Clinical Case Reports

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Kinsbourne syndrome: a case report

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Introduction/Background: Kinsbourne syndrome or opsoclonus mioclonus ataxia is a rare syndrome, commonly post viral or paraneoplastic, characterized by opsoclonus, ataxia, myoclonic jerks of trunk and limbs and behavioral disturbances. Affects both adult and pediatric ages, with greater prevalence between one and three-year-old and equal gender prevalence. Neuroblastoma, hepatoblastoma and glangioneuromas are ordinarily associated with this syndrome. This paperwork aims to present a case report concerning Kinsbourne Syndrome and review literature about it.

Case presentation: We report a case of a one-year-and-two-month-old male, with opsoclonus, gait disturbance and imbalance associated with a neuroblastoma, who has undergone therapy with prednisone 1mg/kg/day and surgical resection, evolving with complete resolution of symptoms after four years and a half of clinical following, presenting himself to the date without neurological deficits, contrary to literature statistics.

Conclusion: KS is ordinarily a post-viral or paraneoplastic rare syndrome, with higher prevalence between 1 to 3-year-old infants, nevertheless also affecting adults. araneoplastic syndrome is majorly associated with NB

Keywords: Kinsbourne syndrome, opsoclonus myoclonus ataxia syndrome, neuroblastoma

INTRODUCTION

Kinsbourne syndrome or opsoclonus mioclonus ataxia is a rare syndrome, commonly post viral or paraneoplastic, characterized by opsoclonus, ataxia, myoclonic jerks of trunk and limbs and behavioral disturbances. Affects both adult and pediatric ages, with greater prevalence between one and three-year-old and equal gender prevalence. Neuroblastoma, hepatoblastoma and glangioneuromas are ordinarily associated with this syndrome. This paperwork aims to present a case report concerning Kinsbourne Syndrome and review literature about it. We report a case of a one-year-and-two-month-old male, with opsoclonus, gait disturbance and imbalance associated with a neuroblastoma , who has undergone therapy with prednisone 1mg/kg/day and surgical resection, evolving with complete resolution of symptoms after four years and a half of clinical following , presenting himself to the date without neurological deficits, contrary to literature statistics.

CASE REPORT

Male patient, 1 year-and-2-month-old, born at full term, without pre or perinatal complications, no reports of previous diseases, was referred to the pediatric ambulatory of the Hospital Universitário do Oeste do Paraná - HUOP with suspicions of KS . One month after the admission, the patient started to present fast and repetitive abnormal ocular movement, gait deficit, unbalance and significant body tremors, besides regression in neuropsych motor development.

According to the physical exam, the patient was in good condition, with adequate weight for his age and vital signs with no alteration . For the abdominal exam, he presented a 5 cm in diameter palpable mass in the right lumbar and umbilical region. For the neurologic exam, the patient presented a Glasgow Coma Score 15 with opsoclonus, level 2 osteotendinous reflexes in left side and upper right limb and level 0 in his right inferior limb, upper and inferior muscles strength level 5, abnormal plantar reflex and slapping gait towards the right side.

After considering KS as a diagnosis, CT scan for the skull, chest and abdomen, MRI of the spine and urine dosage of catecholamine metabolics (vanillylmandelic acid) were executed.

The exams showed an intraspinal extradural solid mass, in the L1-L4 area in right side of lumbar spine, isoattenuating, with uniform contrast intake (Figure 1-3), measuring about 5cm in the largest axis, with exits through the vertebral foramina leading to their stenosis, also showing bulging of the psoas muscle and a ipsilateral deviation of the kidney. Tomographic imaging of the chest, pelvis and skull did not show any signs of metastatic disease.

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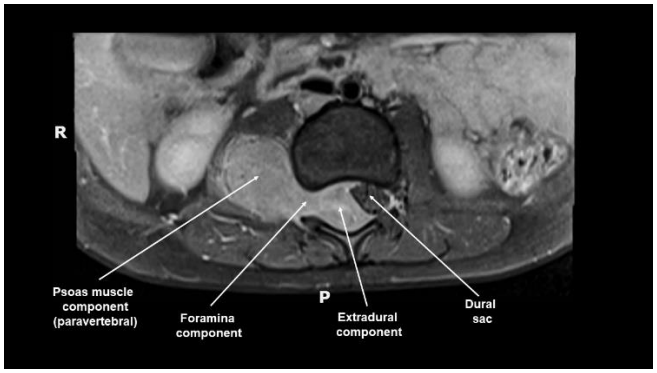

Figure 1 - Spine MRI in axial plane, T1, gadolinium contrasted, lumbar level, exhibiting the NB and its paravertebral, extradural and foraminal components. Personal archive of Marcius Benigno Marques dos Santos, MD.

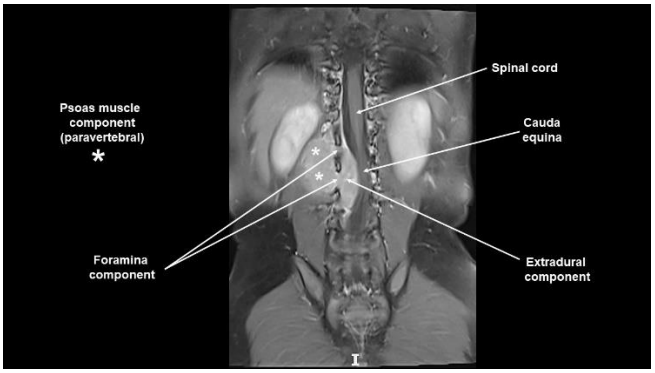

Figure 2 - Spine MRI in axial plane, T1, gadolinium contrasted, exhibiting the NB and its paravertebral, extradural and foraminal components, resulting in swelling of psoas muscle and lateral displacement of the right kidney. Personal archive of Dr. Marcius Benigno Marques dos Santos, MD.

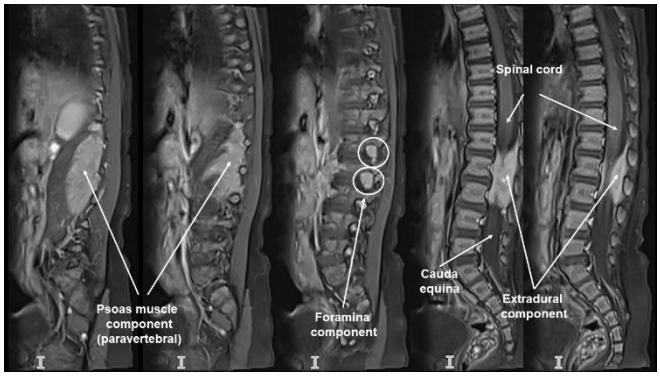

Figure 3 - Spine MRI, sagital plane, right to left, T1, gadolinium contrasted, where are exhibited the extension of tumoral mass and its exit throught vertebral foramina. Personal archive of Dr. Marcius Benigno Marques dos Santos, MD

Lab results showed high doses of lactate dehydrogenase, C reactive protein, and urine dosage of vanillylmandelic acid, about 4,8 mg in 24 hours.

Treatment was initiated with prednisone 1mg per kg per day. The tumor excision occurred in two periods , first by resectioning the spinal extradural portion and then the retroperitoneum one. The anatomopathological exam later determined a NB (neuroblastoma) . After surgical procedures the patient had a good post surgery recovery and was discharged with prednisone 1mg/kg/day, and sent to the pediatric oncology service, where he underwent chemotherapy treatment.

After four years and a half of clinical following , the patient recovered from opsoclonus, myoclonus, unbalance , motor impairments and rehabilitation of the neuropsychomotor development while walking without support. New exams did not show signs of residual or recurrent disease.

DISCUSSION

Most frequent cases of KS present with opsoclonus, torso and members myoclonus, loss of balance, irritability and sleep pattern alterations in infants of 12 months to 3 years of age, although it can also affect adults. It is described the association between KS and atypical viral and bacterial infections such as Epstein-Barr Enterovirus, Haemophilus influenzae, Coxsackie B3, Mycoplasma pneumoniae, Borrelia burgoferi, besides aseptic meningitis and immunizations. It is believed KS pathogenesis to be immune-mediated. About 50% patients of KS present elevated amounts of B cells in LCR exam, which is considered to be a disease activity sign as well as being correlated to the severity of clinical manifestations and treatment resistance [5].

Many kids with paraneoplastic KS present anti-Hu antibodies, which are also found in adults with paraneoplastic neurological syndromes associated with small cell lung carcinoma, and anti-Ri antibodies, found in gynecological neoplasias. Other studies identified the presence of neurofilaments or antibodies against cerebellar neurons dendrites or brainstem in cerebralspinal fluid (CSF) [6,7]. To the exam, CSF presents an inflammatory pattern, with high quantities of IgM and IgG antibodies classes or oligoclonal bands. There is an elevated amount of T gamma-delta cells and a low amount of CD4+. The cytokines pattern suggests prevalence of the Th2 response and an upregulation of B45 lymphocytes.

The NBs are the most common solid tumors in infants and tennagers, mostly untill 10 years old, followed by the central nervous system tumors, which correspond to 8-10% of malignant tumors in children [4]. The NBs consist in a parasympathetic nervous system originated neoplasia, usually developed from the adrenal medulla (47%), although it can also be originated in the abdominal/retroperitoneal (24%), thoracic (15%), pelvic (3%), or cervical sympathetic

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chain (3%)[11]. Most metastases observed in children with stage 4 disease are in bone marrow, bones and lymph nodes, being less common in lungs, central nervous system and skin . A recent KS Case Serie described suggests about 96% of patients with the syndrome don't have metastases in diagnosis, compared to 40-50% in patients with NB without KS associated, since the tumor is commonly small, well-located and well-differentiated [1].

Some authors believe opsoclonus is originated in alterations in the correlation between burst and omnipause neurons in the brain stem and fastigial nucleus of the cerebellum. MRI and PET-SCAN studies reveal alterations in function of the fastigial nucleus and cerebellum vermis [9,10,11]. It is also believed that the GABA transmission in the brainstem may be involved in the opsoclonus pathophysiology.

NBs located in the thoracic region may present through Horner syndrome (miosis, unilateral ptosis and anhidrosis). In cases where the location is paravertebral, signs of spinal cord compression may be evident, such as acute and subacute paraplegia, urinary and bowel dysfunction and radicular pain. In the presented case, the presence of the extradural intrathecal cavity mass with exit through the vertebral foramina to the right, determined its stenosis and the compression of the adjacent nerve roots, resulting in areflexia and gait deficit in the right inferior limb. Besides KS, the NB may relate to untreatable secretory diarrhea syndrome, caused by the tumoral secretion of vasoactive intestinal peptid [4].

The NB treatment consists in complete surgical resection. The impossibility of the total excision, presence of further lymph node metastasis or the unresectability implies in chemotherapy indication, associated or not with radiotherapy.

The immune and tumoral treatment from KS has been executed in the last 30 years using corticosteroids or adrenocorticotropic hormone, which show major effects in decreasing neurological symptoms from the syndrome, improving neurophysiological aspects such as learning, behavior and lessening cognitive impairment. However, most cases of withdrawal lead to recurrence of symptoms [12,13], being the use of Intravenous Immunoglobulin (IVIg) suggested by some authors with similar therapeutic results found with the usage of corticosteroids or adrenocorticotropic hormone [14]. Other immunosuppressive therapies described in literature are the use of monoclonal antibody anti-CD20, Rituximab [15], associated with IVIg and/or ACTH, cyclophosphamide associated with dexamethasone, ciclosporin, plasmapheresis, methotrexate and the monoclonal antibody Ofatumumab [12,13,15].

To the present date, there are no drugs described to be capable of minimizing the ataxia presented by KS patients. For that case, physiotherapy and neurological training have shown great importance in functional improvement of those patients. The opsoclonus can be treated with drugs such as clonazepam, chlormethiazole, gabapentin or topiramate [15].

The natural history of KS can be monophasic or recurrent, not the course of the disease being associated with the NB presence. A small fraction of patients spontaneously recover in a short period of time, whereas most patients become treatment dependent, remaining with neurological damage such as motor deficits, cognitive and language impairment, despite the disease remission.

Contrary to the described in literature, the patient in presented case had complete remission of KS, without motor, cognitive and language impairments or signs of residual or recurrent neoplasia during clinical following.

The amplification of the N-MYC gene is found in 10% cases of NBs, being related to a severe prognosis, to which is recommended extensive investigation and aggressive treatment. In the reported case, the N-MYC amplification was negative. Another factors of worst prognosis are the 11q gene deletion and ploidy of chromosome 17 DNA, which were not verified in this patient, as well as the increase dosage of ferritin and LDH serum levels. The presence of receptors for TrkA neutrophin imply a better prognosis [11].

CONCLUSION

KS is ordinarily a post-viral or paraneoplastic rare syndrome, with higher prevalence between 1 to 3-year-old infants, nevertheless also affecting adults. Paraneoplastic syndrom is majorly associated to NB.

In the presented case, the patient was included in higher prevalence age and exhibited opsoclonus and abnormal gait associated with a palpable abdominal mass. Complete resection of the tumoral mass and immunosuppressive treatment with prednisone 1 mg/kg/day were performed, having the patient complete recovery after four years and a half of clinical following, without gait, language or cognitive impairment to this date, defying the statistics described in literature.

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DISCLOSURES

Ethical approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the local Ethics Committee, number:(CEP – Plataforma Brasil), opinion number 55506022.7.0000.0107.

Consent to participate

The patients gave consent to use their information and images for research purposes. *Consent for publication*

Conflict of interest

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper."

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Artificial intelligence

No artificial intelligence was not used in this paper work

CONTRIBUTIONS

-**Thayanne Jacinto**: Conceptualization, Investigation, Visualization, Writing – original draft, Writing – review & editing
-**Paulo Eduardo Mestrinelli Carrilho**: Conceptualization, Methodology, Project administration, Supervision, Writing – review & editing
-**Lázaro de Lima**: Conceptualization, Methodology, Project administration, Supervision, Writing – review & editing
-Marcius Benigno Marques: Data curation, Supervision, Writing – review & editing

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