Myelolipomas in Adult Goeldi's Monkeys (*Callimico goeldii*)

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ABSTRACT. Hepatic myelolipomas were found in four Goeldi's monkeys (*Callimico goeldii*) from a small colony originated from 3 animals imported from South America and sustained in Monkey Center of Japan, and the histological features were compared with the hepatic extramedullary foci of hemopoiesis in the fetus or newborn monkeys of this species. The histological features were analogous to those of myelolipomas of the liver, spleen or adrenals in other animals and man. The cause of the relatively high incidence of this rare lesion in these monkeys remains nuclear, but, the close genetic background and identical environmental conditions, including diet are mentioned as possible pathogenic factors.—**KEY WORDS:** *Callimico goeldii*, liver, myelolipoma.

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Goeldi's monkey (*Callimico goeldii*) is a tamarin-like species of small new world monkey. The record for the heaviest male animal for the species was 860 g [5], and the average weight is 472 g [9, 11]. They live in the upper Amazonian rain forest and Andean foothills in Bolivia, Brazil, Peru and Colombia [5]. Little information about their behavior, ecology, physiology and anatomy is available because of the very low population and visibility of these monkeys.

In the routine histopathological examinations of dead monkeys from the Monkey Center of Japan at Inuyama, Aichi Prefecture, myelolipomas were frequently detected in the liver of adult callimicos. Myelolipomas have been reported in the spleen and/or liver of domestic cats, cheetahs (*Acinonyx jubatus*), Siberian tiger (*Felis tigris longipilllis*), dogs, in the juxtarenal abdominal cavity of a cotton-top marmoset (*Saguinus oedipus*) and in the adrenal glands of man [3, 4, 6, 8, 10, 13–16]. A myeloliposarcoma has also been reported in a wild monkey, *Perodicticus potto* [2], but this condition seems to be extremely rare in animals compared to man.

The present report describes the microscopic features of the hepatic myelolipomas

of high incidence in the adult callimicos and discusses the morphogenesis of these lesions in relation to the extramedullary hemopoiesis in the liver of the newborns of this monkey.

MATERIALS AND METHODS

Three adult callimicos, two males and one female, imported from a South American country, were kept at the Monkey Center of Japan from June 1975. Animals examined in this study (Table 1) were obtained from a colony started from these three monkeys. Monkey 1, one of these original adult males, died on 14 August, 1983. Monkey 2, an original adult female, died on 23 August, 1983, gestating the 13th baby after the 12th delivery and including a 7th successful weaning of one offspring each time. Monkeys 3 and 4 were born from Monkey 2 on 30 March and 6 October, 1978 respectively. They died suddenly on 17 February 1983, following the oral administration of a helminthic drug (Scolaban 100: bunamidin hydrochloride 25 mg/head, The Wellcome Foundation Ltd., London). Monkey 4 produced offsprings three times before death, but all died within a week after birth. Monkey 5 was a fetus removed

Table 1. Liver weight and macroscopic hepatic lesions of myelolipomas in Goeldi's monkeys (*Callimico goeldii*)

Monkey no.	Age (month)	Sex	Body weight (g)	Absolute liver weight (g)	Relative liver weight ^{a)}	Macroscopic hepatic lesion
1	91	Male	450	19.5	43.3	Several nodules up to 5 mm in diameter
2	97	Female	430	19.7	45.8	Multiple foci up to 1 cm in diameter
3	59	Male	450	13.75	30.6	A small hemorrhagic spot
4	52	Male	620	25.45	41.0	ND ^{b)} (fatty change)
5	Fetus	Male	NW ^{c)}	NW		ND
6	<1	Female	NW	NW		ND
7	<1	Male	NW	NW		ND
8	<1	Male	NW	NW		ND
9	<1	Female	NW	NW		ND
10	<1	Male	NW	NW		ND

a) g/kg body weight.

b) Not detected.

c) Not weighed.

from the uterus of Monkey 2 at necropsy. Monkeys 6–10 were infant animals, born from Monkeys 2 and 4 between June 1981 and October 1982; they died within a week.

All animals were necropsied immediately after the detection of their death. The liver, kidneys, adrenals, spleen, pancreas and heart of the adult animals were removed and fixed in 10% formalin solution, along with other representative organs and tissues. Brain, spinal cord and bone marrow were not examined because of the preservation of the skeletons. The liver, spleen, thymus, kidneys, adrenals, lungs, heart and alimentary tract were removed from infant animals and fixed also in 10% formalin solution. All tissue blocks were trimmed, washed in tap water, dehydrated in an automated processor and embedded in paraffin. Sections were cut at 5 μ m and stained with hematoxylin and eosin (HE).

RESULTS

Macroscopic lesions corresponding to myelolipoma were seen in the 3 adult monkeys (Monkeys 1–3). In Monkey 1, several gray-

ish nodules, 2–5 mm in diameter, were scattered throughout the liver. The nodules were soft, had a fat-like appearance on the cut surface, and were sharply-circumscribed from normal liver tissue. Monkey 2 had many dark red nodules, measuring up to about 1 cm in diameter, which occupied a considerable part of the liver. The color of the nodule was almost the same as that of the red bone marrow. The appearance and consistence of the nodules were similar to those of Monkey 1. Only a single small hemorrhagic spot was detected in the liver of Monkey 3. No focal lesions were seen in Monkey 4, although the liver was mildly enlarged and tan colored. Liver weights seemed not to be influenced by the number or quantity of the nodules (Table 1). No macroscopic abnormalities except congestion were detected in the liver of the newborn monkeys.

Microscopically, the hepatic nodules in two monkeys (Monkeys 1 and 2) consisted of normal bone marrow tissue replacing the liver parenchyma (Fig. 1). The smallest nodule was confined to 2 or 3 hepatic lobules, but large lesions extended into a whole hepatic

Fig. 1. Two small nodules of hepatic myelolipoma in which adipose cells predominate. The smaller nodule (right) is within a few lobules (arrow). HE $\times 56$.

Fig. 2. Large nodule of myelolipoma in which hemopoietic cells predominate extending through a whole hepatic lobe. HE $\times 56$.

Fig. 3. Hepatocytes surrounding the nodule contain fat droplets of varying size. Some hepatocytes are degenerated and shrunken, but neither compression nor distension of surrounding hepatic tissue is evident. HE $\times 564$.

Fig. 4. Fibrous septum surrounding part of a myelolipoma. HE $\times 564$.

Fig. 5. High power view of myelolipoma showing hemopoietic cells of all series at various stages of differentiation. Megakaryocytes are also seen. HE $\times 564$.

Fig. 6. Focus of extramedullary hemopoiesis in the liver of a newborn callimico. Accumulation of granulopoietic and erythropoietic cells. HE $\times 460$.

Fig. 7. Extramedullary hemopoiesis in the liver of a newborn callimico showing two megakaryocytes in hepatic sinusoid. HE $\times 460$.

lobe (Fig. 2). Small lesions with the same histological features were also detected in the remaining two adult monkeys. The ratio of adipose tissue to hemopoietic cells varied among the cases but was almost the same among the nodules in any one case. A small number of hemopoietic cells were aggregated in the narrow spaces among the adipose cells

of the nodules in the case where adipose tissue was predominant. In the cases where hemopoietic cells were predominant the nodules contained only a few adipose cells in the vicinity of the normal liver parenchyma. Although most hepatocytes of Monkeys 2 and 4 showed moderate fatty metamorphosis, the hepatocytes surrounding the nodules contain-

ed fatty droplets of varying size in their cytoplasm (Fig. 3). Some hepatocytes were somewhat shrunken and were enclosed in large droplets of adipose tissue, but there was no evidence of compression or distension of the surrounding hepatic tissue in any case. A fibrous septum surrounded part of some nodules (Fig. 4), but many nodules were not encapsulated (Fig. 3). The hemopoietic cells consisted of the red blood cell series, with granulocytic and agranulocytic series cells at all stages of differentiation (Fig. 5). Megakaryocytes were also seen. The relative proportions of these cell series were almost identical among nodules and monkeys.

In a fetus and 4 newborn monkeys, megakaryocytes and other hemopoietic cells occasionally accumulated in the liver sinusoid (Figs 6 and 7), but neither bone marrow-like masses nor adipose cells were detected.

The red splenic pulp of newborn monkeys also contained some hemopoietic cells, but extramedullary hemopoiesis was not seen in these areas of the adult monkey.

The cause of death on the basis of histological or clinical findings was considered to be chronic interstitial nephritis in Monkey 1, difficult delivery in Monkey 2 and acute dyspnea by drug poisoning in Monkeys 3 and 4. No abnormal changes which would explain death were detected in the newborn monkeys.

DISCUSSION

Myelolipomas have been reported in some species of animals and in man. In the animal cases, the incidence of the neoplasm is somewhat high among species of Felidae; i.e., 8 cheetahs [3, 8, 15], one Siberian tiger [15] and 3 domestic cats [4, 6, 10]. Some recent reports have described the occurrence of myelolipoma in two dogs [16] and a cottontop marmoset [14], but the neoplasms seems to be extremely rare in these species. Many myelolipomas are thought to be non-neoplastic

[1], and some theories on their pathogenesis have been discussed by previous authors; i.e., enlarged mesenchymal rests [13], transformation of mesenchymal cells by hormone imbalance [1, 12], chronic hepatic hypoxia [4] or developmental aberration [10]. A few authors have also suggested chronic anemia as a cause of myelolipomas [2, 13], because the common sites of myelolipomas (spleen, liver and adrenals) are known to be frequent sites of extramedullary hemopoiesis. However, extramedullary hemopoiesis is also seen in the adrenals of domestic animals without any associated hematological abnormalities [7], and no reliable evidence of chronic anemia has been found in animal and human cases of myelolipoma [1, 4, 10, 14].

In the monkey cases under study, no histological changes indicating chronic anemia were seen in the adult animals, although bone marrow tissue could not be examined. There were also no common basic diseases which might depress the hemopoietic function of bone marrow or cause hormone imbalance in these cases. It is unlikely that myelolipomatous tissue is a normal feature of extramedullary hemopoiesis in this species of monkey, because the hemopoietic foci seen in newborn monkeys are similar to those in other wild or domestic animals. The true cause of the relatively high incidence of myelolipomas in our callimicos remains unclear. The very close genetic background in a colony and the identical environmental conditions including diet, of these monkeys might be one factor. However, it is difficult to determine which factors play a role in the pathogenesis of this lesion because few anatomical and pathological data are available for callimicos.

Fatty change of the hepatocytes surrounding the lesion was a constant finding in these monkeys, but this change has never been described in hepatic myelolipomas in the literature [4, 6, 8, 15]. Although it is not clear whether this change is also constant in the hepatic myelolipomas of other animals,

the accumulation of fatty droplets might serve as a suitable condition for the metaplasia or the transformation of the liver mesenchymal cells in the present cases.

REFERENCES

1. Ashley, D. J. B. 1978. Tumor of the Adrenal Cortex. pp. 298–310. In: Evans' Histological Appearances of Tumours 3rd ed. Churchill Livingstone, Edinburgh.
2. Bingham, G., Sembrat, R., and Migaki, G. 1976. Myeloliposarcoma in a potto (*Perodicticus potto*): A case report. *Lab. Anim. Sci.* 26: 473–477.
3. Cardy, R. H., and Bostrom, R. E. 1978. Multiple splenic myelolipomas in a cheetah (*Acinonyx jubatus*). *Vet. Pathol.* 15: 556–558.
4. Gourley, I. M., Popp, J. A., and Park, R. D. 1971. Myelolipomas of the liver in a domestic cat. *J. Am. Vet. Med. Assoc.* 158: 2053–2057.
5. Hershkovitz, P. 1977. *Callimico goeldii* 2. Biology of *Callimico*. vol. 1, pp. 896–911. In: Living New World Monkey (*platyrrhini*), The University of Chicago Press, Chicago.
6. Ikede, B. O., and Downey, R. S. 1972. Multiple hepatic myelolipomas in a cat. *Can. Vet. J.* 13: 160–163.
7. Jubb, K. V. F., and Kennedy, P. C. 1970. The Endocrine Glands. vol. 1, pp. 407–442. In: Pathology of Domestic Animals. 2nd ed. Academic Press, London.
8. Lombard, L. S., Fortna, H. M., Garner, F. M., and Brynjolfsson, G. 1968. Myelolipomas of the liver in captive wild felidae. *Pathol. Vet.* 5: 127–134.
9. Lorenz, R., and Heinemann, H. 1967. Beitrag Zur Morphologie und körperlichen Jugendentwicklung des Springtamarin *Callimico goeldii* (Thomas, 1904). *Folia Primatol.* 6: 1–27.
10. Sander, C. H., and Langham, R. F. 1972. Myelolipomas of the spleen in a cat. *J. Am. Vet. med. Assoc.* 160: 1101–1103.
11. Seibold, H. R., Lorenz, R., and Wolf, R. H. 1972. Giant cell aortitis in a South American monkey (*Callimico goeldii*). *Vet. Pathol.* 9: 230–237.
12. Selye, H., and Stone, H. 1950. Hormonally induced transformation of adrenal into myeloid tissue. *Amer. J. Pathol.* 26: 211–233.
13. Sommers, S. C. 1977. Adrenal Glands. vol. 2, pp. 1658–1679. In: Pathology 7th ed. (Anderson, W. A. D., and Kissane, J. M. eds.) C. V. Mosby, Saint Louis.
14. Stein, F. J., Smallwood, J. E., Tangner, C. H., Jr., Hightower, D., and Joiner, G. N. 1982. A juxtarenal myelolipoma in a cottontop marmoset (*Sequinus oedipus*): A case report. *Am. J. Primat.* 2: 215–221.
15. Wadsworth, P. F., and Jones, D. M. 1980. Myelolipoma in the liver of a cheetah (*Acinonyx jubatus*). *J. Zoo Anim. Med.* 11: 75–76.
16. Zimmer, M. A. and Stair, E. L. 1983. Splenic myelolipomas in two dogs. *Vet. Pathol.* 20: 637–638.

要 約

ゲルジーモンキーの肝臓にみられたミエロリポーマ：奈良間功・永谷真理子・土谷 稔・稲垣晴久¹⁾((株)生物科学技術研究所, ¹⁾(財)日本モンキーセンター)——日本モンキーセンターにおいて飼育・維持されているゲルジーモンキー(アマゾン流域森林に棲息する希少な小型猿)の小コロニー由来成熟動物4例の肝臓にミエロリポーマが認められ、病理組織学的には正常な骨髄組織から構成され異型性を伴わなかった。同種猿の新生仔および胎仔諸臓器を検索して正常な髄外造血巣との形態学的比較を試みたところ、ミエロリポーマの組織像は胎仔あるいは新生仔の肝臓における髄外造血巣とは明らかに異なり、本腫瘍を持つ成熟動物には慢性貧血の証拠は得られなかった。この腫瘍が比較的多発した原因として、動物の遺伝的背景の近似性、飼料・飼育環境等の環境因子の同一性が考えられた。