Türk Pediatri Arşivi
Turkish Archives of Pediatrics

Case Report

Evaluation of two non-myasthenic patients with ptosis

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Cite this article as: Kırık S, Güngör O, Işıkay S, Acıpayam C, Çoban Y, Çelik E. Evaluation of two non-myasthenic patients with ptosis. Turk Pediatri Ars 2017; 52: 240-3.

Abstract

Decreased height of the eyelid or the narrowing of the lid is called ptosis. Ptosis has several causes. Malignancy-related conditions such as Horner's syndrome, which causes unilateral ptosis in the pediatric age group, and patients with malignancy receiving chemotherapeutic treatment, are often secondary to these drugs and ptosis is a clue of underlying diseases. Underlying pathologies can lead to different clinical conditions such as cognitive impairment from coma, the presence of ptosis should be cautionary. In this study, we present two patients with malignancy who were admitted with ptosis. The first patient was diagnosed as having neuroblastoma and treated with neuroblastoma-directed chemotherapeutics. The second patient was diagnosed as having acute lymphoblastic leukemia and developed vincristine-induced ptosis and recovered on treatment with pyridoxine and pyridostigmine. In conclusion, non-myasthenic ptosis may develop due to involvement of the central nervous system during malignancy or neurotoxic effects of chemotherapeutic agents. Therefore, patients who present with ptosis should be evaluated for the etiologic diagnosis.

Keywords: Horner syndrome, malignancy, ptosis

Introduction

Ptosis is drooping of the upper eyelid. Normally, the upper eyelid border is found at the level of the limbus or covers 1-2 mm of the limbus. In presence of ptosis, the upper eyelid border is reduced to lower levels with varying degrees. Ptosis has many causes. In addition to hematologic and neurologic causes, ptosis due to drug toxicity may be observed, albeit rarely. Chemotherapeutic agents that are used to prevent malignancies and central nervous system (CNS) involvement may lead to different pictures including cognitive disorder, encephalopathy, and Horner syndrome. Thus, neurologic findings including ptosis may occur (1, 2). In this article, two patients with malignancy who presented with ptosis are presented. The first patient was being followed up with a diagnosis of neuroblastoma and the second patient was being followed up with a diagnosis of acute lymphoblastic leukemia.

Case 1

A twelve-year-old boy presented with severe headache, ptosis that started 15 days ago, and reduced sweating in the right side of his face. In his history taken from the family, it was learned that the patient's symptoms had increased gradually over the last two weeks and enophthalmos and ptosis advanced day by day. On physical examination, ptosis, enophthalmos, and anisocoria were found in the right eye. The patient's vital findings were found to be normal at presentation. Ipsilateral sweating disorder was found. Congenital causes were excluded because ptosis had developed later. The eye movements were found to be normal. Intra-day alteration was not found in ptosis. Horner syndrome was considered. Bilateral papilledema was found in the fundoscopic examination of the patient whose headache increased gradually. Brain magnetic resonance imaging (MRI) revealed a

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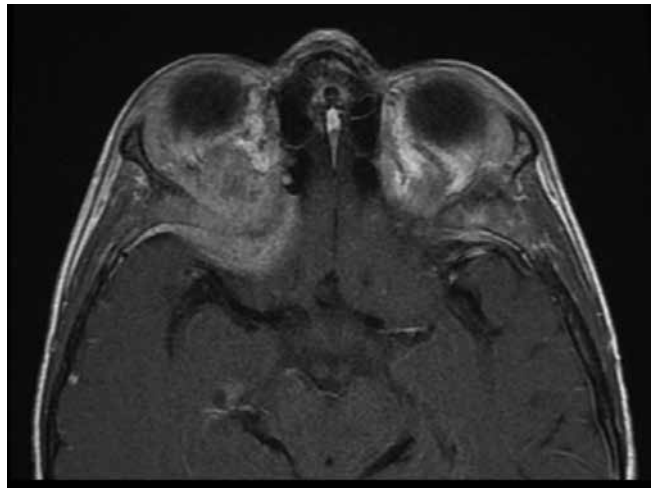
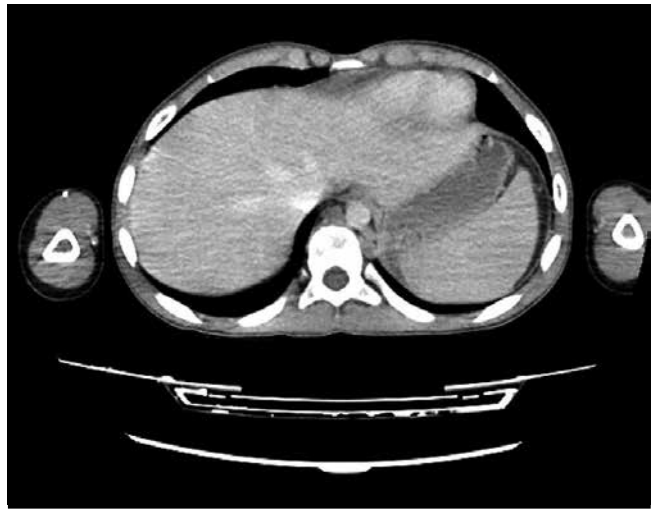
Received: 05.11.2015 **Accepted:** 20.06.2016

DOI: 10.5152/TurkPediatriArs.2017.3535

mass lodged on the dura with a size of 3 x 1.5 cm in the right supraorbital localization (Picture 1). The patient's posteroanterior lung X-ray was found to be normal. A solid mass with a size of approximately 8 x 7 cm was found anterior to the left kidney filling the left upper abdominal quadrant (Picture 2). On abdominal tomography (CT), the left adrenal gland could not be differentiated because of the mass in the abdomen. The laboratory tests were as follows: lactate dehydrogenase (LDH): 638 IU (370-840 IU), ferritin: 12.3 ng/mL (6-24 ng/mL), neuron-specific enolase (NSE): 286.5 ng/mL (0-16.3 ng/mL), vanillylmandelic acid (VMA) in 24-hour urine: 22.718 mg/24h (1.8-8.0). CD56 (+) cells were found in a bone marrow biopsy. A diagnosis of neuroblastoma was made with bone marrow biopsy findings in addition to ocular findings, abdominal mass, and increased VMA and NSE found in the laboratory tests. Chemotherapy was initiated in the Pediatric Oncology Clinic. In the follow-up visit performed one month later, reduction in the abdominal lesion and regression in the ocular findings were observed.



Picture 1. Mass in the right supraorbital localization on brain magnetic resonance imaging



Picture 2. Mass compatible with neuroblastoma anterior to the left kidney on abdominal computerized tomography

Case 2

A seven-year-old girl was being followed up with a diagnosis of acute lymphoblastic leukemia (ALL) for five months. She had symptoms of headache and drooping of the left upper eyelid, which started eight days after administration of two doses of vincristine (3 mg/m^2, maximum 5 mg) one week apart in accordance with the Acute Lymphoblastic Leukemia-Berlin Frankfurt-Munich (BFM) chemotherapy protocol. She had no family history of hereditary neuropathy or neurologic disorder. The deep tendon reflexes were found to be normal. No additional pathology was found in the neurologic examination. The laboratory findings were as follows: white blood cell count: 3,960/μL, absolute neutrophil count: 980 /μL, hemoglobin: 9.7 g/dL, and platelet count: 82,000/μL. Serum electrolyte values were found to be normal. Cranial MRI was found to be normal. Congenital causes were excluded because ptosis had developed subsequently. Deterioration was not found during the day. Third nerve palsy was not considered because eye movements were found to be free. Improvement in ptosis was not observed with the edrophonium test, upward gaze test, and ice test. Acetylcholinesterase receptor antibody was found to be negative. The cumulative vincristine level was found as 3.6 mg. Ptosis in the patient was evaluated to be cranial neuropathy related with vincristine treatment. Ptosis was reduced on the sixth day of pyridostigmine (3 mg/kg p.o.) and pyridoxine (150 mg/m^2 oral) treatment. It was completely regressed on the fourteenth day. Written consent was obtained from the patients' parents.

Discussion

Ptosis is the covering of the cornea by the upper eyelid by more than 1 cm. The eyelid interval is specified by measuring the distance between the light reflected from the center of the cornea and the upper eyelid. This is used for follow-up. To measure the function of the levator muscle, the patient is asked to gaze from below upwards while keeping the eyebrows stable with compression. The upper eyelid should be able to move approximately 14 mm during this procedure. Values of 10 mm and below indicate poor levator function. Congenital causes, oculomotor nerve palsy, myasthenia gravis,

post-traumatic causes, and more rarely, Marcus- Gunn jaw-winking (MGJWS) syndrome and aponeurotic ptosis are considered among the causes. Histories starting from the time of birth support congenital cases and presence of ptosis together with limitation in eye movements supports oculomotor nerve palsy. In MGJWS, improvement in ptosis is observed with mouth movements (1, 3-5).

Horner syndrome develops in relation with blockage of the oculosympathetic nerve pathway between the hypothalamus and the eye. The lesion may be in the cerebral hemisphere, hypothalamus, cervical spinal cord, T1 spinal root, cervical sympathetic chain and carotid plexus because sympathetic sensation belonging to the eye is long (1-3). Enophthalmos, increased amplitude of accommodation, retraction in the ipsilateral eyelid, alteration in lacrimal viscosity, and heterochromia in patients aged below 2 years may accompany these findings in addition to myosis, ptosis, and ipsilateral sweating disorder in the face (2).

Neuroblastoma is a common type of cancer in childhood that is found in the sympathetic ganglia and adrenal glands and originates from the primordial neural crest. It is frequently manifested with palpable abdominal mass and neurologic findings. It is the most common cancer of infancy. At the time of diagnosis, thirty-six percent of patients are below the age of one year, 89% are below the age of 5 years and 98% are below the age of 10 years. The primary tumor is located in the abdomen in 65% of cases. Adrenal localization is observed with a rate of 25% in infants and with a rate of 40% in older children. In addition to these findings, bone pain secondary to metastasis, fever, sweating and opsomyoclonus and diarrhea as paraneoplastic syndrome may be observed; 8.1% of patients present with ocular manifestations. The most common metastases include bone, bone marrow, and orbital soft tissue metastases (2). In the diagnosis, bone marrow biopsy, urinary catecholamine levels, VMA and serum NSE positivity are important. Tumor cells are found to be synaptophysin and NSE (+) on immunohistochemical examination. Although prognosis is worse in cases originating from the adrenal gland, patients with Horner syndrome have been reported to have a better prognosis even in the risky age group (2, 6).

In our first patient, invasion from the adrenal gland to the CNS occurred without thoracal involvement and ptosis and Horner syndrome developed as a result. Recognition of progressive enophthalmos and papilledema while being followed up because of the diagnoses of headache and ptosis was important. The patient's age was not in the age range in which neuroblastoma occurs frequently. Marked improvement was observed in the ocular manifestations belonging to Horner syndrome including ptosis after chemotherapy was initiated in our patient.

Vincristine is a frequently used chemotherapeutic agent in childhood malignancies. The pathogenesis by which it leads to neuropathy is not known clearly. The most widely held hypothesis is that the microtubules in nerve fibers alter and cells die in the metaphasis stage. Its adverse effects occur in a dose-dependent fashion. The main adverse effects include paresthesia, decreased deep tendon reflexes, drop foot, seizure, diplopia, ptosis, photophobia, and optic atrophy. In the diagnosis, the occurrence of manifestations with the initiation of vincristine treatment in patients who were normal before treatment and the absence of signs of neuropathy before treatment are important. In addition, the diagnosis is made with normal MRI findings and complete disappearance of findings with discontinuance of vincristine and initiation of pyridoxine and pyridostigmine. Treatment is generally performed with pyridoxine and pyridostigmine, which are administered for two weeks (1, 4). Our second patient had no known previous neuropathy. His symptoms started with vincristine treatment. MRI was found to be normal. Ptosis completely recovered after pyridoxine and pyridostigmine treatment in 14 days.

Ptosis may develop secondary to CNS invasion and the neurotoxic effects of chemotherapeutic agents. The fact that the patient's age was advanced for neuroblastoma in the first case and the fact that ptosis developed secondary to vincristine neuropathy in the second case were important. Therefore, patients presenting with ptosis should be evaluated very carefully in terms of etiology.

Informed Consent: Writen informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - S.K., E.Ç. Design - O.G., S.I.; Supervision - C.A., E.Ç.; Funding - S.K.; Materials - Y.Ç.; Data Collection and/or Processing - S.K., C.A.; Analysis and/or Interpretation - O.G., S.I.; Literature Review - S.I., S.K.,C.A.; Writing - S.K., E.Ç., O.G.; Critical Review - S.I., Y.Ç.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

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