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CASE REPORT

Presentation of Neonatal Neuroblastoma as Facial Palsy and Vocal Cord Paralysis: a Case Report

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Abstract

Neuroblastoma is the most common malignancy in the first year of life. It can occur in any ganglion of the paraspinal sympathetic chain, but its main location is the adrenal glands. It can evolve from a localized disease to a highly aggressive metastatic tumor, or, in some cases, it can spontaneously regress. Its clinical presentation is variable and depends on the initial location of the tumor, the presence of metastases and paraneoplastic syndromes. The occurrence of facial or vocal cord paralysis is a rare finding, being justified by primary or metastatic tumor infiltration or as a sequel to tumor resection. We report a case of a newborn with neuroblastoma, whose initial clinical findings were facial and vocal cord paralysis at birth. Furthermore, the staging exams did not show evidence of metastatic infiltration in topographies that would justify such symptoms. The description of facial palsy and concomitant vocal cords paralysis as an initial clinical picture is even rarer. The relevance of this case report lies in allowing the recognition of a rare presentation of this disease, increasing the index of suspicion even in atypical contexts.

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INTRODUCTION

Although neonatal tumors are rare, neuroblastomas are the most common malignant neoplasm affecting newborns and young infants.[1-3] These heterogeneous and complex tumors originate from neural crest cells.[4-6] They can arise from any ganglion of the paraspinal sympathetic chain; however, most occur in the abdominal cavity, with the adrenal gland being the primary site in up to 50% of cases.[1,3,5]

Progression can vary from spontaneous regression to terminal metastatic disease.[4] In the neonatal period, more than 50% of patients present with metastases at diagnosis, but the tumor generally exhibits favorable biological behavior,[3] and may even undergo spontaneous regression.[4,5]

Symptoms vary based on the tumor's location, extent, biological behavior, and the presence of metastases or paraneoplastic syndromes.[1,3,4,6] Most children present with a palpable abdominal mass, though other symptoms may also occur.[3]

Facial paralysis is quite rare and has been documented as a result of direct tumor infiltration or secondary implantation.[1,7-9] Similarly, vocal fold alterations have been noted as uncommon symptoms resulting from neoplastic infiltration or as a sequel following tumor resection.[10,11]

Describing facial or vocal cord paralysis as the initial clinical presentation of neuroblastoma is rare, and reports of this tumor occurring with both types of paralysis are even rarer.

CASE REPORT

A mother with hypertensive disease gave birth to a full-term female newborn, appropriate for gestational age, via cesarean section. Prenatal care was uneventful. At birth, the newborn exhibited bradycardia and had a weak cry, which improved following positive pressure ventilation; however, she remained in respiratory distress and exhibited stridor (Apgar scores of 4 and 8). Facial asymmetry and excess interscapular skin were noted (Figure 1). The patient was referred from the maternity ward to a tertiary pediatric hospital for further investigation. She presented with left peripheral facial paralysis, stridor, and an interscapular skin appendage (Figure 1) and required oxygen upon admission. She became hypoxic and cyanotic, particularly during the administration of enteral feeds.

Early screening tests included a transfontanellar ultrasound, an echocardiogram, and an abdominal ultrasound. The first two did not reveal any relevant findings. Still, the third identified a heterogeneous solid mass with interspersed calcifications measuring 4.2 x 3.3 x 2.5 cm between the right kidney's upper lobe and the right hepatic lobe. Computed tomography scans of the abdomen confirmed an expansive mass in the area of the right adrenal gland with interspersed calcifications measuring 5.0 x 2.4 cm (Figure 2).

Magnetic resonance imaging of the abdomen and chest revealed a mass in the right adrenal gland, approximately 4.0 cm in diameter, with a markedly heterogeneous signal and a predominance of hypersignal on T2 while showing areas



Figure 1. Cutaneous appendage in the interscapular region found at birth.

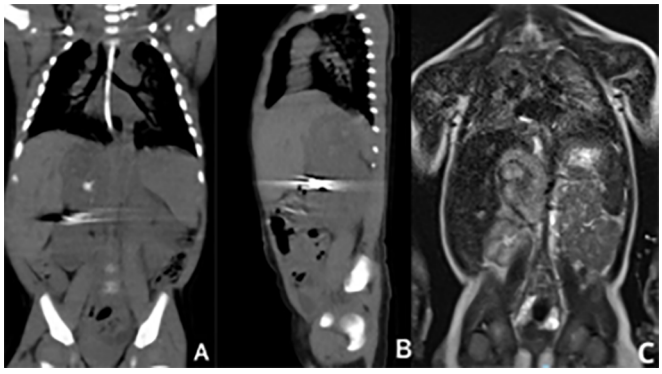


Figure 2. (A) Computed tomography scan displaying a coronal section of the abdomen, revealing an expansive mass in the right adrenal gland measuring 5.0 x 2.4 cm. (A) Computed tomography scan showing a sagittal section of the abdomen. (B) Magnetic resonance imaging scan of the thorax and abdomen featuring T2-weighted images.

of hypersignal on T1 that might correspond to hematic or hyperprotein content within it. Additionally, it presented marked restriction to diffusion and heterogeneous hypervascular enhancement with contrast medium, suggestive of a neoplastic lesion. The mass compressed and displaced the hepatic parenchyma but did not appear to invade it; no images suggestive of secondary pulmonary implants were observed.

A myelogram revealed global bone marrow hypercellularity with agranulocytosis and dyserythropoiesis without identifying syncytia or distinct cells; the bone marrow was not biopsied due to the patient's age and clinical condition. MRI scans of the skull showed no abnormalities, while laryngoscopy indicated left vocal fold paralysis.

An exploratory laparotomy revealed a solid lesion in the right adrenal region that extended toward the inferior vena cava without a cleavage plane separating it; the lesion also extended contralaterally and was close to the left renal vein. The liver surface appeared heterogeneous, with nodules detectable upon palpation. A lymphadenectomy was conducted, but the lesion was only partially resected, leaving some of the tumors in the interaortocaval region.

Histopathology revealed an undifferentiated tumor invading the resected lymph nodes. The diagnosis of neuroblastoma

was confirmed through immunohistochemistry (showing positive synaptophysin, focal positive chromogranin A, and S100, along with negative results for CD99, desmin, CD45, and CK AE1/AE3). The service to which the newborn was referred could not investigate N-myc amplification. The patient underwent an abdominal computed tomography scan after the procedure, which revealed images suggestive of secondary liver lesions.

Initially, the disease was classified as stage 4S, and chemotherapy was started with induction cycles using cyclophosphamide and topotecan, followed by doxorubicin, vincristine, cyclophosphamide, and etoposide.[11] After two cycles, the patient continued to experience hypoxia and cyanosis. Further computed tomography scans of the skull revealed nodules in the cranial vault bones, which led to the patient's reclassification to stage 4.[11] The episodes of hypoxia and cyanosis persisted, raising concerns about potential seizure-like activity. The patient showed clinical improvement after being prescribed phenytoin. A video-electroencephalogram indicated disorganization in the brain's electrical activity without evidence of electrographic or clinical seizures.

The patient developed several infectious complications and became oxygen-dependent, necessitating enteral nutrition and a gastrostomy. Following an extended hospitalization, she was discharged and placed under home monitoring. The pediatric oncology team is currently overseeing her care. The patient continues to experience left peripheral facial paralysis and ipsilateral vocal cord paralysis.

DISCUSSION

Facial paralysis is a common condition. In the pediatric age group, it can be either congenital or acquired.[7] Among the acquired causes are cholesteatomas, parotid lesions, paragangliomas, sarcomas, teratomas, vascular anomalies, metastatic infiltration, and infectious disorders, with neoplastic involvement considered rare.[7,9] In the context of neuroblastoma, it is regarded as uncommon and usually results from direct or metastatic neoplastic infiltration.[7-9]

Vocal cord paralysis results from dysfunction in the nervous components of the larynx, manifesting symptoms such as a weak cry, dysphonia, difficulty feeding, aspiration, and stridor.[12-14] It is the second leading cause of stridor among neonates, and the diagnosis is typically made through flexible nasofibrolaryngoscopy.[13,14] Its origins include perinatal trauma as well as iatrogenic, neurological, and idiopathic causes.[14] It occurs rarely in individuals with neuroblastomas, with few cases reported, most of which resulted from direct infiltration of the cervical nerve chain or resections of cervical tumors.[10,11]

After extensive research in the PubMed, Scielo, and BVS databases using the descriptors "Neuroblastoma, " "Facial Paralysis, " "Facial Palsy, " "Vocal Fold Paralysis," and "Vocal Cord Paralysis," no descriptions were found regarding the simultaneous occurrence of both types of paralysis as the initial presentation of neuroblastoma.

The patient did not show evidence of the most common causes of facial or vocal cord paralysis nor signs of tumor infiltration affecting the topography of the innervations mentioned above, as observed in the imaging exams. Investigations were conducted collaboratively by the neurology and airway teams. Paraneoplastic involvement was considered due to the presence of several classic paraneoplastic syndromes associated with neuroblastoma, such as opsoclonus-myoclonus, secretory diarrhea resulting from tumor production of vasoactive intestinal peptide (VIP)[3,5] and changes arising from catecholamine production, including hypertension, sweating, flushing, and tachycardia.[5]

Generally, when the tumor appears as an abdominal mass, ultrasound is the first examination conducted, followed by computed tomography or magnetic resonance imaging to evaluate the extent of the mass and assist in staging.[3-5] MIBG scintigraphy can also serve as an essential tool.[3,5] Congenital neuroblastoma may be identified as an incidental finding on prenatal ultrasound examination.[3,5]

The diagnosis is determined through findings from imaging tests, a biopsy of the tumor mass, a bone marrow biopsy, or a myelogram with tumor cells accompanied by increased urinary catecholamines.[1,4] The production of catecholamines is attributed to the tumor's origin from the neural crest; however, as in our patient's case, catecholamine production is not commonly detected in neonates.[4,5]

The International Neuroblastoma Staging System (INSS) (Table 1) is the most widely used method for clinically staging the disease, providing details on tumor spread observed in imaging tests, surgical resectability, and lymph node and bone marrow involvement.[1,3,15] Congenital neuroblastomas are typically classified as stages 1, 2, or 4S (INSS), with stage 4S being reported as the most common.[3,5] Stages 1 and 2 are marked by localized tumors that must first be resected and generally have a favorable prognosis. Stage 4S is characterized by progressive growth in the initial weeks of life until it begins to involute, typically without requiring oncological treatment.[2] Throughout treatment in this case, the tumor behavior deviated from this pattern, showing progression with bone metastases in the cranial vault, ultimately leading to restaging to stage 4, which carries a poorer prognosis.[15]

The tumor's risk stratification determines the treatment for neuroblastoma and may involve surgery, chemotherapy, or observation via MRI, taking into account the possibility of spontaneous regression.[3,5] Our patient presented with extensive disease and secondary neurological symptoms, necessitating treatment with both surgery and chemotherapy.

The combination of facial and vocal cord paralysis as initial symptoms is quite rare. Our patient did not exhibit any other common causes for these symptoms or secondary lesions that might explain them, raising the possibility of an associated paraneoplastic syndrome. Further studies are necessary to elucidate the etiopathogenic mechanisms of these alterations and identify possible treatments to improve or reverse them.

Table 1. The International Neuroblastoma Staging System (INSS)[15].

Stage	Definition
Stage 1	Localized tumor with complete gross excision, with or without microscopic residual disease; representative ipsilateral lymph nodes negative for tumor microscopically (i.e., nodes attached to and removed with the primary tumor may be positive).
Stage 2A	Localized tumor with incomplete gross excision; representative ipsilateral nonadherent lymph nodes negative for tumor microscopically.
Stage 2B	Localized tumor with or without complete gross excision, with ipsilateral nonadherent lymph nodes positive for tumor. Enlarged contralateral lymph nodes must be negative microscopically.
Stage 3	Unresectable unilateral tumor infiltrating across the midline, with or without regional lymph node involvement; or localized unilateral tumor with contralateral regional lymph node involvement; or midline tumor with bilateral extension by infiltration (unresectable) or by lymph node involvement. The midline is defined as the vertebral column. Tumors originating on one side and crossing the midline must infiltrate to or beyond the opposite side of the vertebral column.
Stage 4	Any primary tumor with dissemination to distant lymph nodes, bone, bone marrow, liver, skin, and/or other organs, except as defined for stage 4S.
Stage 4S	Localized primary tumor, as defined for stage 1, 2A, or 2B, with dissemination limited to skin, liver, and/or bone marrow (by definition limited to infants younger than 12 months). [14] Marrow involvement should be minimal (i.e., <10% of total nucleated cells identified as malignant by bone biopsy or by bone marrow aspirate). More extensive bone marrow involvement would be considered stage 4 disease. The results of the mIBG scan, if performed, should be negative for disease in the bone marrow.

Source: Brodeur GM, Pritchard J, Berthold F, et al.[15]

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