The Veterinary Journal 240 (2018) 14–18

Contents lists available at ScienceDirect

The Veterinary Journal

journal homepage: www.elsevier.com/locate/tvjl

Original Article

The clinical diagnosis of equine sarcoids—Part 2: Assessment of case features typical of equine sarcoids and validation of a diagnostic protocol to guide equine clinicians in the diagnosis of equine sarcoids

M. Haspeslagh[a], V. Gerber[b], D.C. Knottenbelt[c], G. Schüpbach[d], A. Martens[a], C. Koch[b,*]

[a] Department of Surgery and Anaesthesiology, Faculty of Veterinary Medicine, Ghent University, Salisburylaan 133, 9820 Merelbeke, Belgium
[b] Swiss Institute of Equine Medicine, University of Berne and Agroscope, Länggassstrasse 124, Postfach 8466, CH-3001 Berne, Switzerland
[c] Equine Medical Solutions, Lomond Court, Stirling FK94TU, UK
[d] Swiss Institute for Veterinary Public Health, Vetsuisse Faculty, University of Berne, Schwarzenburgstrasse 155, CH-3097 Liebefeld, Switzerland

ARTICLE INFO

Article history:
Accepted 31 August 2018

Keywords:
Clinical features
Diagnosis
Diagnostic protocol
Equine sarcoid
Scoring system

ABSTRACT

Research has shown that the accuracy of the clinical diagnosis of equine sarcoids (ES) can be improved. Particularly, less experienced veterinarians are often mistaken in their clinical judgement despite a high level of diagnostic confidence. The aim of this study was to develop and assess the performance of a diagnostic protocol (DP) to improve diagnostic accuracy and identify diagnostically challenging cases. The design of the DP was based on typical clinical features of ES and its algorithm was optimised through repeated tests on clinical cases prior to validating its performance in a representative online examination. A total of 22 equine practitioners and 31 veterinary students used the DP to diagnose 40 standardised ES and non-ES cases in an online examination. Scores of these 53 respondents were compared to scores of 128 respondents of comparable levels of expertise, and 14 experts, all assessing the same cases without using the DP. Overall, respondents using the DP were significantly more likely (odds ratio (OR) 1.25; 95% confidence interval (95% CI) 1.09–1.43) to diagnose a case correctly compared to respondents not using the DP and felt significantly more confident of their diagnosis (OR 1.53; 95% CI 1.39–1.67). Thus, the DP proved to be a reliable tool to increase clinical diagnostic accuracy and diagnostic confidence. The DP algorithms may be further improved with experiences gained from its application in equine practice and clinicians will be able to optimise their diagnostic accuracy and selection of lesions requiring a biopsy.

Introduction

Histopathology remains the gold standard for the diagnosis of bovine papillomavirus-induced equine sarcoids (ES), but many clinicians elect not to take biopsies to avoid tumour progression (Knottenbelt and Kelly, 2000). Unfortunately, pathognomonic clinical signs are not readily identified for ES, a condition with a very heterogeneous clinical presentation (Knottenbelt, 2005). While designing an online examination for the accompanying study on the accuracy of clinical diagnosis of ES (Koch et al., 2018), the authors defined a list of features commonly associated with ES disease. These features mainly refer to lesion morphology (Knottenbelt, 2005), number of lesions, recurrence after treatment (Scott and Miller, 2011), observation of growth spurts (Wobeser et al., 2010), and lesions being present in typical anatomic locations (Torrontegui and Reed, 1994).

Based on these features, the authors of the present study have developed a tool to help veterinarians differentiate ES from non-ES lesions. This should increase the clinician's diagnostic accuracy when evaluating a proliferative equine skin lesion and help to identify lesions with less typical clinical features where further histopathological or molecular biological diagnostic assessment are indicated. Furthermore, the results of the accompanying study revealed that the clinical diagnosis of ES has an overall sensitivity of 83.3% and specificity of 79.6%, leaving considerable room for erroneous diagnoses (Koch et al., 2018). In addition, the association between the level of diagnostic confidence and the ability to correctly differentiate ES from non-ES lesions was weaker for observers with less clinical experience (odd ratio (OR) 1.55; 95% confidence interval (95% CI) 1.37–1.75) compared with experts (OR 2.24; 95% CI, 1.81–2.77), implying that inexperienced veterinarians are often wrong in their clinical judgment despite a high level of diagnostic confidence (Koch et al., 2018).

* Corresponding author.
E-mail address: christoph.koch@vetsuisse.unibe.ch (C. Koch).

https://doi.org/10.1016/j.tvjl.2018.08.010
1090-0233/

The working hypothesis for the present study was that the systematic review and weighting of features typical of ES, along with the animal's demographic information, would improve the overall discriminatory accuracy, and in particular for less experienced practitioners, when differentiating between ES and non-ES lesions. Furthermore, it was hypothesised that the use of a clinically applicable diagnostic tool that guides veterinarians through this process would improve the level of confidence with which observers make their clinical decisions. Ultimately, the objective of the present study was to develop and validate a diagnostic protocol (DP) to guide veterinarians in diagnosing ES and to improve case selection for which histopathological assessment of ES biopsies or PCR screening of superficial tumour swabs for papillomaviral infection are advisable.

Materials and methods

Development of the diagnostic protocol

Case features typical for ES, including medical history, number of lesions compatible with ES, lesion localisation and morphology were listed. A weighting coefficient [ranging from 1 (less discriminatory) to 2 (more discriminatory)] was subjectively assigned to each of these case features to reflect their impact in the overall diagnostic decision, as empirically established by the evaluation of clinical case records of skin tumors admitted to the equine clinics of the Universities of Ghent and Berne between 1 January 2012 and 31 December 2016. This resulted in a preliminary DP that would produce a higher total weighted score (TWS) for lesions that were likely ES and a lower TWS for lesions that were unlikely ES. The preliminary DP was used to assess 70 histologically confirmed ES and non-ES cases that were pooled for the accompanying study (Koch et al., 2018) and clinical cases presented to the equine referral hospitals of the Universities of Berne and Ghent between 1 December 2016 and 28 February 2017, to establish cut-off values for the TWS. The resulting TWS was compared to the histological diagnoses for each case and two cut-off values were chosen, so that a maximum of cases with a TWS above the higher cut-off were confirmed ES and a maximum of cases with a TWS below the lower cut-off were confirmed non-ES cases. The cases with a TWS between both cut-off values were considered to have an uncertain clinical diagnosis. The final version of the DP was then generated in a user-friendly spreadsheet program (Excel 2013, Microsoft) to automatically calculate the TWS (see Appendix A: Supplementary material) and advise the user of the diagnostic decision (Table 1).

Online examination to assess inter-observer agreement of the diagnostic protocol

In a first stage, the inter-observer agreement of the proposed DP was assessed. Therefore, an online examination was created, containing ten cases (five ES and five non-ES) selected from a pool of 40 ES and 30 non-ES cases (Koch et al., 2018). The selected cases represented the entire width of the spectrum of TWS as obtained by the developers of the DP. For each case, photographs of the lesion and a brief case description in a standardised format were provided and made accessible online.[1]

Equine veterinarians from the networks of the first and last author were contacted by email to request participation in the online examination. A copy of the DP in form of an automated spreadsheet file (Excel 2013, Microsoft) (see Appendix A: Supplementary material) and supplementary illustrations depicting typical ES morphologies and localisations (see Appendix A: Supplementary material) were attached to the invitation email. Additionally, guidelines on how to use the DP correctly (see Appendix A: Supplementary material) were provided. The study objectives were clearly disclosed, and all candidates were informed that results of the exam would be subjected to peer-review and publication in an anonymised format. For each case, respondents had to provide the exact TWS obtained by using the DP.

Online examination to assess the diagnostic performance of the decision protocol

To assess the diagnostic performance and potential clinical value of the DP, the same online examination was used as described in the accompanying paper (Koch et al., 2018). Briefly, this online examination consisted of 26 ES and 14 non-ES cases out of a case pool of well-documented skin lesions with histologically confirmed diagnoses. The cases included in the examination were selected to represent the proportion of ES vs. non-ES cases and typical vs. diagnostically challenging cases as observed in a clinical setting. For each case, photographs of the lesion and a brief case description in a standardised format were provided.

Respondents were grouped as: (1) 'ES expert', if they had previously published on ES disease in peer-reviewed journals and had at least 2 years of clinical experience; (2) 'Equine practitioners', if they had at least 1 year of clinical experience in equine practice; or (3) 'Novices', including recent graduates with less than 1 year of experience and veterinary students (in their final 2 years of studies, tracking with an equine emphasis). As the online examination for the accompanying study (Koch et al., 2018) was ongoing, the decision was made to test the performance of the DP in the remaining pool of potential respondents designated as 'novice' and 'equine practitioner'. Potential respondents were contacted by email and requested to participate in the online examination. Every other 'equine practitioner' and 'novice' was randomly provided with the DP. Randomisation was performed by providing a DP only to potential candidates listed in an odd numbered line of the spreadsheet (Excel 2013, Microsoft) registers for 'equine practitioners' and 'novices', respectively, but not if listed in an even numbered line. This ensured that half of all potential respondents from these groups received the DP and that the same respondent did not complete the examination twice. By doing so, the effect of using the DP could be evaluated by comparing the results of the following five groups, that all completed the same online examination: (1) 'ES experts'; (2) 'equine practitioners' not using the DP; (3) 'novices' not using the DP; (4) 'equine practitioners' using the DP; and (5) 'novices' using the DP.

Potential respondents who received the DP also received illustrations of typical ES lesion morphologies and localisations (see Appendix A: Supplementary material). The invitational email further included the guidelines on how to use the DP (see Appendix A: Supplementary material). Candidates were instructed that the DP was intended to assist the successful completion of the online examination and that it was a guideline. It was not intended to overrule their personal decisions. Furthermore, the study objectives were clearly disclosed, and all candidates were informed that results of the examination would be subjected to peer-review and publication in an anonymised format.

For each case, respondents were asked if they considered the lesion in question was ES ('yes' or 'no'), and to grade their level of diagnostic confidence on a scale from 1 (not confident at all) to 6 (very confident). Once a respondent had filled in all required fields, the responses were automatically recorded in a spreadsheet (Excel 2013, Microsoft). Results of respondents using the DP were then compared to results of peers not using the DP and a group of ES experts, as described in the previous study (Koch et al., 2018).

Statistical analyses

Descriptive statistics were performed in a spreadsheet (Excel 2013, Microsoft). Further statistical tests were carried out using commercially available software (SPSS 23, IBM). To assess the inter-observer agreement, the intraclass correlation coefficient (ICC) was calculated using a two-way random model testing for absolute agreement. Normality of the data was assessed using probability-probability plots. To assess whether the use of the DP had a significant effect on the ability to correctly diagnose a case, a generalised estimating equations (GEE) procedure was used with a binomial error distribution and a logit link function. The ability to correctly diagnose the lesion (Yes/No) was used as the dependent variable and whether the respondent used the DP (Yes/No) as the independent variable. Estimated marginal means were calculated and pairwise comparisons between groups (expert, practitioner with and without DP, novice with and without DP) were carried out. To find out whether the use of the DP had a significant effect on the level of diagnostic confidence, a GEE with a multinomial error distribution and a cumulative logit link function was carried out, using the level of diagnostic confidence (on a scale from 1 to 6) as the dependent variable and whether the respondent used the DP (Yes/No) as the independent variable. The association between confidence level and the ability to correctly differentiate ES from non-ES lesions was tested by fitting a GEE with binomial error distribution and logit link function, using score (correct or incorrect) as the dependent variable and the level of diagnostic confidence as the independent variable. All models were corrected for the fact that the same respondent scored multiple cases and when multiple comparisons were carried out, a Bonferroni correction was applied. Statistical significance was set at $P \leq 0.05$.

Results

Online examination to assess inter-observer agreement of the diagnostic protocol

The inter-observer agreement test was completed by 55 respondents (response rate 42.0%). The single measure ICC was 0.78 (95% CI 0.62–0.92).

Online examination to assess the diagnostic performance of the decision protocol

The online examination to assess the clinical value of the DP was completed by 195 respondents. The DP was used by 53 of these

[1] See: Google Forms. https://goo.gl/forms/2j6JD4npXi2lAVPx2 (accessed 22 June 2018).