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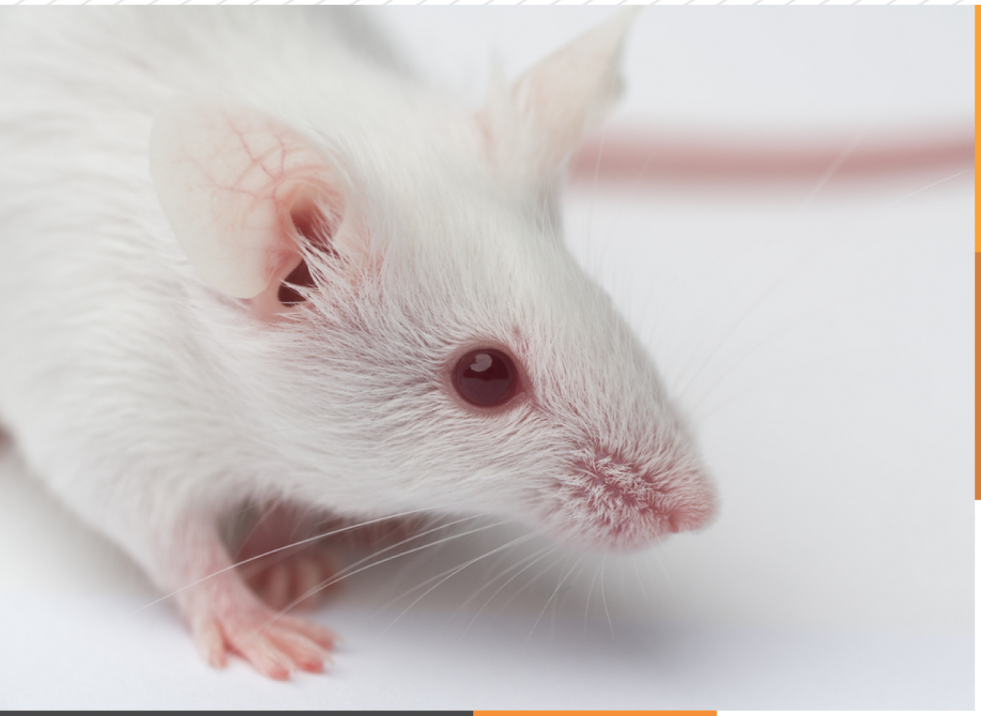

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SHORT COMMUNICATION

Histopathological study of a spontaneous rhabdomyosarcoma in Swiss Albino mouse

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ABSTRACT

A ten weeks old male Swiss Albino mice from a safety assessment study was found with growth at hind leg in the subcutis near inguinal region during necropsy. Tissue was collected, fixed, processed, embedded in paraffin and sliced to produce histology slide. Microscopically, mass was composed of multiple nodules of tumour cells that were incompletely encapsulated with fibrous connective tissue. The neoplastic cells appeared as immature spindles of striated muscle, mononucleated, rounded and polygonal cells with minimal to abundant eosinophilic cytoplasm. Areas of large, multinucleated cells, strap-like cells and a few vacuolated cells were also present. Based on the pathology results, growth was diagnosed as a spontaneous rhabdomyosarcoma in a young mouse.

Keywords: Necropsy, rhabdomyosarcoma, Swiss Albino mouse

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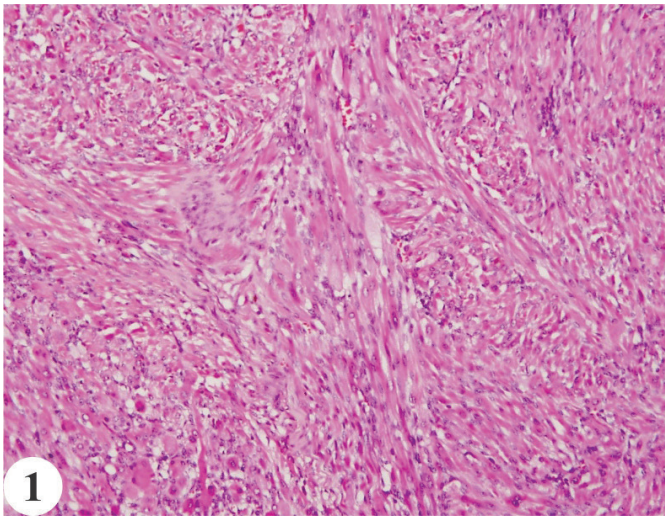
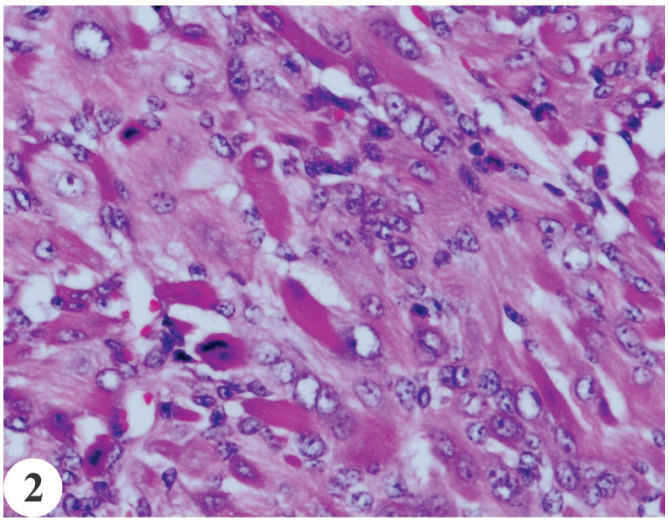
Rhabdomyosarcomas are malignant tumours of striated muscle. Spontaneous rhabdomyosarcomas are rare in humans and in laboratory rats[1]. This is a rare spontaneous tumour in mice and skeletal muscle rhabdomyosarcomas occur more often than those of the heart. However, it can be induced experimentally by exposure to a variety of viruses, metals and chemical carcinogens. Histologically, they are composed of primitive muscle fibres, or myotubes[1]. In the National Toxicology Program, only 14 rhabdomyosarcomas were diagnosed at necropsy in 10,000 mice in one study, most often originating in the quadriceps muscles with a mean age of 4 months[3]. They are uncommon spontaneously developing neoplasms in rodents[4]. Rhabdomyosarcomas have also been reported to develop around inert implants or repeated subcutaneous injection of iron dextran or other poorly absorbed substances[5, 6]. Rhabdomyosarcoma can be a difficult diagnosis to make in carcinogenicity bioassays in rodents, because a variety of other sarcomas may contain large tumour cells with abundant eosinophilic cytoplasm, which superficially resemble rhabdomyoblasts. This difficulty is compounded by the tendency of many sarcomas to infiltrate along skeletal muscle fibres so that degenerate or altered skeletal muscle cells appear as integral parts of the neoplasms. In view of this, a diagnosis of rhabdomyosarcoma is made when there is unequivocal evidence of skeletal muscle differentiation in tumour cells. This can be shown by cross striations at light microscopic level or the presence of Z lines at ultrastructural level. Although various subtypes of rhabdomyosarcoma are reported in humans, these groups have been less well defined in rodents[7].

An approximately 10-week old male Swiss Albino mice (Source of the animals: Vivo Biotech limited, Hyderabad, India) from a safety assessment study conducted at Vimta Labs Limited Hyderabad, India, was presented with a mass at inguinal region during necropsy. A complete necropsy was performed on animal. During gross examination, a subcutaneous mass was observed attached to right hind limb of mice and the growth originating from the thigh region appeared as whitish on cut surface. No other gross lesion were observed during necropsy examination of the animal. Affected tissue was collected in 10% neutral buffered formalin for preservation and processed histologically after fixation. Tissues were embedded in paraffin, and sections were stained with hematoxylin and eosin (H&E) stain. Histology processing and evaluation were performed following standard operating procedures of organization and recommended guidelines. Present study was conducted as per compliance with Organisation for Economic Co-operation and Development (OECD) principles of Good Laboratory Practice (GLP) and animals were provided with a standard diet and water *ad libitum* in a controlled environment (temperature 22°C–25°C, relative humidity 50%–70%), and a twelve-hour light–dark cycle.





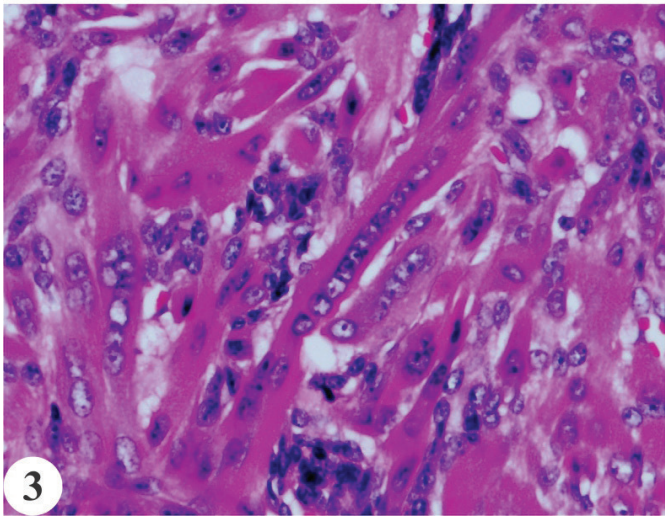


Fig. 1. Tumour cells showing good muscle differentiation and sarcomatous growth characteristics. H&E x20; **Fig. 2.** Pleomorphic tumour cells, round vacuolated cells. H&E x40; **Fig. 3.** Neoplastic multinucleated rhabdomyoblasts with line up nuclei within elongated cytoplasm (strap cells). H&E x40.

Microscopically, the mass was observed as highly pleomorphic and proliferative growth of rhabdomyoblasts with interlacing bundles of well-differentiated muscle fibres (Fig. 1). Cells were mononucleated, rounded and polygonal cells. Sheets of tumour cells were divided by thin, fibrous septa. Rhabdomyoblasts were characterized by cytoplasmic cross striations, a characteristic of striated muscle fibre, visible during light microscopy in some tumour cells. Neoplastic cells had indistinct borders, moderate to abundant eosinophilic fibrillar to vacuolated cytoplasm with myofilaments, and large eccentrically located pleomorphic nuclei (Fig. 2). Multinucleated and karyomegalic cells were numerous and occasionally these cells contained nuclei that line up within elongated cytoplasm and referred as strap cells (Fig. 3). High mitotic activity with abnormal mitotic figures were evident. Anisokaryosis and anisocytosis were marked. Some tumour cells contained large, peripheral vacuolations around nucleus that might be a result of intracellular glycogen accumulation and had been removed while processing of tissues histologically. Areas of necrosis and hemorrhage were frequently observed. Small number of neutrophils were scattered throughout multifocally. Adjacent pre-existing muscle fibres were separated, shrunken with loss of cross striations (atrophy). No encapsulation of the growth was appreciated and the borders of the tumour were indistinct, with tumour cells mixed with normal skeletal muscle fibres. However, distant metastasis of tumour cells was not observed. Based on above histopathological characteristics, the diagnosis of rhabdomyosarcoma was made.

Rhabdomyosarcomas are skeletal muscle neoplasms found in humans and domestic mammals[8]. It is a mesenchymal malignancy associated with the skeletal muscle lineage and is also the most common paediatric soft tissue cancer[9]. They are uncommon and spontaneous neoplasms in rodents. In the *National Toxicology Program* less than 0.2% of Fischer 344 rats developed this neoplasm[10]. Spontaneous rhabdomyosarcomas in young SD rats had been reported earlier by various authors[1, 11-14] (four and nine weeks old). Rhabdomyosarcomas development has been detected upon exposure to carcinogen agents or ionizing radiations, as well as in several different genetically engineered animal models[15].

Rhabdomyosarcomas are occasionally seen in untreated aged mice and hamsters[16,17]. However, in the present case, the neoplasia was observed in a young mice and therefore this was considered spontaneous and rare case.

Histopathological findings of presence of eosinophilic cytoplasm and cross striations in

bundles of well differentiated striated muscle fibres in rhabdomyosarcoma observed in this case during routine microscopy were in agreement with other authors[4,11].

Findings of multinucleated giant cells along with round cells differentiation and cells containing multiple nuclei line up within elongated cytoplasm (strap cells) evident in this case were also reported by many authors[11, 18,19] and supported pleomorphic characteristics of tumour cells. A few cells with peripheral vacuolation around nucleus suggestive of intracellular glycogen accumulation observed in present study was also reported by others[14].

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