The triad of nesidioblastosis, congenital neuroblastoma and glomerulocystic disease of the newborn: a case report

Almıla Bulun, S. Ümit Sarıcı, Özge Uysal Soyer, Özlem Tekşam
Murat Yurdakök, Melda Çağlar
Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey


Neuroblastoma is the most common malignant tumor of the newborn, comprising 20% of all malignancies encountered during the neonatal period. We herein report a newborn who was born after 29 weeks’ gestation and died unexpectedly at the 12th hour of life with no response to vigorous cardiopulmonary resuscitation. Autopsy findings revealed a right pararenal mass; microscopic examination showed neuroblastoma. Although the pancreas was grossly normal, its microscopic sections revealed a reduced number of islets of Langerhans and dispersion of the islet cells throughout the exocrine cells of the pancreas, and immunocytochemistry for the pancreatic hormones confirmed the dispersion of the islet cells. Final pathologic interpretation thus concluded the presence of nesidioblastosis. Furthermore, microscopic examination of the kidney showed glomerulocystic disease. Although the association of congenital neuroblastoma and nesidioblastosis has recently been defined as a new complex, neurocristopathy, the triad of congenital neuroblastoma, nesidioblastosis and glomerulocystic disease of the newborn has not been reported previously. To our knowledge, our case is the first reported newborn presenting with this triad. In conclusion, the association of nesidioblastosis and/or renal glomerulocystic disease should be kept in mind when encountering a case of congenital neuroblastoma. However, whether the presence of glomerulocystic disease in association with those other neurocristopathic pathologies is a coincidental finding or shares a common pathophysiological mechanism remains to be determined.

Key words: nesidioblastosis, congenital neuroblastoma, glomerulocystic disease, complex neurocristopathies.

Congenital neuroblastoma is the most common malignant tumor of the newborn, comprising 20% of all malignancies encountered during the neonatal period. Improvements in prenatal diagnosis with the aid of ultrasonography have led to a marked increase in the number of antenatally diagnosed cases of congenital neuroblastoma. Neonatal neuroblastoma in association with another malignant tumor, nephroblastoma, and with multiple benign anomalies such as as Beckwith-Wiedemann syndrome, DiGeorge anomaly, adrenal cyst, renal agenesis, anal atresia and absence of the right thumb, Ondine-Hirschsprung syndrome, and neurofibromatosis has been reported previously. Although the association of congenital neuroblastoma and nesidioblastosis has recently been defined as a new complex neurocristopathy, to our knowledge, the triad of congenital neuroblastoma, nesidioblastosis and glomerulocystic disease of the newborn has not been reported previously. We herein report a premature newborn who presented with this triad and died unexpectedly at the 12th hour of life with no response to vigorous cardiopulmonary resuscitation.

Case Report

A female infant born to a 39-year-old woman as the second born of the twins after a 29-week in vitro fertilized gestation was transferred to our neonatal intensive care unit
because of prematurity and respiratory distress. Her antenatal follow-up was unremarkable and no pathology had been detected despite routine and serial physical and ultrasonographic examinations. Physical examination revealed a weight of 1100 g (25-50 percentile), length 35 cm (10-25 percentile) and head circumference 27.5 cm (50-75 percentile). Serum glucose levels were 38 mg/dl, 41 mg/dl and 56 mg/dl at the 2nd, 6th and 12th hours of life, respectively. The diagnosis of respiratory distress syndrome was made on the basis of clinical, laboratory and radiological findings, and surfactant replacement therapy was administered at the 6th hour of age. At the 12th hour of life, however, respiratory status of the patient deteriorated rapidly, and she suffered cardiopulmonary arrest and died despite vigorous resuscitative attempts. The cause of death was evaluated as sudden infant death.

An autopsy was performed. The weight of the fetus was normal for her gestational age and no macroscopic anomaly was detected. Macroscopic examination of the lungs showed hypoinflation. Microscopic examination showed intraalveolar hyaline membranes. The most striking histopathological finding in the abdomen was a right pararenal mass. Although the left adrenal gland and kidney were grossly normal in shape and weight, a right pararenal mass was detected at the site of the right adrenal gland. The right kidney was also normal in shape, but the cut section showed a small number of cysts, 0.1-0.2 cm in diameter, in the cortex and corticomedullary region. These cysts were also detected at the same localization of the left kidney. The pararenal mass was 2.8x3x2 cm, weighing 28 g with the right kidney. Bilateral ureters and bladder were normal with the normal genital organs: tuba uterinas, ovaries and uterus.

Microscopic examination of the mass showed a tumor which was composed of small, oval-round hyperchromatic nuclei containing cells with little cytoplasm. These malignant cells had a poor Schwannian stroma (Fig. 1). Immunohistochemical stainings with neuron specific enolase and chromogranin A were positive. The diagnosis was congenital neuroblastoma without a metastatic disease.

Microscopic examination of both kidneys showed cystic dilatation of the Bowman spaces lined by cuboidal or columnar cells with abortive or primitive in appearance glomeruli, especially at the cortex and corticomedullary region of the kidney (Fig. 2). This finding was observed in a focal area with no immature mesenchyme and cartilage formation. This finding was interpreted as focal glomerulocystic disease of the kidney, which was not a part of cystic-dysplastic kidney.

The pancreas was also normal in weight and shape. However, microscopic examination revealed that islets of Langerhans were reduced in number, and single or small groups of clear, pale-staining islet cells were dispersed among the exocrine cells (Fig. 3). Immunohistochemical stainings for insulin, glucagon and somatostatin were also studied and these stainings showed dispersion of the islet cells throughout the pancreas. Some
antibody positive cells formed small groups, but these groups showed irregular shape rather than forming a true island. The most demonstrable staining was accomplished with insulin and glucagon (Figs. 4, 5). A pancreas from a fetus of the same gestational age was also examined and the difference was significant. In hematoxylin-eosin sections, islets were normal in shape and number (Fig. 6). No dispersion of endocrine cells was detected. Immunohistochemical stainings of the normal pancreas revealed insulin cells arranged predominantly in the islet’s center (Fig. 7), and glucagon predominantly at the periphery of the islet (Fig. 8). Micro- or macro-adenoma was not present in serial sections of the pancreas.
Discussion

Neuroblastoma presumably arises from primitive pluripotent sympathetic cells that are derived from the neural crest and that normally differentiate to form the tissues of the sympathetic nervous system, including spinal sympathetic ganglia and adrenal chromaffin cells\(^\text{11}\). Various other tumors also arising from aberrations in the early migration, growth and differentiation of neural crest cells are named as “neurocristopathies”. These are further classified into either simple neurocristopathies, including pheochromocytoma, neuroblastoma, medullary carcinoma of the thyroid, carcinoid tumors, Hirschsprung’s disease and melanocytic progonoma, or complex neurocristopathies such as neurofibromatosis, Sipple’s syndrome-pheochromocytoma, multiple mucosal neuroma syndrome, multiple endocrine adenomatosis, and neurocystic neurofibromatosis\(^\text{11}\).

Certain cells derived from the neural crest are transformed into peculiar neuroendocrine structures, generally designated as the chromaffin bodies. Nesidioblastosis develops from one type of these cells, islets of Langerhans, which belong to the amine precursor uptake decarboxylase cell system and indicate a neuroendocrine function. The association of congenital neuroblastoma and nesidioblastosis has recently been described as a new complex neurocristopathy, and there are only a few reported cases\(^\text{9-11}\). Shuangshoti and Ekaraphanich\(^\text{10}\) reported the first newborn with this association who was born with marked abdominal distention and hypoglycemia, and subsequently died at the sixth week of life. Autopsy findings of the patient reportedly were congenital neuroblastoma with metastases to liver and lymph nodes; severe fatty metamorphosis and glycogen depletion of the liver; advanced hyperplasia of the islets of Langerhans; and diffuse cerebral gliosis with focal encephalomalacia as a sequela of persistent hypoglycemia\(^\text{10}\). Grotting et al.\(^\text{9}\) reported another newborn who suffered from hypoglycemia related with recurrent seizure episodes and died at the third day of life. Autopsy revealed neuroblastoma and nesidioblastosis.

Neuroblastoma resulting from aberrations in the early migration, growth and cytodifferentiation of neural crest tissue is a unique pathophysiological process in the presentation of both congenital neuroblastoma and nesidioblastosis. Although this association represents an extremely rare form of complex neurocristopathy, the additional association of glomerulocystic disease with these two entities has not been reported previously, and our case is the first reported newborn presenting with this triad.

In conclusion, the association of nesidioblastosis and/or renal glomerulocystic disease should be kept in mind when encountering a case of congenital neuroblastoma. However, whether the presence of glomerulocystic disease in association with those other neurocristopathic pathologies is a coincidental finding or shares a common pathophysiological mechanism remains to be determined.

REFERENCES


