Congenital generalized infantile myofibromatosis and neonatal hemochromatosis
An autopsy case report

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SUMMARY: Aksoy F, Göksel S, İlvan Ş, Dervişoğlu S, Ramazanoğlu R. Congenital generalized infantile myofibromatosis and neonatal hemochromatosis: an autopsy case report. Türk J Pediatr 2000; 42: 334-337.

An autopsy case of congenital infantile myofibromatosis and neonatal hemochromatosis is reported. A thirty-six-hour-old baby girl had multiple subcutaneous nodules in addition to multiple visceral involvement of heart, lungs, pharynx, larynx, stomach, small bowel, large bowel, pancreas, kidneys, spleen, thyroid, adrenal glands, lymph nodes, peripheral nerves, meninges and soft tissues. In these tumoral nodules, three types of histological patterns were observed: 1-hemangiopericytoma-like, 2-mixed, and 3-pure spindle cell. Tumor cells were immunohistochemically positive for actin, and negative for desmin, muscle-specific antigen, and estrogen, related protein. The histological and immunohistochemical findings of the case suggested that a close relationship may exist between infantile myofibromatosis and infantile hemangiopericytoma. In addition to infantile myofibromatosis, neonatal hemochromatosis characterized by iron deposition in parenchymatous organs such as liver, pancreas, lungs, thyroid, and adrenal glands was another important characteristic of the case.

Key words: infantile myofibromatosis, neonatal hemochromatosis, congenital fibromatosis infantile hemangiopericytoma.

Congenital generalized infantile fibromatosis is a rare entity characterized by the formation of multiple tumoral nodules or masses localized in the viscera, musculoskeletal system and subcutaneous tissues[1-4]. Infantile myofibromatosis may also arise postnatally or in adolescence[2,3]. After its first recognition by William and Schrum[5] ind 1951 as a congenital fibrosarcoma, Stout[5] indicated that this tumor is benign and denoted it as congenital generalized fibromatosis. Chung and Enzinger[3] renamed it as infantile myofibromatosis (IMF)[3]. It has been reported that IMF can be of multicentric, solitary or generalized types, with the solitary type being the most common[1,36-11].

Neonatal hemochromatosis (NHC) is also a rare and specific entity in the spectrum of childhood liver diseases[12,13]. Three cases of IMF with iron deposition in the liver have been reported in the literature[6,9,14]. To our knowledge, however, there is no reported case of IMF together with NHC. We present an autopsy case of generalized congenital IMF with NHC in a 36-hour-old baby girl.

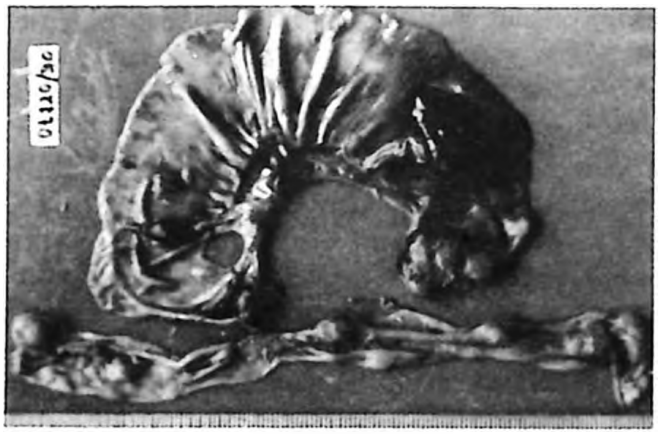
Case Report

The infant, who weighed 2,250 g at birth, was the second child of a 19-year-old multigravida, and was born after 36 weeks of gestation. The first pregnancy of the mother had ended during the first trimester by spontaneous abortion. The infant died in 36 hours as a result of cardiopulmonary insufficiency. There was no kinship between mother and father, no history of disease and no use of drugs before or during pregnancy.

Autopsy Findings: Multiple subcutaneous, polypoid nodules ranging between 0.5 to 1.5 cm in diameter were seen all around the body (face, scalp, trunk and extremities) upon gross examination. Similar types of nodular lesions were seen in many visceral organs such as heart, lungs, gastrointestinal tract, gall bladder,

pancreas, spleen, tongue, pharynx, larynx, adrenal glands, kidneys and meninges (Figs. 1, 2). The same nodules were located in diaphragma and the soft tissues of the body cavities as well. Extrahepatic bile ducts were not obstructed. The internal organs appeared normal both in shape and position, except for these nodules.

(1)



(2)

Figs. 1, 2: Multiple visceral nodules, some of which are hemorrhagic, are seen in heart, kidneys, adrenal glands, and small and large intestines.

Three types of histological patterns of the nodules were observed: 1-centrally located endothelial-lined vascular clefts surrounded by spindle cells (Fig. 3), as revealed by Gomori's reticulum silver staining (hemangiopericytoma-like pattern), 2-centrally located hemangiopericytoma-like pattern surrounded by spindle cells resembling fibroblasts or smooth muscle cells (mixed pattern), and 3-entire nodule composed of fusiform cells arranged in fascicular pattern (pure spindle-cell pattern). All three tumor patterns showed secondary changes such as hyalinization, hemorrhage, necrosis, and calcification.

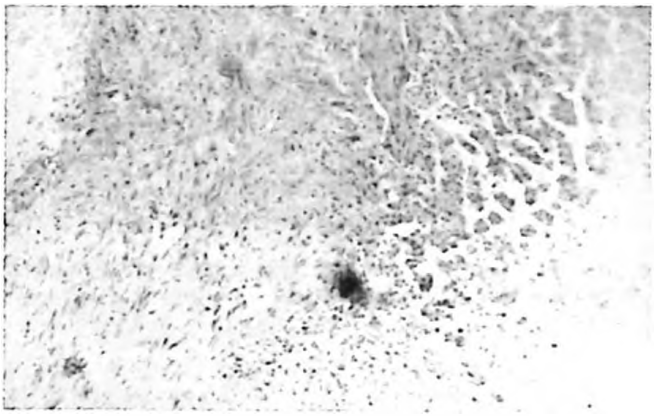


Fig. 3. These well circumscribed nodules exhibit fasicles of spindle-shaped cells in the periphery and prominent vascular features in the center, (hemangiopericytoma-like) (HxE 200).

Immunohistochemically, fusiform cells reacted positively with actin (BioGenex), and negatively with desmin, muscle-specific antigen and estrogen-related protein (BioGenex).

Sections from the liver showed atrophy of hepatocytes and a pseudoacinary arrangement with giant-cell formation. Fibrosis of the sinusoidal walls and portal areas were additional features revealed by silver stain (Gomori's reticulum). Moderate extramedullary hemopoiesis was observed (Fig. 4). Almost all hepatocytes contained accumulation of yellowish-brown pigments in their cytoplasms. Bile thrombi were detected in the intrahepatic bile canaliculi. The heavy accumulation of iron was demonstrated by the application of Lillie's iron staining (Fig. 5). While it was limited to the hepatocytes, no such accumulation was detected in Kupffer cells. Fouchet's bile staining was positive only in intracanalicular bile thrombi. In addition to the liver, the pancreas also showed heavy iron accumulation. Other parenchymatous organs such as lungs, kidneys, and the thyroid gland, contained moderate amounts of iron. Deposition of iron in the tumoral nodules located adjacent to the necrotic and vascular-rich areas was a striking feature. Pathological diagnosis was congenital generalized infantile myofibromatosis with neonatal hemochromatosis.

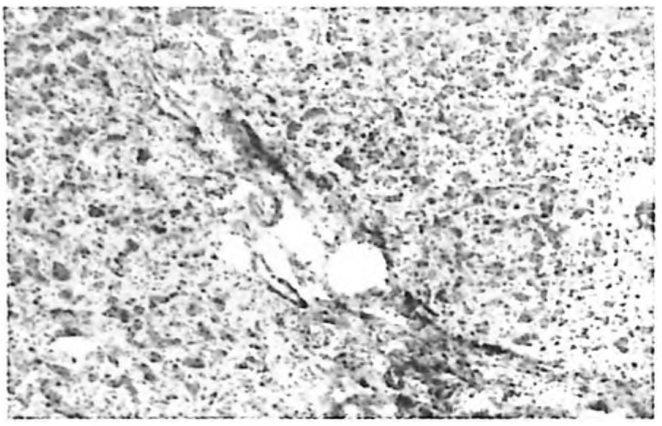


Fig. 4. Atrophy of hepatocytes and pseudoacinary arrangement with giant cell formation is shown (HxE 100).

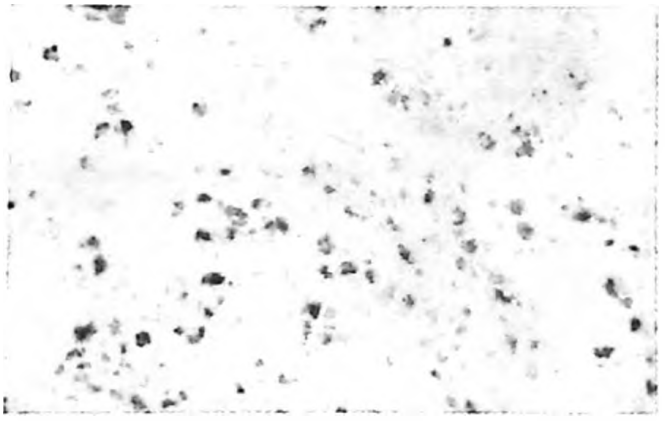


Fig. 5. Lillies's iron staining demonstrating iron accumulation in the liver (Lillies's iron x 200).

Discussion

Infantile myofibromatosis is a rare childhood soft-tissue tumor. Coffin and Dehner[2] reported a large series of infantile myofibromatosis with an incidence of 12 percent in childhood soft tissue tumors and of 22 percent in childhood fibromatosis[2,5,16]. Ünüvar et al.[17] and Kotiloğlu et al.[18] reported two cases of infantile myofibromatosis, one in a 14-day-old neonate, the other in a three-month-old infant, respectively. Our case was a baby born at the 36th week of gestation who lived for 36 hours.

There are some debatable points on the histogenesis of the tumors. Their marked resemblance to smooth muscle and staining reaction specific to smooth muscle were noticed by some authors[6,21]. However, because of the desmin negativity with actin positivity, the possibility of myofibroblastic origin was considered[3,7,9,15,19]. In our case, the fusiform tumor cells were positive for actin, but negative for desmin and muscle-specific antigen. Kotiloğlu et al.[18], in their case of the three-month-old infant with multicentric infantile myofibromatosis, showed the same type of staining patterns in the tumor cell. These findings are not specific for either myofibroblastic or for smooth muscle origin. Chung and Enzinger[3] indicated that infantile hemangiopericytoma should be included in the differential diagnosis of these tumors, and emphasized that the presence of myofibroblasts is a differentiating feature between these two entities[3]. On the other hand, Coffin and Dehner[16] suggested that IMF and infantile hemangiopericytoma are identical tumors[2,20,22]. Ultrastructurally, the tumor cells in IMF have fibroblastic features such as dilated cisternae of rough endoplasmic reticulum, prominent Golgi apparatus, mitochondria and peripheral micropinocytotic vesicles. Furthermore, these tumor cells have the smooth muscle features as well, including irregularly margined nuclear membranes with deep infoldings, abundant longitudinal bundles of parallel cytoplasmic microfilaments, intracytoplasmic dense bodies along microfilaments and basement membrane-like material[7-9].

The above features have also been observed in the ultrastructural examinations of the tumor cells in hemangiopericytoma, and some similarities between pericytes and fibroblasts/ smooth muscle cells have been noted in the literature[14,21,22,24,25]. As a parallel finding, the tumor cells of adult hemangiopericytoma react positively with actin and vimentin, and negatively with desmin and myoglobulin, as in IMF[22-26]. In view of the above, it can either be concluded that pericytic and myofibroblastic cells cannot be differentiated by ultrastructural and immunohistochemical methods, or that these are identical tumor cells. In our case, early lesions determined by light microscopy were in a hemangiopericytoma-like pattern. With this observation and with the observations of the other authors, we suggest that IMF is the same tumor as infantile hemangiopericytoma.

Neonatal hemochromatosis is a rare autopsy finding of the neonatal period with an unknown etiology. The pathologic chances in the liver are the same as with adult type hemochromatosis, containing iron depositions in the hepatocytes

with fibrosis and bile stasis. Iron deposition in the other parenchymatous organs of the body is a constant feature[10,11].

Three cases of IMF associated with iron deposition in the liver are reported in the literature (one is dense, the other is moderate, and the third is slightly higher than normal range)[6,10]. These findings are considered coincidental and not related to IMF[1,15]. Excess iron intake by the mother is a suspected etiologic agent in the development of neonatal hemochromatosis. However, various experimental studies showed that the placenta controls iron transportation and that excess iron in the mother does not affect the fetus in utero. Therefore, maternal iron overload alone is not responsible for the abnormalities seen in NHC[12]. In our case, due to secondary changes like hemorrhage and necrosis of the tumors, excessive free iron and its compounds from the degenerated cells caused hemochromatosis.

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