Equine lymphoma: a review

Lymphoma is the most commonly occurring equine haemopoietic neoplasm, accounting for 1.3–2.8% of all neoplasia identified in horses. The disease broadly takes one of five forms: multicentric, alimentary, cutaneous, mediastinal and solitary extranodal tumours. Lymphoma can be classified by immunophenotype, allowing more accurate prognostication and individualised chemotherapeutic protocols. Clinical signs are usually insidious in onset and clinicopathological changes tend to be broad and non-specific, impeding early antemortem diagnosis. It is not uncommon with internal tumours that a diagnosis is not made until post-mortem examination. Treatment options are limited and often cost-prohibitive, and advanced disease progression at time of diagnosis means that euthanasia is usually opted for, as treatment is very rarely curative. Earlier diagnosis may improve prognosis if therapeutic options are viable to owners, so lymphoma should be considered as a differential diagnosis in many cases.

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Lucy Sheard BSc (Hons) BVSc MRCVS, **Kate McGovern** BVetMed CertEM(IntMed) MS DACVIM DipECEIM MRCVS, Donnington Grove Veterinary Group, Oxford Road, Newbury, RG14 2JB. lucy.sheard.vet@outlook.com

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The term lymphoma describes neoplasia of lymphocytic tissue and is used interchangeably with lymphosarcoma and malignant lymphoma. Generally, the term refers to solid tumours without bone marrow involvement, although metastatic spread can lead to subsequent marrow involvement. Lymphoma has been reported to account for 1.3–2.8% of all tumours diagnosed in horses, although one study of 964 equine neoplastic histology submissions found the incidence of lymphoma as high as 14% (Savage, 1998; Schneider, 2003; Knowles et al, 2015). It is also the most commonly occurring equine haemopoietic neoplasm (Muñoz et al, 2009).

The diverse nature of lymphoma and the number of organs potentially affected results in a broad range of non-specific clinical signs and clinicopathological changes, making antemortem diagnosis challenging. While equine oncology is not as developed as that in other species, there are both palliative and curative treatment options available in certain cases. Generally, there is a paucity of data on the use of chemotherapeutics in equine lymphoma cases, with data limited to single case reports or small case series. This review describes the classification of the various forms of lymphoma, diagnostic methods and explores potential treatment options and chemotherapeutic protocols.

Aetiology

Lymphoma displays no explicit age bias and cases have been reported in fetuses (Haley and Spraker, 1983) through to geriatrics. However, specific forms of the disease have been anecdotally reported to have a predilection for certain ages. Multicentric lymphoma more commonly occurs in horses between 4 and 10 years old, and alimentary in horses aged over 16 years (Schneider, 2003; Meyer et al, 2006; Taintor and Schleis, 2011; Durham et al, 2013). No sex or breed predisposition has been identified, although Quarter horses and Thoroughbreds have been over-represented in some studies (Durham et al, 2013; Miller et al, 2015).

Infection with gamma-herpesviruses is a significant aetiological cause of human lymphoma (Fein et al, 2009). A small number of case reports have presented cases of horses with lymphoma that were positive on polymerase chain reaction (PCR) for gamma-herpesvirus equine herpesvirus 5 (Vander Werf and Davis, 2013; Bawa et al, 2014; Vander Werf et al, 2014). In a case series documenting four cases of equine lymphoma, all four horses were PCR positive for equine herpesvirus-5, irrespective of the topographical form of disease (Miglio et al, 2019). However, equine herpesviruses are endemic to the population and the exact role of equine herpesvirus-5 in equine neoplastic disease has not yet been determined (Van Cleemput et al, 2019). Retroviruses have also been implicated in development of lymphoma in humans, although no formal association has been proven in horses and previous transmission experiments have failed to produce disease (Meyer et al, 2006; Esau, 2017).

Clinical signs and forms of disease

Clinical signs of lymphoma in horses are typically non-specific and insidious in onset, although acute signs may develop depending on the organ system involved. The most common clinical signs include depression, oedema of distal limbs or ventral abdominal wall (*Figure 1*), weight loss and cachexia (Meyer et al, 2006; Muñoz et al, 2009), although some horses develop no clinical signs at all. A case report presented a case where persistently elevated inflammatory markers on routine serum biochemical testing were the only indicator of disease (Hill et al, 2018).

Lymphoma can produce paraneoplastic syndromes such as pyrexia, alopecia, pruritus and hypercalcaemia of malignancy

Figure 1. A horse with ventral oedema of the abdomen.

Case 1

History and signalment: A 23-year-old gelding of unknown breed presented to a UK referral hospital for further investigation of fever and inappetence of one week duration. A moderate improvement had been noted in response to antimicrobial therapy, but the horse's condition had subsequently deteriorated.

Clinical findings and diagnostics: Initial clinical exam showed the horse was tachycardic, tachypnoeic and normothermic.

Imaging: Marked pleural and peritoneal effusions.

Clinicopathology: Hyperfibrinogenaemia, increased serum amyloid A, azotaemia, hypoalbuminaemia, increased liver parameters. Cytology of both the pleural and peritoneal effusions demonstrated large numbers of abnormal cells demonstrating signs of neoplasia: anisocytosis, mitotic figures and prominent nuclei.

Outcome: The horse was immediately euthanised when a diagnosis of multicentric lymphoma was confirmed from cytology of effusion samples. A postmortem examination was conducted (*Figure 1*).

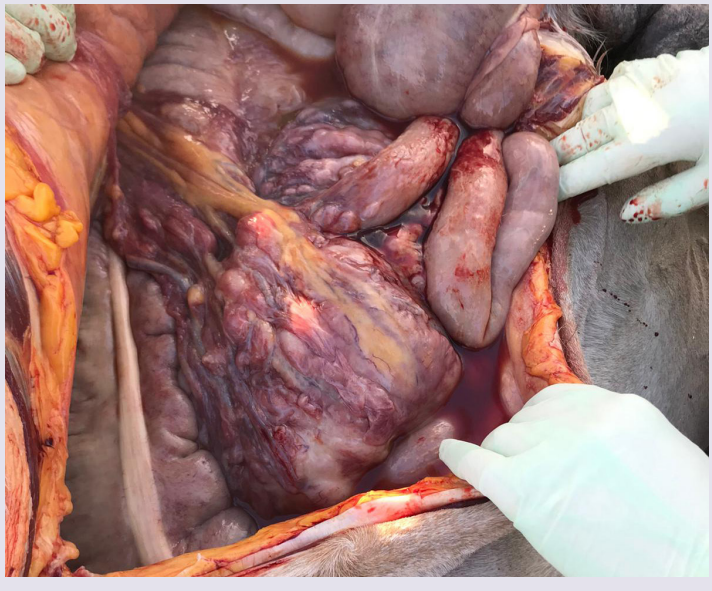

Figure 2. Abdominal organs at postmortem examination.

(Finley et al, 1998; Mendes et al, 2011; Davis and Rush, 2013). Pseudohyperparathyroidism, hypereosinophilia, mucosal ulceration, immune-mediated haemolytic anaemia and thrombocytopenia have also been reported (Meyer et al, 2006; Axiak and Johnson, 2012). In some cases, these may be the only apparent clinical signs.

Lymphoma has been topographically classified into one of five forms:

1) Multicentric
2) Alimentary
3) Cutaneous
4) Mediastinal
5) Solitary tumours of extranodal origin.

Multicentric lymphoma

Multicentric lymphoma is the most commonly occurring form of the disease (Durham et al, 2013), involving the lymphatic system and spleen, liver, intestine, kidney, lung and occasionally bone marrow. Clinical signs vary with the affected organ system, but common signs are oedema, weight loss, and pyrexia. This form typically affects younger horses but can present at any age, as seen in the geriatric patients presented in *Case 1* and *3* (Muñoz et al, 2009; Taintor and Schleis, 2011).

Neurological signs such as ataxia and paresis may develop if the nervous system is also affected (Torrent et al, 2019). Ocular signs may present in some cases of multicentric lymphoma, typically affecting the adnexa, but may also cause acute and chronic uveitis, corneoscleral masses or retrobulbar infiltration (Germann, 2008). Lymphoma should be considered in cases of uveitis that are refractory to treatment. Multicentric lymphoma can also affect the reproductive organs. One case involving the uterus and ovaries in a gravid mare was proposed to be the cause of abortion of a fetus of 9 months' gestation (Canisso et al, 2013).

Alimentary

The alimentary form of lymphoma is reported to be the most common intestinal neoplasm in horses (Spanton et al, 2020; Bacci et al, 2020). Unlike multicentric lymphoma which affects younger horses, middle aged and elderly horses are more likely to be affected by alimentary lymphoma (Spanton et al, 2020).

Alimentary lesions may be the result of primary disease, a component of multicentric disease or a metastatic process from another primary neoplasm. Lesions are more commonly found in the small intestines, predominantly the jejunum, but the large intestine or caecum can also be affected (Spanton et al, 2020). Singular or multifocal tumours may be found within the intestinal wall, or there may be diffuse neoplastic infiltration within the intestinal wall, or a combination of diffuse infiltration and macroscopic lesions such as those found in *Case 2*. Malignant spread to mesenteric lymph nodes is common.

Clinical signs may include weight loss, malabsorption caused by villous atrophy, diarrhoea, melaena, mucosal ulceration and colic (Mair et al, 2006). The formation of pseudodiverticula in the small intestines has been recorded in horses with alimentary lymphoma (Mair, 2011) and these may rupture, leading to acute illness.

Cutaneous

Cutaneous lymphoma is identified in 1.7–3% of equine skin tumours (Miller et al, 2015). Like other forms of the disease, presentation is variable. Cutaneous neoplasms may form solitary or multiple nodules or epitheliotropic scaling disease, disseminated throughout skin (Miller et al, 2015). Nodules may ulcerate or cause local alopecia and inflammation (Muñoz et al, 2009). Lesions are more commonly found on the head, neck and body, but can be found on the limbs.

Mediastinal

Mediastinal lymphoma is encountered in horses of all ages. Masses may produce cardiorespiratory abnormalities including dyspnoea, coughing, jugular vein distension and pleural effusions, sometimes resulting in pulmonary atelectasis and compromised pulmonary function (Ainsworth and Hackett, 2009; Davis and Rush, 2013).

Solitary tumours of extra-nodal sites

Solitary lymphoid tumours have been reported in various sites across the body, such as the mandible, heart, mammary glands and epiglottis (Mendes et al, 2011; Penrose et al, 2012). In these cases, clinical signs depend on tumour location. One case reported a primary peripheral nerve neoplasm led to lameness, weakness and muscle atrophy (Westerman et al, 2014).

Immunophenotyping

Immunophenotyping is routinely used in diagnosis and treatment of lymphoma in human medicine. Use in veterinary medicine may help determine prognosis and develop tailored treatment protocols. A large retrospective study classified 203 cases of equine lymphoma according to the veterinary reference of the World Health Organisation lymphoma classification system, on the basis of immunophenotype and cell morphology (Durham et al, 2013). T-cell-rich, large B-cell was found to be the most prevalent immunophenotype, regardless of the form of lymphoma (Durham et al, 2013).

Tumour infiltration and prognosis varies with immunophenotype. A recent study reported that alimentary lymphoma lesion infiltration and survival time varied with immunophenotype (Bacci et al, 2020). Immunophenotype has also been classified in cases of cutaneous lymphoma. A study demonstrated that different phenotypes have different clinical presentations and some phenotypes were overrepresented in some breeds of horse (Miller et al, 2015). Knowledge of immunophenotype can be used to determine an appropriate treatment protocols and approximate prognosis, although significant further work is needed. This is mainly inhibited by the fact it can be extremely difficult to obtain a diagnosis antemortem in some cases. The lack of availability of thoracic and abdominal magnetic resonance image (MRI) or computed tomography (CT) in horses remains a limiting factor.

Diagnosis

Lymphoma should be considered as a differential diagnosis in horses presenting with non-specific clinical signs, or horses unresponsive to treatment. All horses should be subject to a thorough clinical exam. Blood samples should be taken for complete blood count and serum biochemistry. A rectal examination should be performed to check for abdominal masses such as splenic masses (*Figure 5)* and lymphadenopathy (Davis and Rush, 2013, Janvier et al, 2016). Thoracocentesis and abdominocentesis may be performed if a pleural or peritoneal effusion is present. Neoplastic cells may exfoliate into effusions, though the absence of neoplastic cells does not exclude a diag-

Case 2

History and signalment: A 4-year-old Thoroughbred gelding presented to a UK referral hospital for investigation and treatment of colic signs of several days' duration. The horse was seen 2 years previously for an episode of colic.

Clinical findings and diagnostics: Initial clinical exam showed tachycardia, all other vital parameters within normal limits. On rectal examination a gas distended structure was palpable in the cranial abdomen. It was not possible to determine whether this was distended small intestine or small colon.

Imaging: Abdominal imaging was within normal limits.

Clinicopathology: Increased serum amyloid A, increased creatinine kinase, leukocytosis, abdominocentesis yielded grossly normal peritoneal fluid. Peritoneal lactate was borderline high.

Treatment: The horse underwent a ventral midline laparotomy. An intramural mass was found in the distal small intestine (*Figure 3*) and approximately 10 feet of small intestine oral to the lesion was markedly hypertrophied. There was no gross evidence of spread of the mass. The mass and a portion of the small intestines was resected, an end-to-end anastomosis performed, and the abdomen closed in a routine manner. The horse received intravenous fluid therapy, prokinetic continuous rate infusions, antimicrobial therapy and anti-inflammatory drugs postoperatively.

Outcome: Histopathology on the excised mass confirmed a diagnosis of lymphoma. Complete excision could not be confirmed as abnormal cells were detected extending to the border of the sample, despite appearing macroscopically normal. Immunohistochemistry to further classify the type of lymphoma was declined. The horse was discharged from the hospital 4 days after surgery. A course of oral prednisolone was recommended to delay progression of lymphoma. No further follow up is available.

Figure 3. A small intestinal mass which was histopathologically confirmed as lymphoma.

Case 3

History and signalment: A 27-year-old gelding of unknown breed presented to a UK referral hospital for further investigation of bilateral periocular swelling (*Figure 4*). The swelling was unresponsive to treatment with antibiotics, systemic and intraocular corticosteroids.

Clinical findings and diagnostics: Initial clinical exam showed tachycardia, dullness, mild submandibular lymphadenopathy, marked oedema of conjunctiva, upper and lower eyelids.

Imaging: Thoracic and abdominal ultrasonography was within normal limits.

Clinicopathology: Hyperglobulinaemia, hyperfibrinogenaemia, neutrophilia, atypical lymphocytes on blood smear. Abdominocentesis yielded cloudy yellow fluid with round cells resembling lymphocytes and lymphoblasts.

Outcome: The horse was immediately euthanised when a diagnosis of multicentric lymphoma was strongly suspected on the basis of the clinical signs and cytology results.

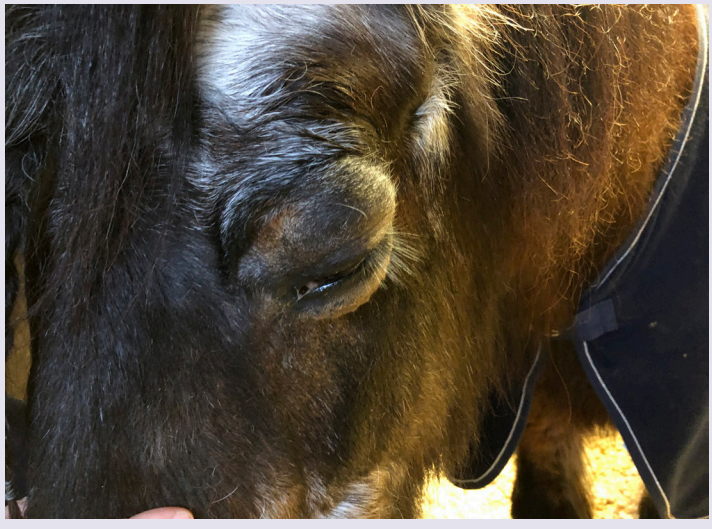

Figure 4. Periocular swelling.

Figure 5. Splenic lymphoma found at post-mortem examination.

nosis of lymphoma (Garber et al, 1994, Recknagel et al, 2012). In one study, cytological analysis of abdominal fluid provided support for the diagnosis of intestinal neoplasia of any kind in 38% of the cases examined (Taylor et al, 2006).

Various imaging modalities can be used to aid diagnosis. Ultrasound can be used to identify both focal and diffuse abnormalities in multiple forms of the disease. Thoracic ultrasonography can identify pleural effusions, pulmonary consolidation and atelectasis, as was found in *Case 4* (Davis and Rush, 2013). Discrete tumours of the liver, spleen and kidneys can be identified by transabdominal ultrasound (*Figure 6*) and subsequently biopsied. Size abnormalities and changes in tissue architecture can also be identified in the liver, spleen and intestines (Janvier et al, 2016; Spanton et al, 2020). Transrectal ultrasound can also be used to evaluate abdominal organ architecture and lymphadenopathy. Ocular ultrasound may be useful to evaluate the globe and adnexa.

Thoracic radiography may be useful for identifying a pleural fluid line, mediastinal or parenchymal abnormalities. A large volume of pleural fluid can obscure image quality so draining pleural fluid may yield a better image. Radiography of peripheral structures such as the head, larynx and limbs may also identify lesions and abnormalities (Oikawa et al, 2003).

Endoscopy can be used for both visualisation of internal structures and for biopsy retrieval. Upper airway endoscopy examines the larynx, trachea and proximal bronchi. Thoracoscopy enables visualisation of the pleural space and mediastinum (Lee et al, 2013). Gastroscopy for examination of the proximal gastrointestinal tract can identify lesions, as well as biopsy of gastric and duodenal mucosa.

Biopsies are proposed to be of greater diagnostic value than fine needle aspirations as biopsies preserve tissue architecture. Cutaneous lesions and peripheral lymph nodes can easily be sampled. Percutaneous biopsies of liver, kidney and spleen can be obtained where indicated. Endoscopically retrieved biopsies, rectal mucosal biopsies bone marrow aspirates, aqueous humour (Germann et al, 2008), pleural and peritoneal effusions (Mair and Hillyer, 1992) can all be used for cytological analysis and immunophenotyped by flow cytometry.

Decreased immunoglobulin subclass concentrations has been found in humans with B cell non-Hodgkin lymphoma (Biggar et al, 2009). One study indicated that horses with high serum IgM (> 23 mg/dl) were unlikely to have lymphoma, although a low IgM could not reliably be used to confirm a diagnosis of lymphoma (Perkins et al, 2003). Measurement of serum immunoglobulin subclass concentration may be useful if there is a high suspicion of lymphoma, but this should not be considered reliable.

In human medicine CT is considered the gold standard imaging modality for diagnosing lymphoma, but this carries inherent risks of radiation damage to the patient. MRI is increasingly being used to diagnose lymphoma and a study found that MRI had high specificity and sensitivity for evaluating nodal and extranodal involvement in humans with mediastinal lesions compared to CT, without exposing patients to radiation (Pereiro-Brea et al, 2020). As use of these modalities in horses increases, so may the potential to diagnose internal tumours such as lymphoma, although current use is limited by patient size and availability of equipment.

Clinicopathological findings

Serum biochemical findings are typically non-specific but commonly include hyperfibrinogenaemia, hypoalbuminaemia, hyperglobulinaemia and hyperlipidaemia. Anaemia, thrombocytopenia and leukaemia are often found on complete blood count (Meyer et al, 2006).

Various biochemical tumour markers have been used as identifiers and prognostic indicators for lymphoma in other species. Serum thymidine kinase (sTK) has been used in humans, dogs and cats. A study found that horses with lymphoma has significantly higher levels of sTK activity compared to clinically healthy horses, as well as horses with inflammatory and non-haematopoietic neoplasia (Larsdotter et al, 2015). Other biomarkers, such as specific lactate dehydrogenase isoenzymes, have been implicated in lymphoma in humans and dogs (Klein et al, 2020). Further study is required to elucidate their potential in equine oncology, but their use may aid earlier diagnosis.

A summary of the characteristics and diagnostics can be found in *Table 1*.

Treatment

Current treatment options for lymphoma are limited. Diagnosis late in the disease course typically means that euthanasia is often chosen for humane reasons. Geographical availability of modalities such as radiation therapy is extremely limited and financial and logistical implications must also be considered before commencing treatment. Survival time is dependent on the form and immunophenotype of lymphoma. Multicentric and alimentary forms carry a poor prognosis, with survival time of weeks to months after diagnosis when diagnosed antemortem (Miller et al, 2015). Cutaneous and solitary lesions carry a better prognosis and partial or full remission can be achieved with appropriate therapy in some cases (Luethy et al, 2019; Bacci et al, 2020).

Surgical excision may be appropriate for some forms and studies have found excision with appropriate margins of cutaneous nodules to be sufficient for preventing recurrence in some horses (Miller et al, 2015). Focal intestinal lesions and solitary tumours may be removed under exploratory laparotomy (Bacci et al, 2020). Surgical debulking can be used to reduce tumour size before chemotherapy or radiative therapy and has been shown to induce complete remission in some cases (Pezzanite et al, 2019).

Chemotherapy

Unfortunately, chemotherapy is rarely indicated in horses because of its vast expense and often, the lateness of (or complete lack of) diagnosis. Chemotherapeutics are cytotoxic and broadly affect stages of cell growth and division, resulting in cell death or inability to undergo mitosis (Mair and Couto, 2006). Drugs are classed on the basis of mechanism of action as alkylating agents, antitumour antibiotics, plant alkaloids, antimetabolites or hormones. These drugs do not target neoplastic cells specifically, although they do display a predilection for them as a result of increased cellular proliferation. A narrow therapeutic window means that rapidly proliferating tissue such as the gastrointestinal mucosa may also be affected by treatment, so dose rate and frequency must be balanced with potential side effects. The most common chemotherapeutic drugs used in treatment of lymphoma in all species but also horses are vincristine, doxorubicin, lomustine, cyclophosphamide and L-asparaginase (Mair and Couto, 2006; Doyle et al, 2013; Luethy et al, 2019). These may be used alone or in combination. For example, cyclophosphamide, vincristine and predniso-

Figure 6. Transcutaneous abdominal ultrasound visualising a splenic mass.

CASE 4

History and signalment: A 12-year-old Warmblood mare presented to a UK referral hospital for further investigation of pyrexia, an elbow wound and markedly increased inflammatory markers.

Clinical findings and diagnostics: Initial clinical exam showed ataxia, tachycardia and tachypnoea. The site of abdominocentesis before admission was dripping blood.

Imaging: Bilateral lung consolidation and B lines were apparent on thoracic ultrasound. Abdominal ultrasound was unremarkable. The trachea was grossly normal on endoscopy. A mild interstitial pattern was present on thoracic radiographs.

Clinicopathology: Anaemia, leukopenia, hyperproteinaemia, hyperfibrinogenaemia, hyperlactataemia, increased serum amyloid A. Clotting parameters were also elevated; prothrombin time was 20 seconds (control 13 seconds) and activated partial thromboplastin time was 135 seconds (control 57 seconds).The tracheal wash sample obtained endoscopically was grossly and cytologically normal. Polymerase chain reaction testing for equine herpesvirus-1/4 was negative.

Treatment: Initial treatment consisted of broad spectrum systemic antimicrobial therapy, analgesia, hyperimmune plasma transfusions and intravenous fluid therapy.

Outcome: The mare became progressively more anaemic, thrombocytopenic and hyperlactataemic. A mild pleural effusion developed. On the fifth day of hospitalisation the mare became severely ataxic and subsequently collapsed. Immediate euthanasia was performed. Histopathology was performed on post-mortem samples and lymphoma was confirmed within the heart, liver and spleen. It was suspected that immune-mediated haemolytic anaemia and thrombocytopaenia secondary to lymphoma were also present.

Table 1. Disease characteristics		
	Summary of lymphoma in horse	
Age	Reported in fetuses, occurs in any age. Alimentary form more common in geriatrics. Multicentric form more common in younger horses	
Sex	No sex predisposition	
Breed	Quarter horses and Thoroughbreds overrepresented in cutaneous lymphoma cases	
General clinical signs	Weight loss, limb or ventral body wall oedema, cachexia, fever, lymphadenopathy	
Forms	Multicentric	Depends on tumour location
	Alimentary	Colic, weight loss, ventral abdominal oedema, diarrhoea
	Mediastinal	Coughing, dyspnoea, tachypnoea, tachycardia, bradycardia
	Cutaneous	Singular or multiple skin nodules
	Solitary	Depends on tumour location
Immunophenotype	T-cell-rich, large B-cell lymphoma most common immunophenotype in all forms	
Haematology	Anaemia, neutrophilia, lymphocytopenia	
Serum biochemistry	Hyperfibrinogenemia, hyperproteinaemia, hypoproteinaemia, hypoalbuminaemia	
Ultrasonographic findings	Transcutaneous thoracic	Pleural effusion, atelectasis, identification of discrete masses
	Transcutaneous abdominal	Diffuse changes in echogenicity, focal or diffuse intestinal thickening, identification of discrete masses, displacement of organs
	Abdominal per rectum	Diffuse changes in echogenicity, focal or diffuse intestinal thickening, identification of discrete masses, displacement of organs, lymphadenopathy
Radiographic findings	Thoracic masses, pleural effusion, masses in peripheral structures	
Cytology	Pleural and peritoneal effusions, biopsy samples, aqueous humour	
Endoscopy	Visualisation of airways, proximal gastrointestinal tract, bladder, vagina, biopsy retrieval	

From Meyer et al (2006); Muñoz et al (2009); Taintor and Schleis (2011); Davis and Rush (2013); Durham et al (2013); Miller et al (2015); Janvier et al (2016); Spanton et al (2020); Luethy et al (2019)

Table 2: Summary of clinical outcomes in response to chemotherapy for treatment of lymphoma in 15 horses				
	Complete remission*	Partial response†	Stable disease‡	Median survival time in months (range)
Multicentric	2	6	1	7 (1–32)
Cutaneous	3	0	0	34 (21–46)
Alimentary	0	3	0	7 (2–36)

*complete remission; defined as disappearance of all evidence of disease and clinical signs; † partial response; defined as >30% decrease in size of baseline pathological lesions; ‡ stable disease; defined as <30% decrease or <20% increase in the lesions. Adapted from Luethy et al (2019)

lone can be given concurrently, referred to as the COP protocol (Taintor and Schleis, 2011). Although typically palliative, chemotherapy has been curative in some cases. Median survival times for 15 horses treated with chemotherapy are illustrated in *Table 2* (Luethy et al, 2019). Intralesional chemotherapy using cisplatin has been used successfully in some cases of cutaneous lymphoma (Théon et al, 2007).

Corticosteroids can be used as monotherapy or as an adjunct to treatment, as they have been shown to reduce tumour mass and temporarily ameliorate some clinical signs. They may also be indicated for the treatment of paraneoplastic syndromes such as immune-mediated anaemia that may arise as a result of lymphoma (Mair and Couto, 2006; Luethy et al, 2019). However, they should not be considered curative.

Radiation

Radiation therapy is commonly applied in cancer treatment in humans and companion animals, but use in horses is limited because of patient size. The principle of radiation therapy is the disruption of DNA bonds, resulting in either immediate cell destruction or progressively non-viable tumour cells. Primitive tumour cells are more susceptible to radiation (Bradley et al, 2015). Radiation can be delivered as brachytherapy, which uses a radiation source at short range or in direct contact with the tumour (Donaldson, 2014; Bradley et al, 2015), or as teletherapy, which uses a linear accelerator further away from the patient (Hollis, 2019; Gillen et al, 2020). Both forms have limited use in horses and repeated doses, often under a general anaesthetic, are required. Implantation of radioactive isotopes within masses leads to prolonged periods of radioactivity, posing a risk to handlers (Donaldson, 2014; Bradley et al, 2015; Hollis, 2019).

The logistics of treatment must be considered. In the UK there are a limited number of facilities offering radiation and chemotherapy to horses and such treatment is expensive. Owner and handler safety is also a consideration. Administration of chemotherapeutic drugs is not risk-free, as cytotoxic drug residues are excreted in urine and faeces. Some therapeutic methods require prolonged periods of hospitalisation which may be distressing for the horse or owner.

Adverse effects of treatment may occur when horses are treated with radiation or cytotoxic drugs (Gillen et al, 2020). The Veterinary Cooperative Oncology Group-Common Terminology Criteria for Adverse Events, released in 2011 and revised in 2021, is a set of descriptive terminology proposed for adverse event reporting in cats and dogs undergoing investigative treatment (LeBlanc et al, 2021). These criteria have been applied to horses in recent studies. Luethy et al (2019) found hypersensitivity to be the most frequently occurring adverse effect, although others such as alopecia, colic and neurotoxicity have been recorded. Doxorubicin administration was associated with higher grade adverse effects (Luethy et al, 2019).

Conclusions

Lymphoma is a complex disease that presents with a wide variety of clinical signs. Consequently, definitive antemortem diagnosis is often challenging, delayed or impossible. Treatment options are limited, and euthanasia is often elected for on humane grounds. When warranted and feasible, treatment can be curative for cutaneous lesions and solitary tumours, but this is dependent on tumour type, size and spread.

Further study exploring the potential role of equine herpesvirus-5 in the disease process is warranted, as this may lead to the investigation of antiviral use in treatment of lymphoma with concurrent equine herpesvirus-5 infection. As human oncology continues to develop, the extrapolation of tumour markers in horses may aid earlier diagnosis. EQ

KEY POINTS

- There are many forms of lymphoma, leading to a broad range of clinical signs.
- Lymphoma should be considered as a differential diagnosis in horses with non-specific disease that is unresponsive to initial therapy.
- A range of diagnostic methods can be employed in both first opinion and referral settings.
- Treatment options are limited, and prognosis is often poor. Some forms of the disease can be cured.

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