious agent under a new guise. It gave the impression too, of spread in that it was recognized in certain areas of the country before others. This, from what we have heard, would parallel the situation with Grass Sickness. Other infectious diseases in small animals have appeared from nowhere in recent years. The classic would be canine parvovirus, but in the feline world disease associated with coronavirus infection appeared to show a very real increase some years ago. However, cats living in multi-cat households do not appear to be predisposed, nor do other cats in households with a diseased cat seem to be commonly affected. While we have anecdotal evidence that in-contact cases do occur, they are not the rule and this condition certainly does not cluster or appear as outbreaks in a group of cats in a way which might be expected of an infectious condition. However, this should not be completely off-putting. One can envisage a situation where disease is the unusual manifestation of infection rather than the norm. This begs the question, therefore, as to whether this infection, if it is such, is now widespread throughout the cat population, but with disease as only the clinical tip of this infectious iceberg.

Here we need to turn to the pathologist for a little more help, because it would be useful to know if there is any pathological evidence of sub-clinical disease. In other words, are the sorts of changes we are seeing in the clinically ill animal present as incidental findings in animals which are showing no clinical signs? In a household of five cats in which one is diseased, are they all losing neurons, but perhaps at different rates or in different numbers? We also noted in the epidemiology that young cats seem to be predisposed. This might be taken as supporting an infectious aetiology, because it is normally the young in the population, without previous experience of an infection which might be considered more at risk from the disease. However, this is not wholly consistent with the suggestion that this is a new condition, when presumably the whole population would be susceptible. The histopathology of FD is
not supportive of an infectious aetiology, being dissimilar to other known infectious neurological diseases: that however, may be a failing of our understanding. Immuno-pathology has been unhelpful in suggesting or supporting an infectious aetiology. Some, albeit very limited, trials have been carried out using immuno-fluorescence to look for the presence of immunoglobulins in ganglion tissue, and for the presence of known feline infectious agents. All of this has drawn a blank so far. Limited transmission studies, where affected and unaffected cats have been kept in contact, have been carried out, but without any success. In a low incidence disease, however, this may not be the way to succeed. Perhaps Dr Gilmour would like to comment on this, relating to his work where serum from horses with Grass Sickness was given to so-called susceptible horses. He did not reproduce the disease, but I understand was successful in reproducing the pathology. Those, then, are some thoughts on infectious aetiology which may provoke discussion. The evidence, such as it is, is often contradictory, but on balance not convincing for a conventional infectious disease.

The other front-runner has been a toxic aetiology. As I said in discussing the epidemiology, we felt initially that this was a distinct possibility, and searched without success for evidence of exposure to one or more toxins. I have to say, however, that it is difficult to imagine a source of toxin which would become so suddenly available to a wide cross-section of the cat population, having previously been unavailable. Similarly, we are led to understand that the pathological changes and their distribution in this condition are unlike those seen with any previously recognized neurotoxin. Such observations are important, but do not progress the argument very far, and tempting though a neurotoxin is as a cause for these conditions, it is hard to support on the information currently available.

So far, it would seem, much of the information on aetiology has been negative and the cause(s) of FD and Grass Sickness remain unknown. Let us hope that whatever progress is made in one, is at least of immediate relevance to the other and also to other, seemingly much less frequent, animal dysautonomias.