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Neoplasie interne: linfosarcomi e patologie mieloproliferative

*Internal neoplasia:
lymphosarcoma and myeloproliferative disease*

Domenica, 2 Febbraio 2003, 17.15

Sunday, February 2nd 2003, 17.15

SALA PACINOTTI

MEDICINA INTERNA

Chairperson: Alessandro Frione

Riassunto

Le malattie linfoproliferative sono un gruppo importante di affezioni neoplastiche degli equini. Il linfosarcoma, nelle sue varie forme, è probabilmente la più comune ed autentica neoplasia interna del cavallo. Si riconoscono parecchie forme differenti e ciascuna è caratterizzata da propri problemi diagnostici, prognostici e terapeutici. Nel cavallo, il linfosarcoma si riscontra in quattro forme differenti:

1. Intestinale (forme focali o diffuse)
2. Toracico (forme mediastiniche e timiche)
3. Multicentrico
4. Linfosarcoma istiocitario cutaneo

La lesione primaria è raramente evidente nel momento in cui è possibile attuare l'escissione chirurgica, ma un numero ridotto di casi intestinali è stato trattato mediante asportazione radicale del tumore e dei linfonodi associati. L'estesa disseminazione delle neoplasie comporta il coinvolgimento di molti organi di maggiore e minore entità, come i polmoni, il cuore, la milza, il rene, le ovaie, ecc... Sono stati identificati anche tumori secondari nel sistema nervoso centrale.

Gli effetti clinici sono di solito intensi, ma non patognomonicamente. Nella maggior parte delle affezioni linfoproliferative si riscontrano perdita di peso, compromissione dell'immunità e talvolta anemia. È comune l'accumulo di fluidi nelle cavità corporee, che può interessare elevati volumi di liquidi (tipicamente limpidi o leggermente striati di sangue). Molti dei tumori possono raggiungere dimensioni considerevoli ma, nonostante ciò, di solito non sono esfoliativi, per cui spesso non risulta utile la diagnosi citologica del fluido aspirato dall'addome. L'esame ecografico e laparoscopico/toracoscopico sono importanti ausili diagnostici. Possono essere utili anche la radiografia del torace e, in alcuni casi, l'endoscopia. Spesso è possibile formulare un sospetto diagnostico sulla base del solo esame clinico. In tutti questi tumori sono comuni le sindromi paraneoplastiche e la cachessia neoplastica. L'anemia è un riscontro frequente e, in alcuni casi, il midollo osseo può essere quasi totalmente obliterato, per cui l'anemia risulta grave. Tuttavia, spesso è solo marginale.

Sono stati descritti alcuni casi di mieloma plasmocellulare. Si osserva usualmente una gammapatia monoclonale con una lieve zoppia che si sposta da un arto all'altro (in associazione con le lesioni ossee) e lievi alterazioni ematologiche. È interessante notare che sembra che nel mieloma plasmacellulare degli equini (a differenza di quanto avviene nella stessa neoplasia nell'uomo e nel cane) non siano rilevabili le proteine di Bence-Jones.

La prognosi per tutte le forme di malattia mieloproliferativa o linfoproliferativa è molto sfavorevole. Sono stati tentati dei trattamenti, che però invariabilmente falliscono. Talvolta si può ottenere una remissione temporanea utilizzando agenti chimici citotossici ed antimetabolici, ma il costo è proibitivo ed i risultati sono molto insoddisfacenti. Una volta confermata la diagnosi il cavallo deve essere abbattuto il più rapidamente possibile per evitare ulteriori sofferenze.

Il linfosarcoma istiocitario cutaneo è la forma di linfosarcoma che comporta la prognosi migliore (che però non è affatto buona!). Alcuni casi possono sopravvivere per molti anni dopo la diagnosi, mentre in tutte le altre forme il massimo che ci si può aspettare è una sopravvivenza di 6-12 mesi. Di conseguenza, risulta utile la formulazione di una diagnosi rapida e definitiva. Al momento attuale non esistono trattamenti, ma la forma cutanea è talvolta associata a tumori delle cellule della granulosa e l'eliminazione di questi ultimi può risultare utile (ma non risolutiva) per la condizione sottostante.

Summary

Lymphoproliferative disease is an important group of neoplastic diseases in horses. Lymphosarcoma in its various forms is probably the commonest true internal neoplasm of horses. Several different forms are recognised and each has its own diagnostic, prognostic and therapeutic problems. Lymphosarcoma occurs in 4 different forms in horses:

- 1. Intestinal (focal or diffuse forms)*
- 2. Thoracic (Mediastinal and thymic forms)*
- 3. Multicentric form*
- 4. Cutaneous histiocytic lymphosarcoma*

The primary lesion is seldom evident at a time when surgical excision can be used but a few intestinal cases have been treated by radical excision of the tumour and the associated lymph nodes. Extensive dissemination of tumours occurs with involvement of many major and minor organs such as the lungs, heart, spleen, kidney, ovary etc. Secondary tumours have been identified in the central nervous system also.

The clinical effects are usually profound but are not pathognomonic. Weight loss, impaired immunity and sometimes anaemia are encountered in most of the lymphoproliferative diseases. Fluid accumulation in the body cavities is common and this can involve large volumes of fluid (that is characteristically clear or slightly blood stained). Many of the tumours can reach considerable size but in spite of this they are not usually exfoliative and so diagnostic cytology of fluid aspirated from the abdomen is not often helpful. Ultrasonography and laparoscopy / thoroscopy are important aids to diagnosis. Thoracic radiography and in some cases endoscopy can also help. It is often possible to make a tentative diagnosis from clinical examination alone. Paraneoplastic syndromes and cancer cachexia are common with all these tumours. Anaemia is a frequent finding and in some cases the bone marrow can be almost totally obliterated and so the anaemia is profound. Many cases however are marginally anaemic.

Few cases of plasma cell myeloma have been described. A monoclonal gammopathy with a mild shifting lameness (associated with bone lesions) and mild haematological alterations are usual. Interestingly it seems that Bence-Jones Proteins are not detectable in equine plasma cell myeloma (by contrast to human and dog PCM cases).

The prognosis for all forms of myeloproliferative or lymphoproliferative disease is very poor. Treatments have been attempted but invariably fail. A temporary remission can sometimes be obtained using cytotoxic and antimitotic chemicals but the expense is prohibitive and the results very unsatisfactory. Once a diagnosis has been confirmed the horse should be destroyed as soon as possible to relieve further suffering.

Cutaneous histiocytic lymphosarcoma is the one form of lymphosarcoma that carries a better prognosis (though it is by no means good!). Cases can survive for many years after diagnosis whereas in all the other forms a prognostic of 6 – 12 months is the maximum that can be expected. Therefore a rapid and conclusive diagnosis is helpful. Treatments are not feasible as yet but the cutaneous form is sometimes associated with granulosa cell tumour and removal of the latter may help (but will not resolve) the underlying condition.

The term lymphosarcoma covers a wide range of myeloproliferative and lymphoproliferative disorders in the horse. Leukaemia is a name that covers both lymphosarcoma / lymphoma and myeloproliferative disorders. The term lymphoma is more synonymous with lymphosarcoma but the whole group of diseases is often referred to as lymphosarcoma or leukaemia. All these names have limited value in the diagnosis but owners often relate to them by inference from human experiences.

Fortunately all these disorders are much rarer in horses than in most other species, but, because the prognosis varies markedly from hopeless to fairly good, an early diagnosis is important. Progress in the management of these disorders in other species has been impressive in other species but this has not been translated to or matched by the equine disease. Therapy is bound to be expensive and difficult and humane considerations usually take precedence.

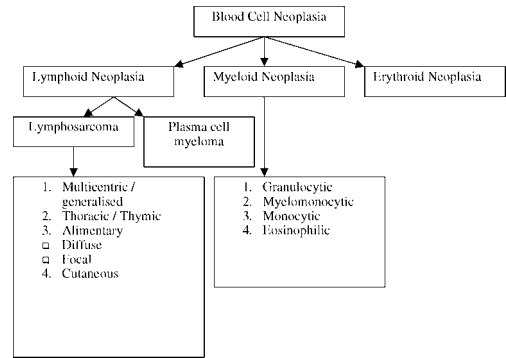
One of the main problems with equine lymphosarcoma cases is the subtlety of the early signs (at stages when perhaps some sort of treatment might be possible). Most cases are presented late in the course – sometimes because the course is rapid but more often because the onset is insidious and therefore the subtle initial signs pass unnoticed. The signs are no specific in the large majority of cases being manifest in either systemically variable signs or cutaneous nodules that could easily be attributed to other more benign conditions.

Neoplastic proliferation of the erythroid series is singularly rare in horses but a few cases of 'polycythaemia vera' have been reported.

When considering the group of neoplastic diseases as a whole, leukaemia can be classified with respect to the:

- Type of cell involved (either lymphoid or myeloid) or
- Degree of tumour differentiation (as acute or chronic) or
- Number of circulating abnormal cells (leukaemic or aleukaemic).

Pathologists may also have specific morphological categories based upon histochemical stains for the tumours but also classify them as malignant or benign, infiltrative or localised.



LYMPHOSARCOMA

Pathogenesis

Lymphosarcoma (lymphoma) is the most common internal tumor of the horse and is by far the most common of the tumors of the haemopoetic system.

There are several different forms of lymphosarcoma.

The incidence in the UK is less than 3 cases per thousand horses. No specific risk factors are reported and there is no sex or breed predilection. Most cases are between 4 and 10 years of age but cases have been reported in the fetus and in much older horses also. For the most part however, lymphoma is a condition of the younger – middle-aged horse.

Four specific types of lymphosarcoma are recognized:

Generalised / Multicentric lymphosarcoma

Alimentary lymphosarcoma (focal and diffuse subforms).

Mediastinal (including thymic) forms

Cutaneous forms (including cutaneous histiocytic lymphosarcoma)

The extent of malignancy is variable and so the tendency to metastatic spread is also variable and can mask the differences between the various forms. Thus a mediastinal form may cause alimentary or splenic secondary tumour formation and a primary in the alimentary tract may result in metastatic spread to the lungs.

Clinical Signs

There is a wide range of clinical syndromes associated with the various forms of lymphosarcoma / lymphoma and the signs have a wide overlap between the various types of lymphosarcoma. General signs are part of most of the conditions and include:

Anorexia and weight loss

Depression / lethargy (these are often in association with the periods of fever – see below)

Ventral oedema

Lymphadenopathy may be present. In some sites this causes secondary oedema as a result of lymphatic obstruction. In the thymic / mediastinal forms this results in pleural effusion – this is the only cause of massive accumulation of slightly blood stained, non-infective fluid within the pleural cavity. Accumulation of peritoneal



Ventral oedema with filling of the left forelimb characteristic of thoracic / mediastinal lymphosarcoma.

fluid is less prominent but can still be severe in some cases – this results also in ventral oedema. Lymphadenopathy can cause localised oedema such as a single front leg – usually the earliest sign of mediastinal lymphosarcoma is oedema of one front leg (often the right one).

Recurrent (undulant) fever is a common finding if the rectal temperature can be taken twice daily. Very often a diagnosis of infection is made and antibiotics administered. The subsequent fall in body temperature may then give the impression of a therapeutic effect only to find that the fever returns.

Secondary effects include:

Effects resulting from specific location of the tumours including:

- forelimb and neck oedema and jugular engorgement with pleural effusion in thoracic / mediastinal forms.
- Colic, diarrhoea and / or peritoneal fluid accumulation (with consequent ventral oedema) in intestinal forms.
- Immune mediated anaemia or Thrombocytopenia
- Paraneoplastic syndromes (weight loss, cancer cachexia, hypercalcaemia and hyperfibrinogenaemia, hypoalbuminaemia (as a result of both malabsorption and of consumptive reduction by fast growing tumour cells)

Specific Signs associated with the various types of lymphosarcoma include:

GENERALISED / MULTICENTRIC LYMPHOSARCOMA

The tissues most often involved in this form (in decreasing order of frequency) are:

1. Lymph nodes (including the palpable peripheral lymph nodes although in many cases the only enlargement is in internal lymph nodes – it is often useful to examine the pharyngeal lymph nodes from within the guttural pouch)
2. Liver (causing metabolic derangements and post hepatic / obstructive icterus)
3. Spleen (splenic nodules may be palpable per rectum or may be detected by trans-abdominal ultrasonography)

4. Intestine (inducing colic or malabsorption syndromes with diarrhoea or both)
5. Kidney (inducing haematuria or chronic renal failure)
6. Lung (inducing a chronic cough and mediastinal fluid accumulation with pleural effusion)

More rarely tumours can invade the upper airway (causing respiratory obstructions and coughing), spinal cord (causing spinal compression and various neurological symptoms including paraplegia and hemiplegia), heart (causing arrhythmias and altered valvular function), retrobulbar space (causing exophthalmos). Other signs that may be present include icterus (as a result of autoimmune haemolytic anaemia).

MEDIASTINAL (THYMIC) LYMPHOSARCOMA

Enlargement of the mediastinal lymph nodes secondary to tumour invasion may compress the intrathoracic structures (particularly the lymphatic vessels such as the cranial and caudal lymphatic ducts) and the veins. This results in fluid accumulation within the forelimb(s) and chest cavity (followed by peritoneal fluid accumulation) and also venous distension (resulting in jugular engorgement and subsequently obstruction of the caudal vena cava (with consequent portal hypertension and peritoneal fluid accumulation). In any case ventral oedema is a common finding.

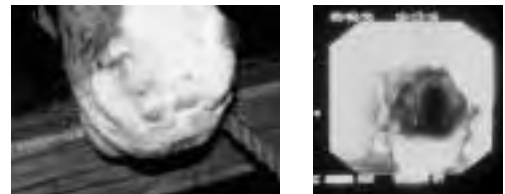
ALIMENTARY LYMPHOSARCOMA

Diffuse involvement of the small intestine is more common than other forms although the stomach and the large colon may be affected. In the former cases there is a failure of digestion and more significantly absorption although in the early stages at least the normal large colon capable of counteracting the malfunction (and so the condition may pass unnoticed). Discrete masses in the small intestine may cause a no-strangulating obstruction [colic – interestingly the focal form is more often seen in older horses while the diffuse form is more often in younger animals (under 10

years)]. In both cases the mesenteric lymph nodes are invariably affected and the root of the mesentery (at which the majority of the lymph nodes occur) may be palpably enlarged and nodular in form. Diarrhoea is rare unless the condition affects the large colon. Weight loss, anorexia and lethargy / depression are usually present. Metastases tend to occur late in the disease so if a diagnosis can be made early there is a slight hope of successful removal of the affected portion of small intestine. The large intestinal forms and those forms that involve larger lengths of small intestine carry a grave prognosis. Occasionally the intestine develops a severe mechanical obstruction.

CUTANEOUS (HISTIOCYTIC) LYMPHOSARCOMA

Multifocal, firm, subcutaneous nodules in the skin are the common findings. Some will ulcerate and exude honey coloured plasma like substance. The nodules may be alopecic and may become inflamed (either from sterile necrosed



Cutaneous nodules on the muzzle of a pony diagnosed with cutaneous histiocytic lymphosarcoma. Picture b shows the appearance of the pharynx of the same pony – there are numerous large lymphoid nodules over the pharyngeal mucosa.



Post mortem specimen of the pharynx of a 12-year-old Thoroughbred that was presented for investigation of dysphagia. The lesion was easily appreciated endoscopically and no other lesion was found either clinically or at post mortem. The diagnosis of lymphosarcoma was made Histologically from a pre mortem biopsy and confirmed post mortem.

or from secondary infections). The onset of systemic disease or metastases is usually delayed for up to 5 years but may be far sooner.

Differential Diagnosis

Each form of lymphosarcoma has its own differential diagnosis. Probably the most difficult differentials occur when the tumours are in the early stages where the signs are subtle and the diagnosis difficult.

Focal forms have localised signs that are attributable to space occupying nature (e.g. orbital lymphoma causes exophthalmos) or to functional disability (e.g. pharyngeal lymphosarcoma causes dysphagia and epistaxis with a fetid breath).

The focal skin forms may be single and ulcerate early or may be static for many years. There is usually no outward sign except where these interfere with function in some respect.

Diagnosis

A thorough and systematic clinical examination (including rectal palpation, abdominocentesis, pleurocentesis and haematological examination) are essential if only to eliminate other conditions that do not carry such a poor prognosis – it is singularly disappointing to

find at post mortem examination that the diagnosis was wrong and that the animal had a treatable condition. The diagnostic tests may need to be repeated before a definitive negative or positive diagnosis can be made. The value of a good cytopathologist cannot be overstated. Collection of high quality specimens is clearly central to the diagnosis and the accurate assessment of the stage and type of the disease.

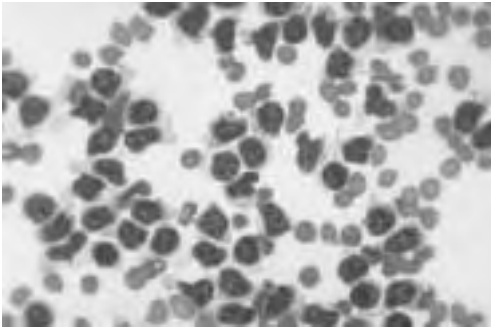
Ultrasonographic and if necessary radiographic or endoscopic examinations (including laparoscopy or pleuroscopy) can be very useful in the diagnosis.

A definitive diagnosis requires specific recognition of the cell type and its rate of proliferation (see above). The main problem is that most forms of lymphosarcoma are non-exfoliative and so abnormal cells may not be obvious in peritoneal or pleural fluid. Furthermore abnormal lymphocytes do not often appear in the blood (where they do, diagnosis is easy if the smear is examined by a skilled cytopathologist). Abnormal (blast) cells are easily recognised by their extensive cytoplasm and nuclear chromatin clumping, prominent nucleoli and basophilic cytoplasm. However, they may resemble large, well-differentiated lymphocytes.

Bone marrow involvement is also rare in horses and so biopsy and aspirates may not help.

DIFFERENTIAL DIAGNOSIS FOR TUMOUR TYPE

<i>Generalised</i>	<i>Mediastinal Pleural /</i>	<i>Alimentary / Mesenteric</i>	<i>Cutaneous</i>
<input type="checkbox"/> Infection Parasitism	<input type="checkbox"/> Pleural bacterial infection	<input type="checkbox"/> Alimentary infections	<input type="checkbox"/> Nodular skin disease
<input type="checkbox"/> Chronic inflammatory process	<input type="checkbox"/> Fungal infection	<input type="checkbox"/> Parasitism	<input type="checkbox"/> Ulcerative lymphangitis
<input type="checkbox"/> Gastric squamous cell carcinoma	<input type="checkbox"/> Pulmonary infection	<input type="checkbox"/> Granulomatous enteritis	<input type="checkbox"/> Glanders / Farcy
<input type="checkbox"/> Equine Infectious anaemia	<input type="checkbox"/> Mesothelioma	<input type="checkbox"/> Maldigestion / Malabsorption	<input type="checkbox"/> Nodular Sarcoid
<input type="checkbox"/> Purpura haemorrhagica	<input type="checkbox"/> Equine Infectious anaemia	<input type="checkbox"/> Peritonitis	<input type="checkbox"/> Fibroblastic sarcoid
	<input type="checkbox"/> Purpura haemorrhagica	<input type="checkbox"/> Hepatic disease	<input type="checkbox"/> Cutaneous collagen necrosis
		<input type="checkbox"/> Renal failure	<input type="checkbox"/> Dermoid cysts
		<input type="checkbox"/> Mesothelioma	
		<input type="checkbox"/> Squamous cell carcinoma	



A rare case of leukaemic lymphosarcoma in which the absolute lymphocyte count was $750 \times 10^9/L$.

LABORATORY FINDINGS

These are often disappointing given the severity of many of the cases on initial presentation. Very few cases are leukaemic (peripheral lymphocyte counts are often normal!). About 50% of cases show:

- Neutrophilia (with left shift)
- Hyperglobulinaemia: usually there is a gammopathy of some sort – often slight increase or decrease in gamma globulins. Monoclonal gammopathy may be detected but this is more often seen in myeloma
- Hyperfibrinogenaemia.
- Normocytic normochromic anaemia (seldom profound and often slowly progressive becoming static)
- Hypercalcaemia
- Leukaemia is a rare finding but of course when present is immediately recognisable. White cell counts of up to $750 \times 10^9/l$ are encountered.

Treatment

Successful long-term treatment is not possible at present. Transient improvement in signs may follow high dose corticosteroids or specific antimetabolic drugs such as vincristine or cyclophosphamide. The more aggressive approaches are simply an expensive way of prolonging the animals suffering. In any case the cost of all forms of therapy and the late diagnosis in most cases make therapy a poor op-

tion. Early euthanasia is the most sensible way forward. However, the one interesting form is the cutaneous histiocytic lymphosarcoma. Recently it has been suggested that some of these are oestrogen dependent or at least are oestrogen exacerbated. It is always worth performing a rectal examination and ovary palpation and ultrasonography in mares presented with cutaneous histiocytic lymphosarcoma. Some affected mares have a concurrent granulosa cell tumour and this should be removed before condemning the horse. Some cases are improved markedly (though possibly not permanently). The rate of progression is reduced and the secondary effects are less obvious.

Prognosis

The prognosis for most forms is largely hopeless. Usually progression is rapid. The exception to this rule is the cutaneous form. In these cases the rate of progression can be very slow and a survival rate of around 2 – 6 years can be expected (although it is still unwise to predict that this will indeed be the case). Before such a prognosis is offered, the clinician will need to be sure that the skin manifestations are not the result of a multicentric form or metastatic spread from another malignant form.

MYELOGENOUS (MYELOID) LEUKAEMIA

Pathogenesis

This group of neoplastic conditions is characterised by unregulated proliferation and incomplete differentiation of primitive bone marrow stem cell clones from medullary and extra-medullary bone marrow including those of the erythroid, granulocytic, monocytic and megakaryocytic series. Specific forms that have been described include:

1. Acute myelomonocytic leukaemia
2. Acute monocytic leukaemia
3. Chronic myelocytic (neutrophilic) leukaemia
4. Eosinophilic leukaemia

These tumours are classified by the histochemical characteristics of the predominate cell type present within bone marrow. Thus a diagnosis is heavily reliant upon bone marrow examination. The chronic forms tend to be less aggressive and more differentiated. For example chronic myeloid leukaemia involves neutrophils and late precursor cells whereas the acute forms tend to involve myeloblastic cells.

There is no breed or sex predisposition and most cases fall into the 3 – 12 year age group.

Clinical Signs

The signs are not pathognomonic and may be so subtle as to belie the diagnosis.

The onset of clinical signs is usually rapid (over some days) with an inexorably rapid course over 1 – 4 months. All reported cases show peripheral pitting oedema (particularly of the hind limbs) with ventral midline oedema being a common sign. There is usually an obvious purpuric petechiation with depression, anorexia and anaemia.

Recurrent or persistent pyrexia (that is non-responsive to antibiotics but may respond to non-steroidal anti-inflammatory drugs), weight loss, lymphadenopathy, coagulopathy and pulmonary infections are common.

Differential Diagnosis

All severe wasting diseases with a course of less than 3 – 6 months including:

- severe parasitism, internal sepsis / abscessation.
- Peritonitis, pleuritis.
- Other disseminated neoplastic disease (e.g. Mesothelioma / melanoma).

Diagnosis

The diagnosis is usually made with the help of blood samples – and indeed it may be made accidentally / incidentally. The finding of undifferentiated leukocytes in the circulation is

highly suggestive but by no means definitive. The laboratory findings are usually central to the diagnosis but can be almost insignificant. Usually there is a profound leucopaenia but there may be a leucocytosis! There is usually some degree of anaemia but this is seldom profound and may be static or slowly progressive. There may be a thrombocytopaenia (both this and the anaemia may be immune mediated and the later can result in a mild icterus).

Bone marrow cytology is essential if the diagnosis is suspected. Bone marrow depression can be associated with increased serum iron with decreased iron binding capacity.

Treatment

Treatment with cytosine arabinoside (at 10 mg/s metre body surface area) q 12h for 21 days has been attempted but was unsuccessful. There are no reports of successful treatment in any case so far. Early euthanasia is indicated.

Prognosis: Hopeless!

PLASMA CELL MYELOMA

Pathogenesis: Plasma cell tumours are singularly rare in horses. These are myeloproliferative diseases characterised by uncontrolled replication of single clones of plasma cells (this results in the characteristic monoclonal gammopathy – see below). The literature contains around 4 – 6 cases¹. Plasma cells are differentiated B-lymphocytes and these can develop into several forms of neoplastic proliferations.

- Chronic B-cell lymphocytic leukaemia
- B-cell lymphoma
- Plasma cell tumour

¹ Edwards DF, Parker JW, Wilkinson JE and Helman RG (1993) Plasma cell myeloma in the horse. A case report and literature review. *Journal of Veterinary Internal Medicine* 7; 169-176.

The clones of plasma cells produce paraproteins that are globulin like but have no globulin functions. Most cases are Multiple Myeloma but solitary plasma cell tumour has been reported. The age of reported cases is between 3 months and 22 years and there is no obvious sex, breed or other predisposition.

Clinical Signs

The signs are related to organ infiltration by neoplastic cells or to systemic effects of the paraproteins that are produced. Weight loss, anorexia, lameness, neurological defects, renal disease, haemorrhagic diatheses, and recurrent chronic infections are reported in individual cases. These signs are characteristically non-specific.

The lameness is an interesting sign that is possibly due to osteoclastic activity and that is a result of the paraproteins (osteoclast activating factors) but direct bony invasion may also be possible. Hypercalcaemia and a high urinary paraproteins production may be present and contribute to the renal disease. There may be an immune mediated antithrombotic effect when the platelets become coated with the paraproteins and lose their function. Anaemia as result of bone marrow suppression can also occur in theory at least. Secondary infection is a common cause of death in other species but so far the disease is so rare in horses that few guidelines can be stated.

Differential Diagnosis

Lameness and vague neurological problems (particularly involving the hind limbs) are possibly the major differential diagnosis. Other forms of lymphoid and myeloproliferative disease may also be considered. Other causes of renal failure and anaemia and clotting problems must be considered also.

Diagnosis

All horses with non-specific signs of systemic illness, hyperglobulinaemia / hypopro-

teinaemia and concurrent anaemia are affected by some chronic inflammatory process. Serum electrophoresis is a useful aid to identification of the gammopathy involved. A polyclonal gammopathy usually indicates a chronic inflammatory process of any origin but a monoclonal gammopathy is virtually diagnostic.

A definitive diagnosis is made when a bone marrow aspirate reveals a plasma cell proportion of over 10% especially if there is a concurrent monoclonal gammopathy. Circulating plasma cells are rare.

Radiographic evidence of "punched out" radiolucencies may be supportive but it is not certain whether this is a practical diagnostic option in horses.

Bence-Jones proteinuria is not reported to occur in horses but this may be related to the technology rather than the absence!

Treatment

This is probably not practical but treatment in one case with melaphan (at 7 mg / sq metre) q 24 h for 5 days every three weeks resulted in remission / stabilisation of signs that lasted for up to a year. Supportive broad-spectrum antibiotics are also necessary. Most cases die within 3 months and so early euthanasia is the best option.

Prognosis

The prognosis is hopeless at present.

ARE WE MISSING THIS DISEASE?

POLYCYTHAEMIA

Pathogenesis

This is a singularly rare disorder in horses (and other species) and results from the abnormal / uncontrolled proliferation of the red cell mass. It is far more common to have a relative polycythaemia due to reduction in plasma volume (dehydration is the commonest

cause of this) – this is a very common event in horses. There are also some physiological states that result in an abnormal increase in the volume of red cells (Haematocrit) such as splenic contraction (excitement, catecholamine activity and possibly a result of phaeochromocytoma activity). Also there is a well-recognised syndrome of “haemoconcentration” in young racing stallions in hot humid climates. The latter cases may respond to castration but this may be unacceptable for the better class of horse!

Genuine increases in red cell production with increased circulating red cell mass (absolute erythrocytosis) may be primary or secondary.

Primary absolute erythrocytosis occurs extremely rarely and is due to genuine autonomous proliferation of erythroid progenitor cells or genuine neoplastic proliferation of red cell precursor cells and uncontrolled release into the blood stream.

Secondary erythrocytosis is due to abnormal production of erythropoietin from the renal cortex. This in turn may be due to abnormal stimulus (low general circulating oxygen tension) or reduced renal perfusion.

Clinical Signs

The absolute erythrocytosis (polycythaemia vera) causes an increase in blood viscosity and expanded blood volume. There is a generalised venous engorgement (even at rest superficial vessels are prominent). The mucous membranes have a dense muddy hyperaemic colour.

A marked decrease in cardiac output occurs with poor tissue perfusion, which is responsible for the dark brownish red mucous membranes. The consequences include lethargy and weight loss. Epistaxis, gastrointestinal haemorrhage or thrombotic complications including laminitis and focal cutaneous necrosis and renal failure may occur.

Differential Diagnosis

Secondary or relative erythrocytosis.

Diagnosis

Very high haemoglobin, red cell count and PCV without dehydration.

There is no detectable abnormality of red cell structure but immature nucleated red cells may be present.

Treatment

Repeated bleeding is essential – bleeding with return of plasma is helpful and should continue until the haematocrit returns to the reference range. This may need to be repeated at daily intervals. The haematocrit should be kept below 50%. Once iron deficiency is induced by the repeated bleeding the need for phlebotomy is reduced. Specific drug therapy is not applicable to horses.

Prognosis: Grave.

Note

There are many suggestions that homeopathic remedies are effective for these disorders. The reality is that if they work the diagnosis was probably wrong.

Veterinary surgeons need to be sure of the diagnosis before making major decisions.... owners are inclined to try anything once the diagnosis has been made and if they turn to the alternative treatments and the animal survives then they will never trust conventional medicine again. The problem is in the diagnosis!