Journal of Perinatology (2008) 28, 160–162

www.nature.com/jp

PERINATAL/NEONATAL CASE PRESENTATION

Congenital high-grade sarcoma presenting as skin nodules and respiratory distress in a neonate

JW Powers[1], M Teitell[2] and V Milisavljevic[1]

[1]Division of Neonatology and Developmental Biology, Department of Pediatrics, Institute for Stem Cell Biology and Medicine, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA, USA and [2]Department of Pathology and Laboratory Medicine, Institute for Stem Cell Biology and Medicine, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA, USA

We report, to our knowledge, the first case of a congenital, widespread, aggressive high-grade sarcoma, presented as multiple skin nodules and respiratory distress in a neonate that had a t(9;22)(q22;q11–12) cytogenetic abnormality suggestive of a more indolent extraskeletal myxoid chondrosarcoma (EMC). EMC is generally thought of as a slow-growing tumor that presents between the fourth and sixth decades of life. Our patient was a 45,XY, t(13;14) newborn who presented at birth with subcutaneous nodules involving the face, scalp, back and extremities, as well as multiple intrathoracic, intraabdominal and intracranial masses. Diagnosis was made using electron microscopy and immunohistochemical and cytogenetic studies. Despite attempts to control rapid growth of lesions using high–dose steroids and *cis*-retinoic acid, patient's clinical status continued to deteriorate and life support was withdrawn at the 26 day of life.
Journal of Perinatology (2008) **28,** 160–162; doi:10.1038/sj.jp.7211890

Keywords: sarcoma; respiratory distress; skin nodules; neonate

Introduction

Respiratory distress is one of the most common problems newborns present. It can be caused by respiratory distress syndrome, transient tachypnea of the newborn, neonatal pneumonia, meconium aspiration, persistent pulmonary hypertension, pneumothorax or congenital heart disease. However, other less frequent causes of respiratory distress have to be considered in the differential diagnosis. This is the first report of a neonate with multiple skin nodules and respiratory distress presenting with a sarcoma containing a t(9;22) that normally characterizes a typically indolent extraskeletal myxoid chondrosarcoma (EMC) in older patients. Neonatal tumors are extremely rare, and soft tissue sarcomas represent less than 6% of all pediatric sarcomas.[1] EMC is generally considered a slow-growing disease affecting older age groups. However, there have been a handful of case reports of children presenting with this tumor. Aggressive local control is the current standard of practice. In cases where surgical excision is not an option, very few effective alternatives exist.

Correspondence: Dr V Milisavljevic, Division of Neonatology and Developmental Biology, Department of Pediatrics, David Geffen School of Medicine at University of California Los Angeles, 10833 Le Conte Avenue, Room B2-375 MDCC, Los Angeles, CA 90095, USA.
E-mail: vmilisavljevic@mednet.ucla.edu
Received 9 July 2007; revised 15 October 2007; accepted 23 October 2007

Case report

The patient was a full-term, appropriate for gestational age male born to a 38-year-old gravida 2, para 1 to 2 Armenian mother via a Cesarean section secondary to a non-reassuring fetal heart rate tracing. Prenatal labs were unremarkable. Amniocentesis showed a 45,XY fetal karyotype, with a balanced translocation between chromosomes 13 and 14. The mother carries the same translocation. Apgar scores were 8 and 9 at 1 and 5 min, respectively.

After birth, subcutaneous nodules on the left cheek and the back were noted. The baby was taken to the NICU due to respiratory distress. He was intubated and placed on high-frequency ventilation within 4 h after birth. The initial chest X-ray showed opacification of the right upper lobe of the chest, which was initially thought to represent atelectasis (Figure 1). The baby failed several attempts at extubation with what was thought to be stridor, for which he was treated with steroids. A CT scan was performed, which showed a mass in the right chest displacing the mediastinum to the left and compressing the trachea, as well as bilateral adrenal masses and several paraspinal masses. An echocardiogram reportedly showed normal cardiac anatomy. The infant was transferred to our institution at day of life (DOL) 8 for further evaluation and management.

On DOL 11 the infant underwent an excision biopsy of the left paraspinal mass. Fluorescent *in situ* hybridization studies of the tumor cells showed X and Y chromosomes, eliminating maternal origin of the tumor. On DOL 15, the infant had episodes of focal seizures. A CT scan of the head showed marked communicating hydrocephalus and enhancing masses in the left cavernous sinus, left superolateral orbit, left subauricular area, as well as facial lesions (Figure 2). The infant was started on phenobarbital.

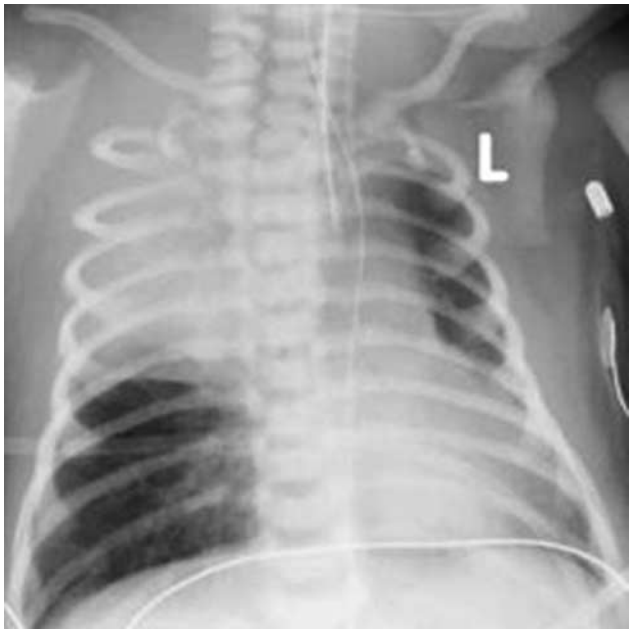

Figure 1 Chest X-ray showing right upper lobe lesion. Nasogastric tube is shifted to the left, suggesting a space-occupying lesion.

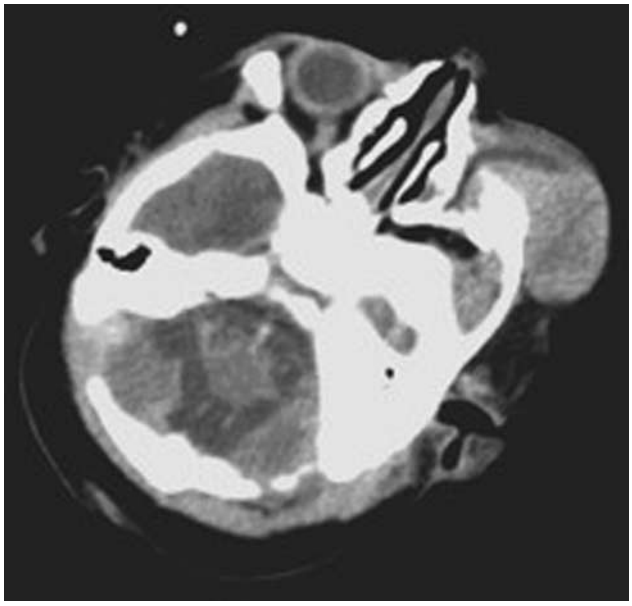

Figure 2 Head CT showing facial lesions.

External ventricular shunt was placed on DOL 16. Repeat CT scans of the chest and abdomen showed large upper lobe mass, bilateral lower lobe lung masses, multiple subcutaneous nodules and masses in the chest, abdomen and pelvis, right psoas mass and exophytic masses of the right kidney. The right upper lobe mass resulted in the left shift of the cardiomediastinal content and compression of the trachea. On DOL 17, due to the deterioration of the patient's clinical status and rapid tumor growth, high-dose dexamethasone was started, although a definitive pathological diagnosis for the tumor had not yet been obtained. On DOL 20, seizure activity recurred. Repeat CT scan of the head showed massive intraventricular, subarachnoid, prepontine cistern and suprasellar cistern hemorrhage.

Pathological evaluation proceeded to electron microscopy, which showed sheets of closely opposed neoplastic cells with large oval to polygonal nuclei and prominent nucleoli. The aggressive histological appearance (Figure 3), lack of extracellular matrix and electron microscopic findings, combined with a relatively nonspecific immunohistochemical staining profile, suggested a rhabdoid tumor. Cytogenetic studies indicated a translocation, t(9;22)(q22;q11−12), in the tumor cells, which is characteristic of EMC. Isotretinoin was started in an attempt to promote differentiation of the cells, but, unfortunately, no clinical improvement was observed. The patient developed blood pressure instability requiring vasopressor support secondary to compression of the inferior vena cava. His clinical status was deteriorating due to the rapid and aggressive growth of tumors, despite treatment attempts. Resection of the lesions was not an option due to the extensive and generalized nature of the disease and locations of vascularized tumor metastases. Life support was withdrawn on DOL 26 in agreement with the parents' wishes.

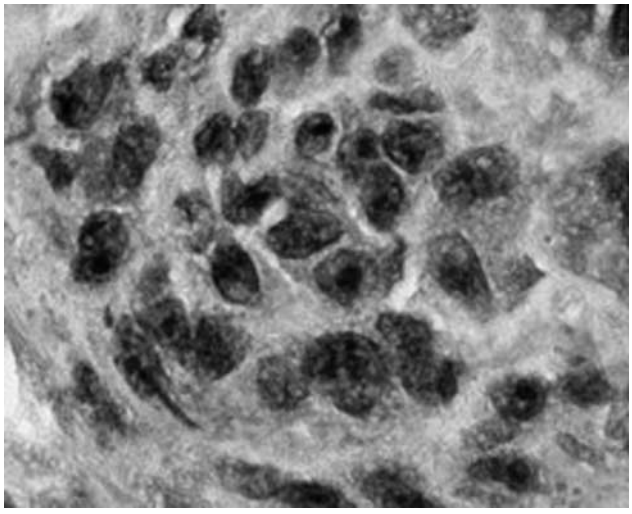

Figure 3 Hematoxylin- and eosin-stained tissue section showing high-grade sarcomatous appearance (magnification 400 ×).

Discussion

The most common causes of cutaneous and subcutaneous nodules in neonates are dermoid cysts, subcutaneous fat necrosis, nevi and benign tumors including hemangiomas, lipomas, teratomas, juvenile xantogranulomas, infantile myofibromatosis and congenital self-healing reticulohistiocitosis.[2–4] Depending on the

localization and growth rate, tumors can have severe clinical presentation, such as airway and vascular compromise, even when pathologically benign. Malignant tumors are rare in newborn period and they can be an initial presentation of a serious systemic disease (neuroblastoma, leukemia, rhabdomyosarcoma, infantile fibrosarcoma, lymphoma).

Mediastinal masses in infants are extremely uncommon. The majority has neurogenic origin and is usually located in the posterior mediastinum. In the anterior mediastinum, a mass can represent lymphangioma, teratoma, thymic enlargement (physiological and pathological), lymphadenopathy, lipoma or lipothymoma.[5,6] Soft tissue sarcomas represent less than 6% of all pediatric sarcomas, and the most common are embryonal rhabdomyosarcoma, Ewing sarcoma, congenital-infantile fibrosarcoma and undifferentiated sarcomas.[7]

To our knowledge, this is the first reported case of a congenital sarcoma with a chromosomal aberration that is characteristic of EMC. The next youngest reported patient with this genetic abnormality was a 21-month-old infant with bulbous urethra involvement.[8] This is also the first reported case of such extensive disease with this translocation, involving numerous sites of metastasis. Tumors with t(9;22)(q22;q11–12) are characteristic of a relatively indolent EMC and usually present between the fourth and sixth decade of life, with a 2:1 male predilection.[9,10] Primary EMCs are located mostly in the proximal extremities and limb girdles (64%), distal extremities (23%) and trunk (13%). Rarely, tumors have been reported to involve the mediastinum, retroperitoneum, fingers and intracranial cavity.[9] EMCs are generally thought of as slow-growing tumors with a propensity for recurrence and metastasis.[11] In a comprehensive review of 117 patients, Meis-Kindblom *et al*.[12] reported a 46% rate of metastasis, and a survival after metastasis ranging from a few weeks to 17 years. The most common sites of metastasis are the lungs, followed by soft tissues, lymph nodes, bone and brain.[12,13] The current mainstay of treatment is aggressive local control with surgical resection. Adjuvant therapy with radiation may be used in cases of complete resection. Current regimens of chemotherapy employed in the case of sarcoma show poor success rates, with one study reporting response in only two of the six patients.[14] These treatment modalities, unfortunately, were not an option in our young patient with numerous inoperable rapidly growing tumors.

This particular case is either a very unusual presentation for an EMC, or it may be that the t(9;22) chromosome mutation may not be as pathognomonic for this entity as previously believed. It is possible that association of the t(13;14) with t(9;22) in this neonate elicited a tumor with more aggressive pathology that either chromosome aberration by itself would normally cause.

Acknowledgments

We thank thank Dr Brigitte Gomperts of the Division of Pediatric Hematology/Oncology at University of California Los Angeles for her expertise and help in management of the patient, and Drs Nagesh Rao and Sunita Bhuta of the Department of Pathology at University of California Los Angeles for cytogenetics and electron microscopy. MAT was supported by National Institutes of Health (NIH) Grants CA90571 and CA107300, by CMISE, a NASA URETI Institute (NCC 201364) and is a Scholar of the Leukemia and Lymphoma Society. VM is supported by NIH, National Institute of Child Health and Human Development (NICHD) Career Development Award (K12) K12HD034610-11.

References

1 Chandler JC, Gauderer MW. The neonate with an abdominal mass. *Pediatr Clin Am* 2004; **51**: 979–997.
2 Cohen BA. Neonatal dermatology In: Cohen BA (ed). *Pediatric Dermatology*. 3rd edn. Elsevier Mosby: Philadelphia, 2005, pp 57–59.
3 Buyukpamukcu M. Solid tumors in the neonatal period. *Clin Pediatr* 2003; **42**: 29.
4 Ricart J, Jimenez A, Marquina A, Villanueva A. Congenital self-healing reticulohistiocytosis: report of a case and review of the literature. *Acta Paediatr* 2004; **93**(3): 426–429 (Review).
5 Paterson A. Imaging evaluation of congenital lung abnormalities in infants and children. *Radiol Clin of Am* 2005; **43**: 303–323.
6 Harvey JG. Chest wall, mediastinum and pleura In: Freeman NV, Burge DM, Griffiths DM, Malone PSJ (eds). *Surgery of the Newborn*. Churchill Livingstone: Edinburgh, 1994; 455–456.
7 Alaggio R, Ninfo V, Rosolen A, Coffin CM. Primitive myxoid mesenchymal tumor of infancy: a clinicopathologic report of 6 cases. *Am J Surg Pathol* 2006; **30**(3): 388–394.
8 Yi J, Yong-Koo P, Yong-Mook C, Hong H, Chang S. Bulbous urethra involved in perineal extraskeletal myxoid chondrosarcoma in a child. *Int J Urol* 2004; **11**: 436–439.
9 Hisaoka M, Hashimoto H. Extraskeletal myxoid chondrosarcoma: updated clinicopathological and molecular genetic characteristics. *Pathol Int* 2005; **55**: 453–463.
10 Jorg S, August C, Stoll W, Alberty J. Myxoid chondrosarcoma of the maxilla in a pediatric patient. *Eur Arch Otorhinolaryngol* 2005; **263**(3): 195–198.
11 Palmer H, North P, Nicholas RW, Allison JW, Parham DM. Pathologic case of the month: extraskeletal myxoid chondrosarcoma. *Arch Pediatr Adolesc Med* 1999; **153**(10): 1107–1108.
12 Meis-Kindblom JM, Bergh P, Gunterberg B, Kindblom LG. Extraskeletal myxoid chondrosarcoma: a reappraisal of its morphologic spectrum and prognostic factors based on 117 cases. *Am J Surg Pathol* 1999; **23**(6): 636–650.
13 Takeda A, Tsuchiya H, Mori Y, Nonomura A, Tomita K. Extraskeletal myxoid chondrosarcoma with multiple skeletal metastases. *J Orthop Sci* 2000; **5**: 171–174.
14 McGrory JE, Rock MG, Nascimento AG, Oliveira AM. Extraskeletal myxoid chondrosarcoma. *Clin Orthop Relat Res* 2001; **382**: 185–190.