Eosinophilic granuloma presenting as periorbital cellulitis


We report a case of eosinophilic granuloma, a localized form of Langerhans' cell histiocytosis, in a young child who presented with fever, catarrhal symptoms, and periorbital inflammation resembling periorbital cellulitis. After treatment with systemic antibiotics without improvement, she developed proptosis. Plain radiographic examination showed an orbital mass extended to the intracranium without lytic bone lesion. Diagnosis of eosinophilic granuloma was confirmed by biopsy of the mass, and absence of bone, soft tissue or other organ involvement. After treatment by surgical removal and chemotherapy, the proptosis subsided as well as the mass, as shown in radiographic examination. No significant complications were observed.

We report this case to ensure clinician's awareness in diagnosing inflammatory orbital masses that show no response to antibiotic treatment. Although rare, eosinophilic granuloma is a treatable disease, and should be considered as one of differential diagnoses of periorbital cellulitis.

Key words: Eosinophilic granuloma, Langerhans' cell histiocytosis, Periorbital cellulitis, Orbital mass.

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Received for publication. February 5, 2000.
รายงานผู้ป่วยโจชิโธสินฟิลิคกรุญโองมา 1 รายที่พยาบาล โรงพยาบาลแทยมคดว
อาการไข้ ไม่ดี ผิวสีปุ๊บปีน และมีการเข้าสู่บริเวณรอบกายครุยต์ ผู้ป่วยได้รับการรักษาด้วยยาปฏิชีวนะทาง
การศึกษาและออกแบบ แต่อาการไม่ดีขึ้น ต่อมาผู้ป่วยมีตาไปขึ้น ภาวะชร้างทางข้างฝั่งก่อนเนื้อในบริเวณ
รอบกาย จึงได้คัดชันนี้เพื่อก่อนบริเวณรอบกายไปตรวจ ผลชิ้นเนื้อพบว่าเป็น แดงเกินานซ์สลด
ฮิสติโอซิส ซึ่งเป็นอาการตามที่ไปตรวจ ได้ให้การรักษาด้วยยาปฏิชีวนะ ซึ่งได้รับผลิตฟิลิค-
กรุญโองมา ผู้ป่วยได้รับการรักษาโดยดีต่อเนื่องเนื้อรอบกาย รวมกับการให้คอมัมป์ หลังได้รับการรักษา
ผู้ป่วยมีอาการดีขึ้น ภูมิภูมิ และไม่พบมีผลแห่งข้อของการรักษา

การรายงานผู้ป่วยรายนี้มีวัตถุประสงค์เพื่อให้แพทย์ที่สูงส่งรักษาได้มีการปฏิบัติ ซึ่งเป็น
ที่พยาบาล โรงพยาบาลแทยมคดว ได้รับการรักษาด้วยยาปฏิชีวนะดีต่อเนื่อง ทั้งนี้เนื่องจากผู้ป่วยโจชิโธสินฟิลิคกรุญโองมาเป็น
โรคที่พบได้บ่อยแต่สามารถรักษาได้
Langerhans’ cell histiocytosis (LCH) is the most common histiocytic disorder in children. Eosinophilic granuloma is a localized form of LCH. Orbital involvement of eosinophilic granuloma is rare. In a Thai literature review, we found only one report of orbital involvement of this disease. Most patients with orbital involvement present with proptosis caused by orbital masses. We report herein a case of eosinophilic granuloma initially presented with a rare manifestation, peri-orbital inflammation.

**Case report**

A Thai girl was in good health until 14 months age when she developed a low-grade fever and rhinorrhea, followed one month later by rapid onset of mild pain, erythematous and a swollen right upper eyelid. She had been treated with topical and systemic antibiotics for 10 days at a private clinic for peri-orbital cellulitis, but without any clinical improvement. Her family history and past history, including eye trauma or previous infection, were noncontributory.

She was then referred to King Chulalongkorn Memorial Hospital. Physical examination was completely within normal limits except for the right orbital region. A 2 x 3 cm. mass was found beneath the inflamed right upper eyelid. The initial ophthalmologic evaluation revealed that the patient’s vision was central, steady and maintained fixation (CSM) in both eyes. The extraocular movement was full. There was no evidence of strabismus by Hirschberg testing. Pupils were equal, reactive to light, and without relative afferent pupillary defect. The right eye was slightly proptosed and showed temporal fullness by resiliency testing. The peri-orbital area was inflamed. A 2 x 3 cm. firm and tender mass was detected by palpation (Figure 1A). Both anterior and posterior eye segments were normal. The left eye and left orbital area were unremarkable.

Complete blood cell counts and blood chemistry, including electrolytes and liver function tests, were within normal limits. Urinalysis was normal, with a specific gravity of 1.020. Urine vanillomandelic acid (VMA) was within normal range for her age. The chest radiography was normal. Plain films of the skull showed the mass without lytic bone lesion. A radionuclide bone scan detected abnormally increased uptake at the right temporal bone, and upper part of orbit and maxilla but without other bone lesion. Computed tomographic (CT) study of the brain and orbit with contrast enhancement showed a large homogeneous enhancing soft tissue mass involving supra- and infrayzygomatic masticator spaces, the right retrobulbar space, orbital apex, and with intracranial extension into the anterior and middle cranial fossa. By CT study of the orbit, bony destruction was demonstrated (Figure 2A). CT scan of whole abdomen was normal, without any abnormal mass detected. An incisional biopsy of the mass was performed, but yielded only adipose tissue without any evidence of malignancy.

Ten days after the first biopsy, the patient came in and showed rapid progressive growth of the right orbital mass to 5 x 3.5 cm. displacing the globe in an inferonasal direction, and which increased proptosis and mild limitation of lateral gaze of the right eye. Vision was still CSM in both eyes. A second deeper biopsy showed abnormal proliferation of histiocytes and eosinophils (Figures 1B, 1C). Immunohistochemical study was positive for S-100 protein supporting the diagnosis of Langerhans’ cell...
histiocytosis. Rhabdomyosarcoma, which was also in the differential diagnoses, was then ruled out by the pathological examination and immunohistochemistry. The patient was later treated by gross total removal of the extradural tumor. Pathology from the total excision again confirmed the diagnosis. Postoperatively, the patient significantly improved but there was residual tumor in the right temporals muscle and its medial aspect as shown in both bone scan and CT scan (Figure 2B). Subsequently, the patient was treated with a course of weekly intravenous vinblastine and daily oral prednisolone. After chemotherapy, the tumor regressed and disappeared from the intracranial portion in CT scans. The patient was followed for 3 months and there was no recurrence.

Figure 1-A: A 14-month-old girl with periorbital mass at temporal part of right upper Eyelid.

Figure 1-B, 1-C: Pathological examination demonstrating proliferation of histiocytes (arrow) and eosinophil (arrow head) (Hematoxylin and eosin)

Figure 2-A: Preoperative CT scan of brain and orbit showing large, homogeneous, enhancing soft tissue mass involving right temporal region, retrobulbar space, orbital apex and intracranial extension. (white arrow head) A large lytic bone lesion is shown. (arrow)

Figure 2-B: CT scan at 2 months after surgery and adjuvant chemotherapy showing no recurrence.
Discussion

Langerhans’ cell histiocytosis (LCH) is the abnormal proliferation of histiocytes. It is not a malignant disease, and can undergo spontaneous regression and recurrence. LCH was formerly classified as eosinophilic granuloma, Hand-Schuller-Christian disease and Letterer-Siwe disease which reflect localized unifocal, multifocal and diffuse forms of histiocytosis, respectively. Letterer-Siwe disease most commonly occurs in infants and young children, while eosinophilic granuloma are mostly found in adolescents and young adults. Based on the biology of Langerhan cell, the three diseases are now considered a spectrum of LCH. Since there is a wide spectrum of the disease, severity depends on subtypes.

The incidence of Langerhans’ cell histiocytosis is 1:200,000. It is uncommon for it to involve the orbit. Less than one-fourth of the patients have orbital involvement. Eosinophilic granuloma constitutes to less than 1% of all orbital tumors. Unifocal eosinophilic granuloma of bone is the most benign condition of histiocytic proliferative disorders. The most common age of onset was reported to be under 2 years of age. The younger age carries worse prognosis since the younger patients have a higher risk for transforming to the disseminated type. Ophthalmologic presentation has been reported as rapid progressive proptosis caused by an orbital mass, especially in the lateral or superior-temporal areas, which may extend intracranially. Whenever a young patient presents with orbital mass, neuroblastoma should always be suspected. Bone marrow examination, urine VMA and CT whole abdomen should be performed, the results of which were normal in our patient. The diagnosis of neuroblastoma was then excluded. Orbital involvement of eosinophilic granuloma may present with unusual manifestations, including bilateral xanthelasma and non-resolving chalazion which have been reported in older age groups. Bilateral choroidal osteoma associated with histiocytosis has also been reported.

By radiographic examination, bony lesions may be found in the skull, especially the frontal bone, and in the ribs, proximal long bone, vertebrae and pelvis. Plain films are characterized by circumscribed, lytic bone lesions without surrounding sclerosis. CT findings are non-specific. They may show an orbital mass of irregular density, which may extend into the intracranial cavity through the lytic bone lesion. Eosinophilic granuloma is usually isodense or slightly hyperdense compared with brain parenchyma and enhances homogeneously with intravenous contrast media. Our case presented radiographically as an orbital mass which CT scan later demonstrated to be a lytic bone lesion.

When a Langerhans’ cell histiocytosis is suspected, hematologic evaluation and biopsy (fine needle aspiration, incisional or excisional biopsy) should be performed for definite diagnosis prior to treatment. Microscopic findings of Langerhans’ cell histiocytosis include proliferation of histiocytes admixed with numerous lymphocytes and plasma cells resembling most small round blue cell tumors, including neuroblastoma, lymphoma, rhabdomyosarcoma and primitive neuroectodermal tumor (PNET), which should always be considered and excluded. Immunohistochemical studies are helpful to rule out such diseases. Langerhans’ cell histiocytosis reacts positively to S-100 and monoclonal Ab OKT-6 (CD)}
protein. Furthermore, electron microscopy is used to confirm the diagnosis by demonstrating Birbeck granules or Langerhans' granules in the tumor cell cytoplasm.\(^{(1)}\) There is no pathological difference between localized and disseminated disease. Rhabdomyosarcoma, one of the important differential diagnoses, can be excluded definitely by pathologic examination. In our case, the pathological report excluded rhabdomyosarcoma and PNET, and concluded the diagnosis of Langerhans' cell histiocytosis. The diagnosis of eosinophilic granuloma (localized disease) was made by clinical investigation excluding other systemic foci of the lesion.

Treatment of unilateral eosinophilic granuloma is variable, and usually depends on the clinician's decision, and the location and extension of the tumor. Several reports describe incisional biopsy with curettage,\(^{(4,9)}\) intralesional corticosteroid injection,\(^{(3)}\) low dose radiation therapy,\(^{(8)}\) surgical removal\(^{(10)}\) and chemotherapy\(^{(6,11)}\) in unifocal eosinophilic granuloma. Vinblastine and prednisolone were the most common chemotherapy agents used in these cases. However, spontaneous regression was surprisingly reported in a 13 year-old patient who declined low dose radiotherapy.\(^{(8)}\)

In our case, we decided on surgical removal of the tumor combined with adjunctive postoperative chemotherapy for several reasons. Firstly, the patient was very young, which carries a high risk of progression to the disseminated form. Secondly, the lesion at the lateral wall of the orbit also extended posteriorly into the intracranial cavity, which may compromise the optic nerve. After treatment the tumor regressed without recurrence but we were also mindful of the complications that may occur after radical treatment. Chemotherapy is superior to radiation therapy in terms of reossifying bone after treatment. However, chemotherapy may result in transient immunosuppression and myelotoxicity.

Orbital involvement of eosinophilic granuloma is rare. Previously, there was only one case reported in Thailand.\(^{(12)}\) The authors present this case in order to confirm the existence of this rare disease. Ophthalmologists are urged to be aware of it and not overlook its diagnosis. A definite pathological diagnosis should be obtained whenever the disease is suspected, since the prognosis is favorable and the disease is curable if the patient receives early diagnosis and treatment. On the other hand, if left untreated, the disease could progress and morbidity can occur due to its mass effect.

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