Histol Histopathol (1999) 14: 845-860

http://www.ehu.es/histol-histopathol

Histology and Histopathology

Invited Review

Malignant fibrous histiocytoma (MFH). A comparison of MFH in man and animals. A critical review

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Summary. This review gives information about localization and types of MFH in man and animals such as mouse, rat, cat, dog, opossum, cattle, horse and birds [e.g. mallard (a wild duck)]. Furthermore, this paper reports about cell culture dealing with MFH.

The aim of this publication is to show that MFH originates from a primitive mesenchymal stem cell, fibroblastoid cell and fibroblasts. Histiocytes are, according to the literature in a small amount constituents of MFH and are reactive cells or without any meaning.

In our own studies using rats [*strain*: Chbb: THOM (SPF)] the characteristic storiform or cartwheel pattern of tumour cells were evident. The cells were elongated, rich in endoplasmic reticulum and possessed no or very few lysosomes. The cells were predominantly fibroblasts and fibroblastoid cells. These cells were intermingled with giant cells. In other species mentioned above, the MFH showed very similar histological features. Our own results and findings obtained from the literature support our concept that the MFH represents a primitive phenotype or pleomorphic sarcoma which may differentiate in one or more directions. Histiocytes are not a neoplastic component.

Key words: Malignant fibrous histiocytoma, MFH, Man, Animals, Electron microscopy

Introduction

The human MFH, a not uncommon type of soft tissue sarcoma (Zagars et al., 1996), is a neoplasm of late adult life (Kirchner et al., 1984b; Cole et al., 1993; Fang et al., 1996) but often found in children too (Cole et al., 1993; Kodet et al., 1993; Malone, 1993; Corpron et al., 1996; Hari et al., 1996; Palmer et al., 1997; Shah et al., 1996).

According to Burke and Virmans (1993) who studied MFH in great vessels (see below; next chapter), the mean age of adult patients suffering from MFH was, e.g., 62.3 years (aorta) or 49.9 (inferior vena cava). The average span of lives was 23-93 years.

MFH was first described as a distinct type of sarcoma by O'Brien and Stout (1964). The tumour is called synonymously as malignant fibrous xanthoma or pleomorphous fibrous xanthoma according to Weiss and Enzinger (1978). Little and McCarthy (1993) designated this tumour as a high-grade primary bone sarcoma. Requena et al. (1997) emphasized that an atypical fibroxanthoma was a superficial variant of pleomorphic MFH.

MFH is often a consequence of therapy, mostly after radiotherapy or chemotherapy with doxorubicin and cyclophosphamide (Costa, 1994). This neoplasm is also induced by 4-hydroxyamino-quinoline-1-oxide (Mii et al., 1982), 7,12-dimethylbenz(a)anthracene (Nikitin et al., 1993) or by a similar agent (Sakamoto, 1986) in rats. Narita et al. (1997) described a family aggregation of soft tissue sarcomas which they designated in part as MFH. The authors concluded that the observed features closely resembled the Li-Fraumeni syndrome because they noted different neoplasms (liposarcoma and gastric carcinoma) seen at the very same time as MFH.

MFH is sometimes a consequence of primary diseases e.g. fibrous dysplasia (Ruggieri et al., 1994; Ohmori et al., 1996) a benign disease which often occurs predominantly in the area of femur, tibia and face's skull (monoostotic, Morbus Jaffe-Lichtenstein; the polyostotic variant mostly found in girls is named Albright-syndrome). After fibrous dysplasia a fibrosarcoma or osteosarcoma could also be a consequence (Ruggieri et al., 1994). According to Little and McCarthy (1993) MFH is sometimes the consequence of post-radiotherapy, Paget's disease, osteosarcoma or giant cell tumour.

The question arises as to whether the designation as MFH is justified. It is the aim of our review to clarify this. Since the publication by Leder (1967) it is well-known, that phagocytic cells such as histiocytes, macrophages but also resident phagocytes like Kupffer's cells of the liver originate from monocytes. Because malignant cells possess characteristics of stem cells the MFH must actually derive from monocytes. Mature

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phagocytes could then form at the most benign neoplasms.

A very important review about human soft tissue tumours has been published by Kirchner and Wünsch (1981). In this monograph, amongst other things, the distribution and differential diagnoses are discussed. Similar statements were given by the same authors (Wünsch and Kirchner, 1982). Wünsch and Müller (1982) emphasized that in differential diagnosis for hemangiopericytoma different mesenchymal neoplasms, also a MFH, have to be taken into consideration.

The literature on MFH is extensive. About 600 references are available. The papers are for the most part those dealing with therapy (cytostatic agents, surgery and radiation). We used only such literature where pathology was the predominant part or where pathology was integrated as an important factor into a paper.

We intended to use the exact morphological definitions to describe anatomical sites and structures. Here, we orientated ourselves by Krstic (1984).

Localization and types of MFH in man

Localization

MFH is mostly localized within soft tissues of the extremities, bone (Little and McCarthy, 1993; Hartmann et al., 1997; Nishida et al., 1997) trunk or limb girdles (Pritchard et al., 1993) but also in other organs or regions of the body such as paranasal sinuses (Bültmann et al., 1981), pleura (Aozasa et al., 1994), lung (Rosemberg et al., 1993; Gal et al., 1994; Halyard et al., 1996; Suster, 1995; Shah et al., 1996; Barbas et al., 1997; Hartmann et al., 1997) - a benign fibrous histiocytoma must be taken into consideration in differential diagnosis of lung MFH (Schneider and Wünsch, 1980), heart (Beck et al., 1985; Okita et al., 1994; Teramoto et al., 1995; Fang et al., 1996), larynx (Benett and McFarlane, 1993; Kuwabara et al., 1994; Scott and Carter, 1995; Soh et al., 1996), spleen (Lieu et al., 1993; Bonilla et al., 1994), head and neck together

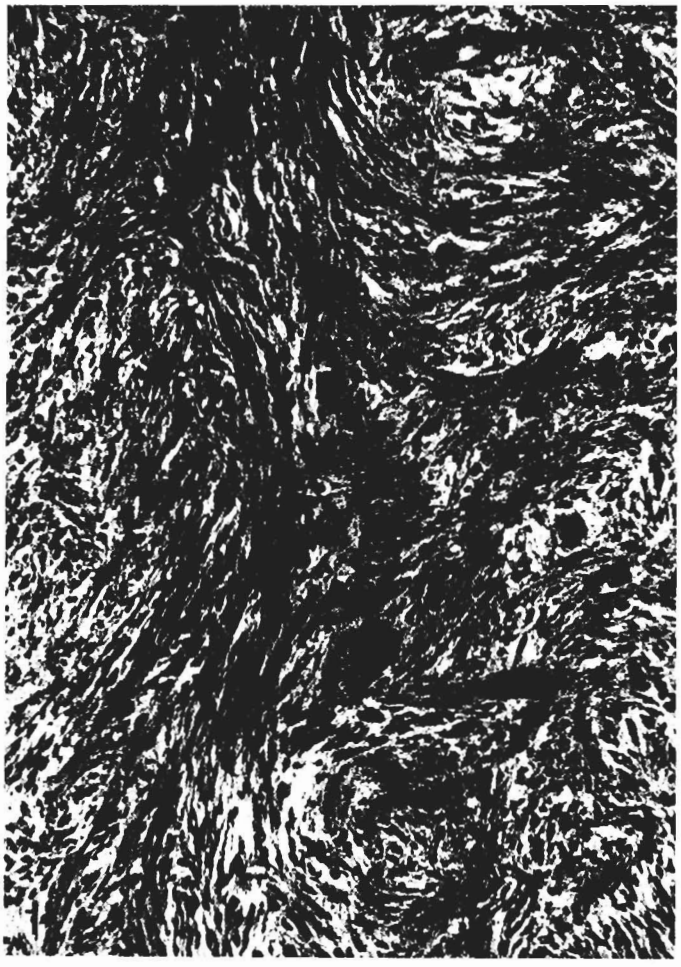

Fig. 1. MFH, overall view, typical storiform-pleomorphic pattern or structure respectively, cell-dense, fusocellular, giant cell containing, sarcomatous tumour. H-E, x 240

Fig. 2. MFH, magnification of a sector, pleomorphic bizarre giant cells. The MFH includes spindle cells similar to fibroblasts and histiocytes. H-E, x 400

with larynx, tonsils and/or regional lymph nodes (Bremer et al., 1982; Singh et al., 1993; Zapater et al., 1995), axilla (Fukunaka et al., 1996), spermatic cord (Glazier et al., 1996), pancreas (Haba et al., 1996), leptomeninges (Hari et al., 1996) as well as peritoneum, retroperitoneum, mesentery and intestine (Hauser et al., 1993), large vessels such as aorta, inferior vena cava and/or pulmonary artery (Burke and Virmani, 1993; Khan et al., 1997), intracranial localization (Kirchner et al., 1984b), urinary bladder (Kunze et al., 1994; Weingärtner et al., 1995), liver (Lieu et al., 1993), kidney (Lopez et al., 1996), brain (Martinez-Salazar et al., 1997), oesophagus (Naganuma et al., 1996), mandible (Onyango and Awange, 1993; Sohail et al., 1995; Narvaez et al., 1996), pleura (Rizkalla et al., 1994) and trachea (Sennaroglu et al., 1996).

Bültmann et al. (1981) stressed the fact, that more than 60% of the cases are found in the area of extremities. The retroperitoneum, abdominal walls and chest wall are the organs closest to MFH-development (30%).

Types of MFH

Different authors have described the types of MFH: histologically the MFH can be subdivided into: 1) storiform-pleomorphic (the most common type); 2) myxoid type; 3) giant cell type; 4) inflammatory type; and 5) angiomatoid type

There are only slight differences between the investigators who proposed and described this nomenclature. All those who studied the types of MFH considered this matter as a similarity (Weiss and Enzinger, 1978; Bültmann et al., 1981; Kirchner et al., 1984a,b; Müller et al., 1984; Wünsch and Dubrauszky, 1987; Cole et al., 1993; Nascimento, 1993; Kunze et al., 1994; Miller et al., 1994; Costa et al., 1995; Meister, 1995; Riede and Sterry, 1995; Unnik, 1995; LeDoussal et al., 1996; Zagars et al., 1996). The MFH in man is illustrated by Figs. 1-4. We studied this malignant

Fig. 3. MFH, magnification of a sector, mainly a picture of fibroblastic spindle cells together with some multinucleated giant cells. H-E, x 480

Fig. 4. MFH, magnification of a sector, beside multinucleated bizarre giant cells and fibroblasts ("histiocytic" cells); there are also inflammatory cells. H-E, x 480

tumour in approx. 250 cases.

MFH in animals

Mouse

Tillmann et al. (1997) implanted microchips in CBB/y mice. Subcutaneous soft tissue tumours occurred at the site of these microchips. Although the neoplasms developing at the implantation site had a mixed histological appearance, two main tumour types were identified. The majority of the neoplasms were fibrosarcomas. The other main tumour type was a typical MFH. This tumour showed populations of histiocyte like and fibroblastic cells with focal collagen production. The storiform cartwheel pattern was characteristic. Bizarre multinucleated giant cells were found corresponding to the pleomorphic subtype of MFH. Some MFH's looked like a hemangiopericytoma, while others resembled malignant schwannomas.

Yamamoto and Yamamoto (1996) detected an MFH in a hind leg tissue of a ddY-mouse.

Mouse uterine tumours similar to MFH were observed by Turusov et al. (1993). Trukhanova et al. (1998) described 1,2-dimethylhydrazine (DMH)-induced uterine sarcomas, including several MFHs.

Roholl et al. (1988) registered MFH in mice of all test groups including controls during a cancerogenicity study. There are also different data from studies in mice which suggested that neoplasms resembling MFH may develop from mouse bone marrow cells or peritoneal macrophages transformed by SV 40 virus (Yumoto and Morimoto, 1980).

Rat

MFH exists as spontaneous neoplasms or chemically or mechanically induced tumours.

Subcutaneous tumours comparable with human MFH were described by Zackheim et al. (1990). The neoplasms could reach huge proportions. Distant metastasis was frequent. The authors cited Greaves and

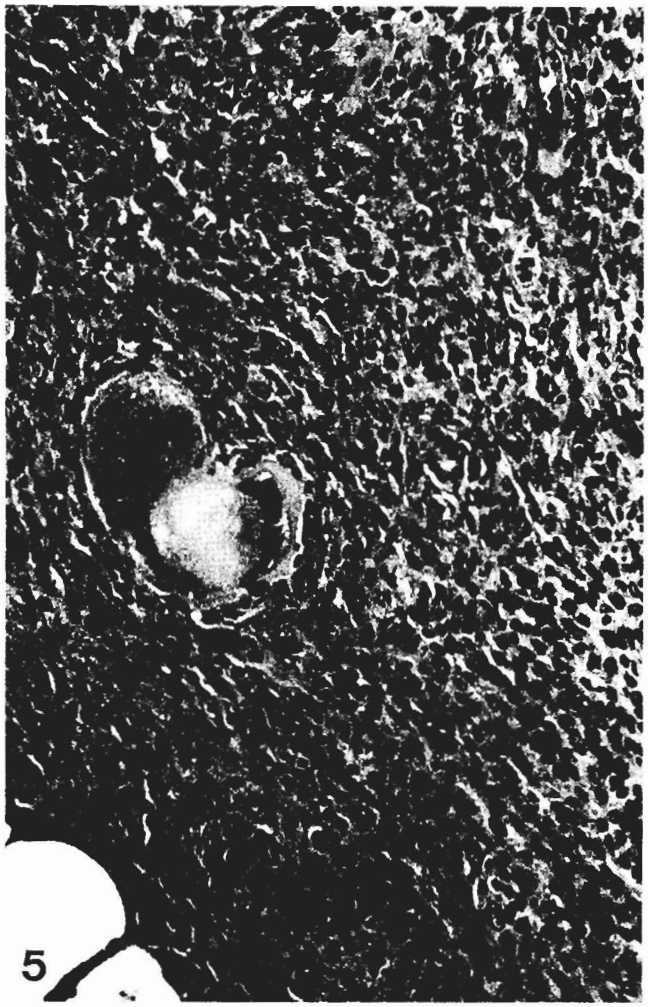

Fig. 5. MFH of lung. Most of the cells are similar to fibroblasts. Above the centre one recognizes a Langhans' giant cell. x 160

Fig. 6. MFH of bone marrow. Cells are small, round to elongated. Histiocytes and macrophages are not visible. x 55

Faccini (1992) who had observed MFH previously. Greaves and Barsoum (1990) also reported on MFH too.

Ogasawara et al. (1993) described the MFH as synonymous with malignant histiocytoma, malignant histiocytosis or Kupffer cell sarcoma. The authors used Donryu - and F-344 rats for their studies. They stressed the fact that although histiocytic sarcomas in rats are considered to originate from the liver, peritoneum or subcutis, the results they obtained strongly suggested that some of these malignancies could also originate from bone marrow and lymph nodes.

MFH induced chemically in rats has already been mentioned in the introduction of this paper. Here, we would like only to repeat the authors Mii et al. (1982), Nikitin et al. (1993) and Sakamoto (1986). It should be completed that Tanuma et al. (1993) induced MFH by administration of 4-hydroxyaminoquinoline 1-oxide. Tsuchiya et al. (1993) used 9,10-dimethyl-1,2-benzanthracene to induce MFH. Konishi et al. (1982) induced MFH by 4-(hydroxyamino) quinoline 1-oxide. This neoplasm occurred in the subcutaneous tissue and bone. The histological subtypes were fibrous, myxoid and giant cell MFH.

Hatanaka et al. (1993) reported on 5 kinds of foreign bodies (silicone, cellulose, polyvinyl chloride, zirkonia and alkyl-alpha cyanoacrylate) implanted into subcutaneous tissue of female Fisher rats. All substances caused, apart from cellulose, MFH.

Different compounds were tested by s.c. administration using new-born female rats (Imaida et al., 1995). MFH was observed in 12%, 100% and 100% of the rats treated with a total dose of 6.3 μmol 1,3-, 1,6- and 1,8-dinitropyrene (DNP). 1,6- and 1,8-DNP also induced leukaemia.

Litvinov and Soloviev (1990) wrote that osteolytic osteosarcomas in rats usually show a considerable degree of anaplasia, rapid growth and destruction of the pre-existing bone. A variant of these malignancies can be polymorphic cell sarcoma or MFH respectively.

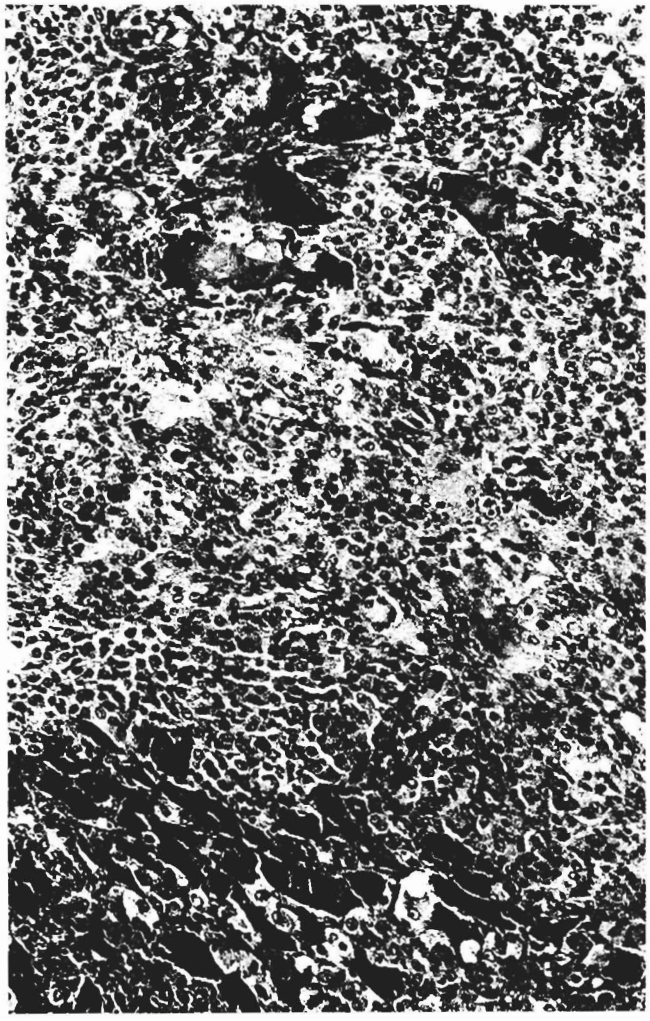

Fig. 7. MFH of pancreas. Several giant cells can be observed. x 100

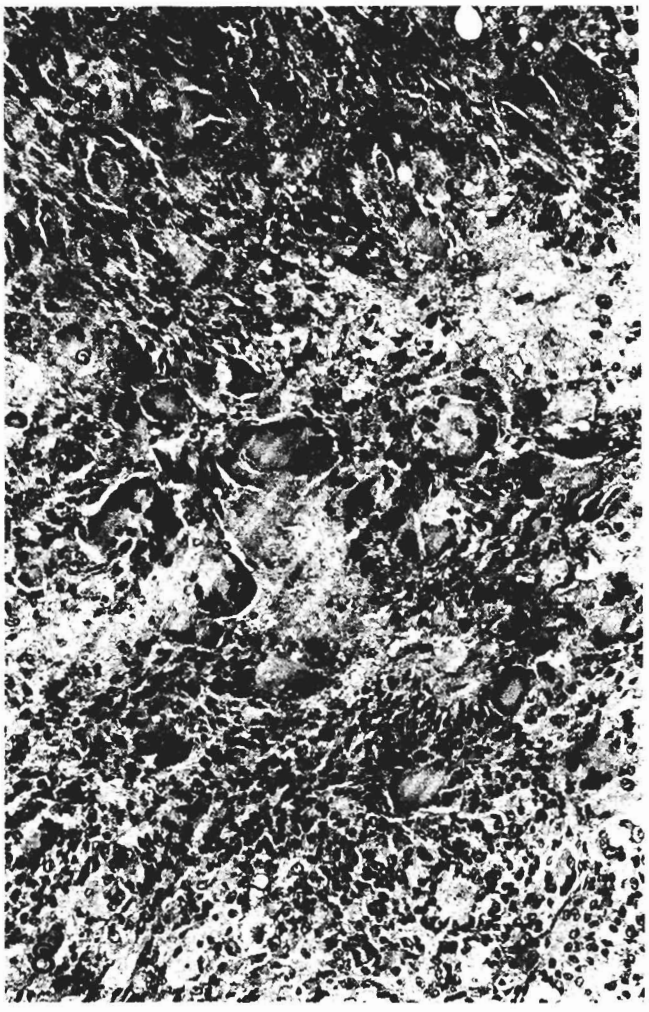

Fig. 8. MFH of pancreas. One can recognize, apart from some giant cells, necroses palisaded by histiocytes. x 100

MFH in the Chbb: THOM-rat

During a 2-year carcinogenicity study using male rats (strain: Chbb: THOM) Schneider et al. (1998) investigated all organs and tumours histologically. Neoplasms suspicious of MFH were also studied by electron microscopy.

MFH was observed in 14 out of 250 rats, i.e. approx. 5 percent. The characteristic storiform or cartwheel pattern was evident. The cells were similar to fibroblasts intermingled with giant cells (Figs. 5-9). The cells were rich in rough endoplasmic reticulum and possessed no or very few lysosomes. Histologically, the tumour looked like a fibrosarcoma focally. We could not recognize histiocytes with certainty. The neoplastic cells were not only elongated as fibroblasts but also pleomorphic in character (Figs. 10-12). This was shown by light - as well as by electron microscopy (Figs. 13-17).

The origin of rat MFH is commonly the abdomen and it spreads by «metastasis per continuationem» to all organs and body regions.

Our findings supported our concept that MFH represents a primitive phenotype or pleomorphous sarcoma which may differentiate in one or more directions (Greaves and Faccini, 1992).

Cat

Pace et al. (1994) diagnosed MFH in 7 cats from biopsy specimens. The diagnoses were made at the University of Missouri Veterinary Diagnostic Laboratory during a 4-year period from 1987-1991. Other scientists who mentioned MFH or soft tissue tumours related to MFH were Nielsen (1952), Alexander et al. (1975), Ford et al. (1975), Gleiser et al. (1979) Seiler and Wilkinson (1980), Confer et al. (1981) Renlund and Pritzker (1984), Allen and Duncan (1988) and Gibson et al. (1989), Hendrick et al. (1994) noted after rabies

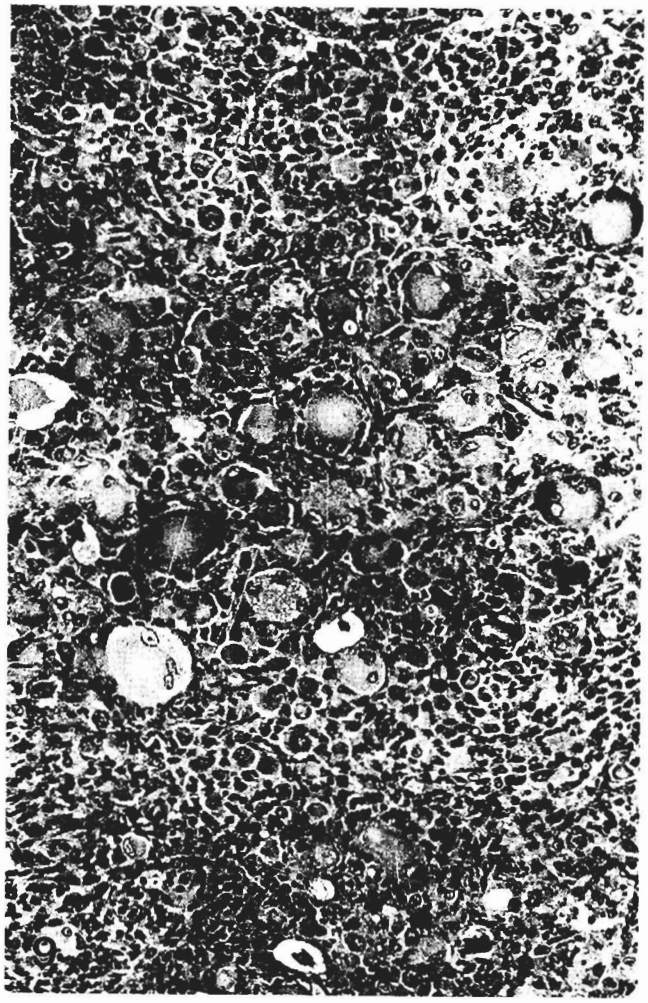

Fig. 9. Pleomorphic MFH of a lymph node partly showing very small cells, partly distinct fibroblasts and cells similar to epithelioid cells as well as many giant cells. x 100

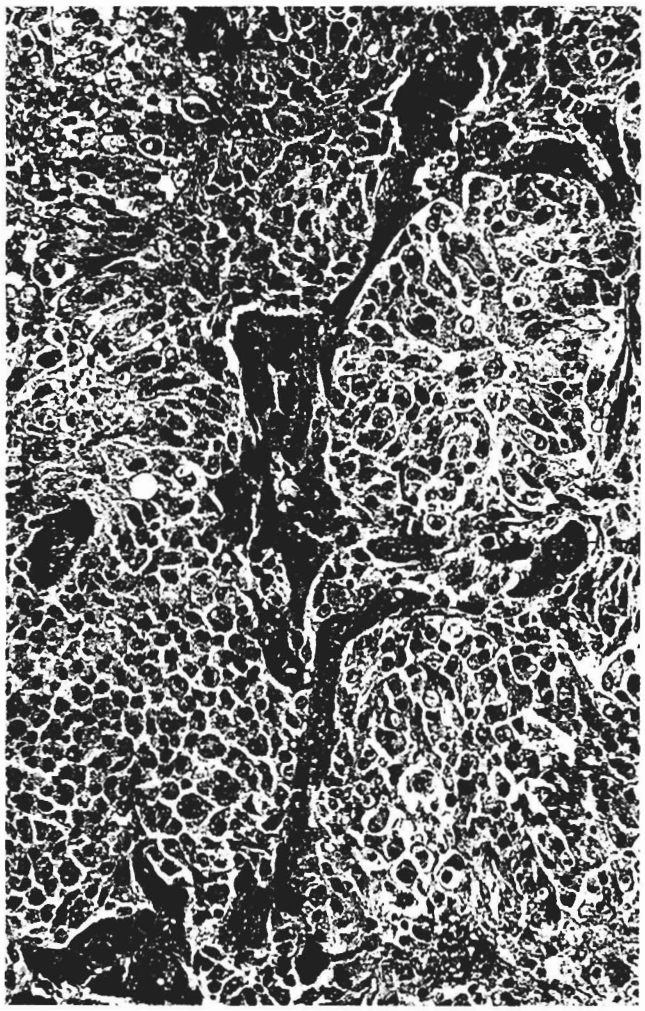

Fig. 10. MFH of liver. Extensive granulomas consisting of neoplastic cells. Marked anaplasia together with polymorphic nuclei and some mitoses. In some areas of the tissue atrophic hepatocytes of hepatic cords can be seen. x 250

vaccination an increase in fibrosarcomas, but also that osteosarcomas and MFH had occurred.

Rabbit

A total of 40 rabbits were used to induce sarcoma by administration of 9-10-dimethyl-1-2-benzanthracene (DMBA). DMBA caused MFH and occasionally fibrosarcoma (Homma and Wünsch, 1983). The authors mentioned that all malignant mesenchymal neoplasms result from a pluripotent stem cell.

Dog

Two dogs found to have splenic masses were histologically diagnosed as MFH (Rogers et al., 1994). The authors stressed that the MFH is a rare tumour of the spleen in domestic animals. They further wrote that, as most malignancies of the canine spleen have an aggressive behaviour, MFH appears to be no exception. Vilafranca et al. (1995) reported on MFH found in a kidney of a dog. Waters et al. (1994) described a giant cell variant of MFH found in 10 dogs. Common clinical findings included subcutaneous masses, anorexia, weight loss and lethargy. The most common sites of this neoplasm were subcutaneous tissues, lymph nodes, lungs and liver. MFH was determined to be a highly metastatic tumour in dogs, which may be responsive to radiotherapy, surgical excision or chemotherapy. Kerlin and Hendrick (1996) observed many canine soft tissue sarcomas that had an appearance of both MFH and malignant histiocytosis.

Pig

MFH was described in the spleen of a six-month-old pig at slaughter. This neoplasm was characterized as having a predominantly storiform and pleomorphic pattern. Besides the primary tumour in the spleen, there were disseminated, miliary, metastatic lesions in the

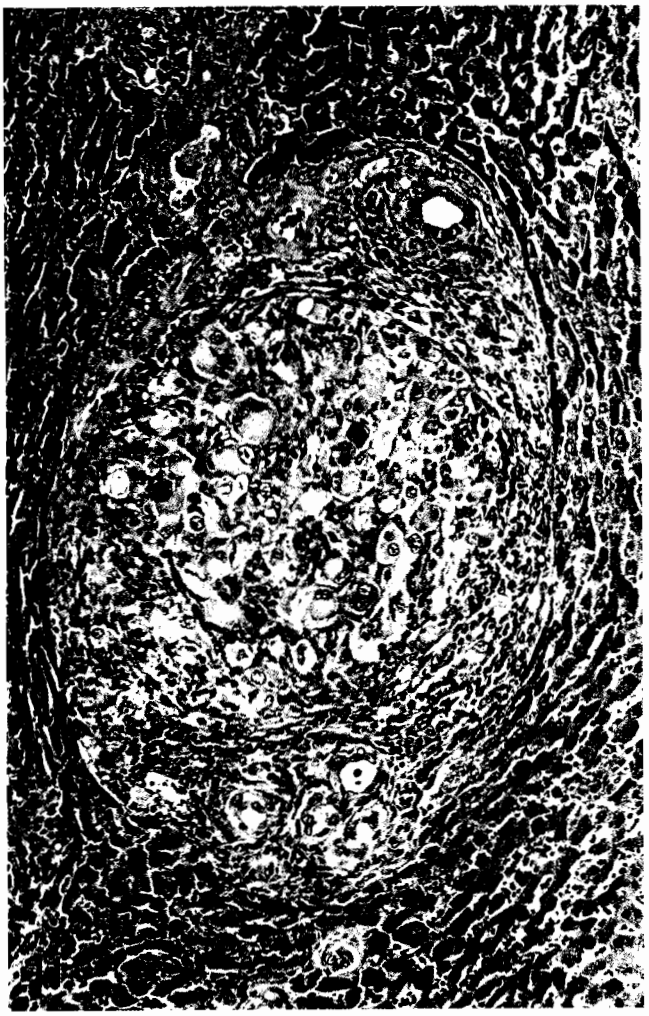

Fig. 11. MFH of liver in a granulomatous shape. x 96

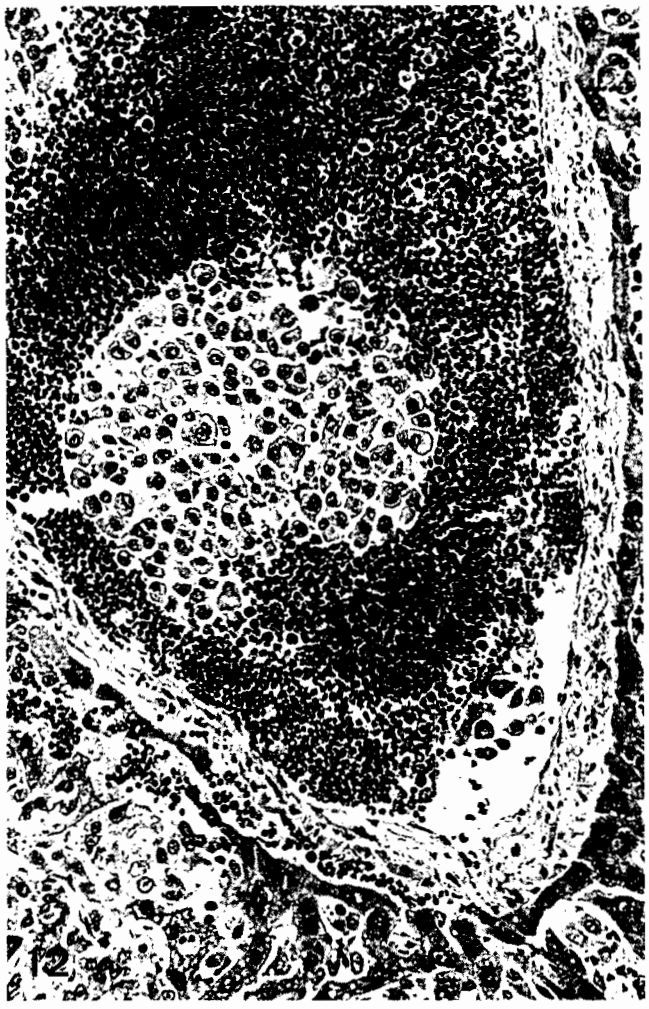

Fig. 12. MFH of liver. One can see intravascular metastatic tumour cells. The malignant cells are epithelioid or have a shape similar to plasma cells. x 205

liver and in the cortex of one kidney. The cells were different, with principally fibroblasts in the spleen and cells similar to histiocytes in the liver and in one kidney (Tanimoto et al., 1988).

Cattle

An invasive MFH associated with the left cornual process was diagnosed in a cow (Sartin et al., 1996). The masses compressed the left cerebral hemisphere focally and extended into the frontal sinus and ethmoid as well as nasal turbinates. They were composed of pleomorphic to spindle-shaped cells with evidence of fibroblastic, myofibroblastic and fibrohistiocytic differentiation. The authors concluded that trauma and chronic inflammation could be the predisposing factors for this neoplasia in

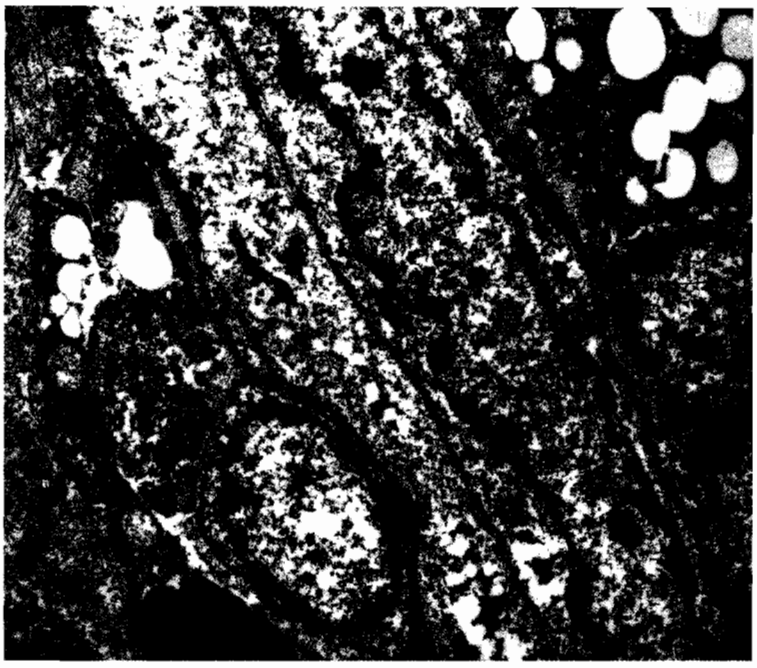

Fig. 13. Typical picture showing longitudinal tumor cells similar to fibroblasts in the center; liver. x 11,000

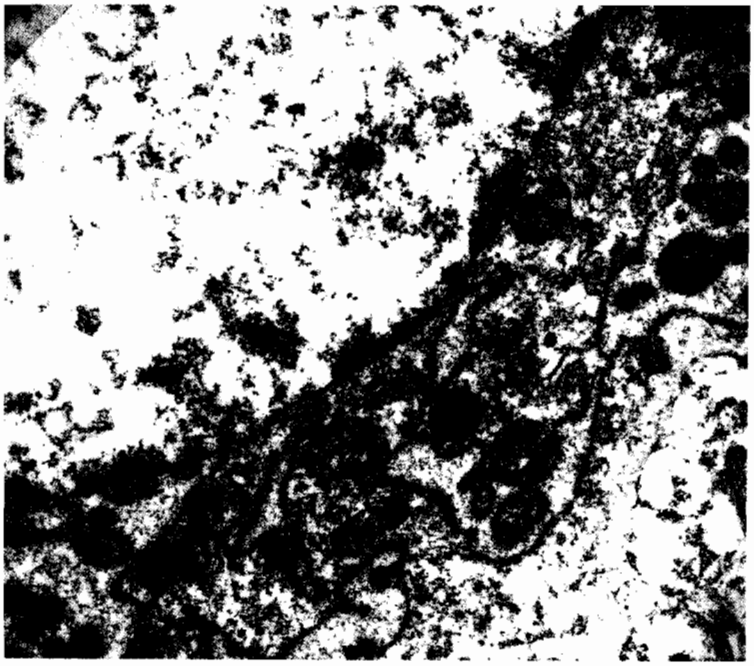

Fig. 14. Details of organelles. One can recognize extended rough endoplasmic reticulum; liver. x 14,735

cattle.

Horse

It is very interesting to note that MFH occurs in horses too. A giant cell type was seen in one horse by Ford et al. (1975) and in 6 horses by Render et al. (1983).

South American opossum

Chronic exposure of this species (*Monodelphis domestica*) to ultraviolet radiation induced 154 primary tumours of the cornea in 152 eyes (Sabourin et al., 1993). The opossum is a mammal being one of the marsupials, such as wombats, koala and kangaroos living in Australia (Grzimek, 1979). Histologically, the majority of neoplasms appeared to be fibrosarcomas, in part similar to MFH, but about 12 percent of these malignancies seemed to be haemangiosarcoma.

Birds

Roffe (1987) described an unusual pleomorphic sarcoma from a mallard (*Anas platyrhynchos*), a species of wild duck. Rhabdomyosarcoma was considered originally but then rejected due to the lack of specific features generally seen in these tumours. The histological characteristics observed were consistent with mammalian sarcomas recorded in the literature as MFH.

Cell culture

A continuous cultured cell line was established from human MFH of bone (Sekiguchi et al., 1994) The cultured cells were considered to be of at least 3 types of neoplastic cells. The authors recognised polygonal, spindle and giant cells.

By means of electron microscopy mostly immature cells could be seen which had poorly developed organelles and very few lysosomes. Allotransplantation of MFH cells into athymic nude mice produced tumours at early passages. Some cloned sublines isolated from parent line also exhibited essentially an identical morphology with that of the parent cell line, indicating that 3 cell types were interchangeable.

A fibrous histiocytoma cell line, NMSG 10, was derived from an MFH of human tibia (Yokota et al., 1995). Primary culture cells revealed a mixture of histiocyte-like cells, fibroblast-like cells and giant cells. The fibroblast-like cells became the major population after several passages in vitro.

To clarify the origin and nature of "histiocytic" cell in MFH immunoreactivities to rat, macrophage/histiocyte-specific monoclonal antibodies and monocyte chemoattractant protein-1 (MCP-1) production were investigated using rat transplantable MFH-derived cloned cells (Yamate et al., 1996). In rats with these tumours, the number of circulating monocytes was significantly increased. This and other results suggested the existence of non-neoplastic, infiltrated macrophages of host origin that were probably induced by MCP-1. The studies indicated the presence of heterogeneities in the original "histiocytic» cells in rat MFH.

Differential diagnoses and origin of MFH

Differential diagnoses

Goodlad and Fletscher (1991) described a malignant

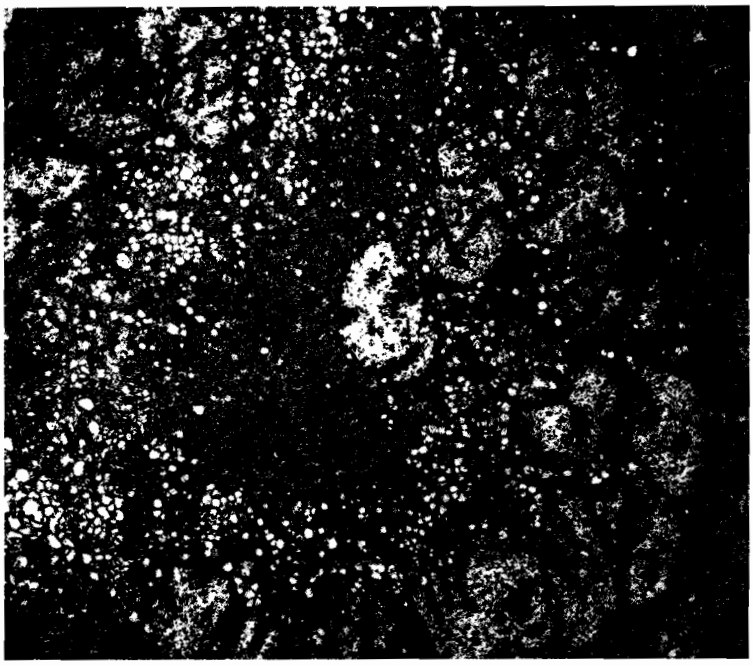

Fig. 15. Tumor giant cell of Touton's cell type; spleen. x 14,720

peripheral nerve sheath tumour (MPNST) mimicking very closely pleomorphic MFH. The authors stated that the nature and nosology of MFH were a matter of controversy. The true nature of MPNST was only disclosed by ultrastructural examination.

The morphological definition of childhood anaplastic pleomorphic rhabdomysarcoma (RMS) does not clearly separate this type from other variants of RMS. Moreover, the identification of MFH as a classifiable tumour has changed the proportions of neoplasms previously diagnosed as RMS (Kodet et al., 1993).

More than 300 soft tissue sarcomas were studied by Schurch et al. (1996). Amongst them were RMS, leiomyosarcomas (LMS), pleomorphic liposarcomas (LS) and MFH. By light microscopy, the pleomorphic RMS, LMS and MFH were indistinguishable, as each was dominated by pleomorphic cells in a haphazard growth pattern.

Lazova et al. (1997) described differential diagnoses of various tumours. They distinguished 102 spindle cell neoplasms including dermatofibroma, dermatofibrosarcoma protuberans, atypical fibroxanthoma, leiomyoma, neurofibroma and MFH by means of monoclonal antibodies.

Meister et al. (1980, 1982) found out that a group of soft tissue sarcomas could not be unambiguously classified histogenetically. It was assumed that these malignancies involved in the first instance MFH, liposarcomas, LMS and synovial sarcomas. Several authors, mainly the team around Mentzel (Mentzel et al., 1994) emphasised that leiomyosarcomas with osteoclast-like giant cells may mimick the "giant cell variant" of MFH. They further argued (Mentzel et al., 1996) that a myxofibrosarcoma varied from a hypocellular, mainly myxoid to high-grade pleomorphic MFH. Ultrastructurally, neoplastic cells had a fibroblastic phenotype. The authors emphasised that, e.g., an unusual myxoid/round cell liposarcoma was juxtaposed to a high-grade non-lipogenic component resembling non-pleomorphic storiform MFH. In another case they called a high-grade myxofibrosarcoma a so-called myxoid MFH (Mentzel and Fletcher, 1997).

The paper of Unnik (1995) provides an overview of the classification of soft tissue sarcomas. The author wrote that an important point must be mentioned regarding the definition of MFH. The fibroblast appears to have enormous divergent differentiations. The multinucleated giant cells are reminiscent of the histiocytic giant cells found in some types of chronic inflammation. In other parts of MFH the presence of lipoblasts allows diagnosis of a pleomorphic liposarcoma.

Origin of MFH

Imai et al. (1989), Katenkamp (1988), Squire et al.

Fig. 16. Many tumor cells are totally undifferentiated. This figure shows one mitosis. Mitoses are often seen in rats' MFH. x 3,600

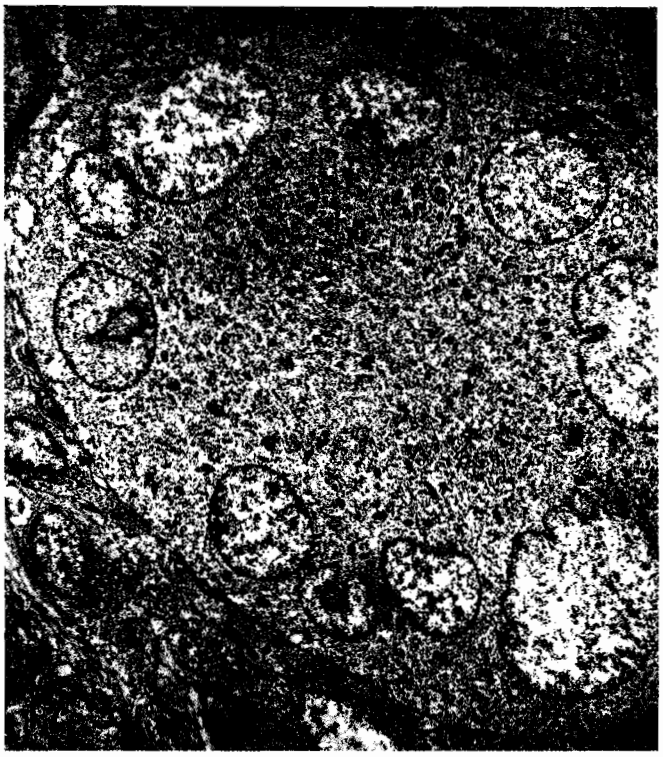

Fig. 17. A second type of tumor giant cell showing nuclei at the cells' periphery like a Langhans' giant cell; skin. x 2,800

(1981) and Wünsch (1984a,b) emphasized, as did Goodlad and Fletscher (1991), that often, apart from histiocytoid elements, fibroblastic or only fibroblastoid cells are primarily found.

Wünsch et al. (1981) and Wünsch (1984a,b) also stated that induced soft tissue tumours (e.g. by chemical carcinogens) proved to be multiform. The observed structures were comparable with fibro-, leiomyo-, lipo-, rhabdomyosarcoma as well as with MFH. The fact must be emphasized that some of these components can be encountered within one and the same tumour. Wünsch (1984a,b) brougt up the question as to whether the varying sarcomas develop from a common mesenchymal stem cell.

Wünsch (1984 a) outlined the following schemes:

I. Alternative pathways of neoplasm histogenesis

Histogenesis
- Neoplastic transformation of defined specific cell lines (e.g. fibroblast, lipoblast, myoblast etc.)
- Neoplastic transformation of common pluripotent stem cell

and

II. Representation of mesenchym differentiation

Pluripotent mesenchymal stem cell
- fibroblast, lipoblast, rhabdomyoblast, leiomyoblast, histiocyte/macrophage, endothelial cell, adventitial cell/ hemangiopericyte, mesothelial cell,osteoblast, chondroblast, Schwann cell

A similar scheme was published by Meister (1995). He asked whether the MFH originated from a «fibrohistiocytic» or primitive fibroblastic sarcoma.

Meister (1996) argued further that during the past years MFH had obviously been used as a diagnostic waste basket to classify neoplasms of all kinds. Thus, a number of neoplasias originally diagnosed as MFH could be reclassified.

According to Leder (1967) all phagocytes and resident phagocytes like Kupffer cells, originate from the monocyte being a blood-borne stem cell. The monocytes invade the periphery and then develop to histiocytes and mature macrophages, different giant cells such as foreign-body giant cells, Langhans' cells (e.g. tuberculosis) or Touton's giant cells, which typically occur in the case of some MFH types: for example the malignant fibrous xanthoma or pleomorphic fibrous sarcoma (Weiss and Enzinger, 1978).

Many authors used distinct neoplasms, for example the myxofibrosarcoma and the myxoid variant of MFH as synonyms. Kirchner and Wünsch (1983) stated that a morphological and conceptual distinction appears to be justified because the group of MFH-types could be defined only descriptively by the histiocytic character, but not at all histogenetically - in the sense of a histiocyte process of malignity. This quotation should serve for the argument that a great confusion exists in relating different soft tissue sarcomas to MFH.

A case of a patient with an intrasplenic MFH was reported by Bonilla et al. (1994). This neoplasm was accompanied by chronic myelogenous leukemia (CML). Because of the parallel occurrence of both the MFH and the CML it seemed to be possible that the origin of these neoplasias was the very same. Thus, the authors' opinions are similar to those of Leder (1967; see above).

Costa (1994) investigated 2 cases of pleomorphic sarcoma with MFH phenotype. He described an unusual finding of "differentiation" rather than "de-differentiation". The transformation to osteosarcoma and leiomyosarcoma demonstrated the potential for phenotypic changes in soft tissue sarcomas and suggested that the MFH phenotype and more differentiated sarcomas such as extraosseous osteosarcoma or leiomyosarcoma are related in a common pathway in differentiation from a primitive mesenchymal stem cell.

Since the early descriptions MFH has been a controversial diagnosis because of its uncertain histogenesis (Cole, 1994). The author emphasized that MFH shows varying proportions of spindled fibroblastic cells and plumper histiocytic cells lacking the features of differentiation, other than collagen production. Cole (1994) concluded that the origin of MFH from primitive mesenchymal cells is established.

Hanau and Miettinen (1995) studied 29 tumours from 26 patients diagnosed as solitary fibrous tumours (SFT). The features resembled MFH, malignant hemangiopericytoma or fibrosarcoma. Some areas showed typical characteristics of benign SFT. It was concluded that SFT is a neoplasm of fibroblasts or primitive mesenchymal cells with characteristics of multidirectional differentiation.

Sohail et al. (1995) presented a case of an MFH arising in the mandible and oral cavity of a 26-year-old woman. They stated that the exact nature of this unusual soft tissue sarcoma was uncertain. Microscopically, it may resemble other neoplasms such as sarcomatoid squamous carcinoma. An accurate diagnosis requires the use of immunohistochemistry and/or electron microscopy.

Hollowood et al. (1995) informed all scientists who dealt with MFH that the initial notion of this malignancy would be a true histiocytic tumour showing facultative fibroblastic differentiation. The MFH had also been disproved due to the lack of definable, reproducible criteria. Several studies had expressed considerable doubts about MFH as an "entity" and had suggested that it represents a common morphological manifestation of a host of poorly differentiated sarcomas.

A contribution to the origin of MFH in dogs was

presented by Kerlin and Hendrick (1996). They described MFH and malignant histiocytosis (MH) and notified that the tumours were neoplasms with different appearances of both MFH and MH - a different putative cell of origin. Many canine soft tissue sarcomas have the gross and histological appearances of both MFH and MH within the same animal. Age, sex, breed, predispositions and distribution of lesions in various organs were remarkably similar between the 2 categories. The hybrid neoplasms containing MFH-like and MH-like regions may be the result of divergent or convergent phenotypic differentiations.

Conclusion

The examples outlined in the present paper should indicate, that the designation MFH does not meet the character of the neoplasias described by various authors. The cells of this specific tumour are mesenchymal stem cells which develop to fibroblastoid cells and fibroblasts.

Merchant et al. (1995) studied inflammatory leiomyosarcomas. Many of these tumours were diagnosed originally as inflammatory MFH. This study-group mentioned that at least one subset of neoplasms showed smooth muscle differentiation. The team required further investigations to demonstrate that other tumour types or lines of differentiation could be represented within the category of so-called MFH.

Papadopoulos et al. (1995) emphasized that great confusion had arisen over the years due to the diversity of nomenclature used to describe a group of cutaneous and soft tissue neoplasias, including MFH.

The results of Pace et al. (1994), who studied cats, did not support the theory that MFH originate from histiocytes. One tumour of a cat was more similar to a fibrosarcoma.

Altmannsberger et al. (1986) stressed the fact that histiocytic markers were more constantly provable in malignant histiocytosis than in MFH. They were also of the opinion that MFH originate, as other soft tissue sarcomas, from a mesenchymal stem cell. Akerman (1997) meets our criteria by asking "malignant fibrous histiocytoma - the commonest soft tissue sarcoma or a non-existent entity?"

Quite a similar statement was made by Takeya and Takahashi (1994) as well as by Takeya et al. (1995). They stated that the term MFH is inappropriate because this tumour contains neither histiocytes nor macrophages. Instead of MFH, this neoplasm should be renamed as a special type of mesenchymal tumour differentiating toward fibroblasts producing monocyte chemoattractants and macrophage differentiation factors. We propose to call this tumor only pleomorphous sarcoma.

From the above mentioned details we cite Takeya et al. (1995) who stressed that the histiocytic-like cells in MFH are not a neoplastic component but rather infiltrated macrophages.

Acknowledgements. We would like to thank Mrs. Monika Bach, clinical data manager (D-88447 Warthausen) and Mr. Florian Schneider, high school pupil (D-88400 Biberach), who wrote the manuscript. We thank Mr. Hilmar Kopp (Department of Documentation and Information services, 1), who made enquiries about references. We also thank Mrs. Dagmar Rädel, Mrs. Waltraud Stöhr and Mr. Manfred Kasper (medical technicians, Laboratory for electron microscopy, department of experimental pathology and toxicology, 2), who provided figures 1 and 2: D-88397, Boehringer Ingelheim Pharma KG, Pharmaceutical Company, Biberach/Riss, Germany.

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Accepted November 26, 1998