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Fatal Disseminated Multiple Intracranial Juvenile Xanthogranuloma without Cutaneous and Other Organ Involvement: A Rare Case Report

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Established Facts

- Juvenile xanthogranuloma (JXG) is a disorder of histiocytic proliferation among young children that usually presents as spontaneously regressing cutaneous lesions.
- Rare intracranial involvement.
- Solitary intracranial lesions are more frequently observed than multiple lesions.

Novel Insights

- Extensively dural, sellar-suprasellar region, orbit, and parenchymal involvement noted in our case patient at the time of diagnosis, which is extremely uncommon.
- Multiple central nervous system (CNS) involvement at the time of diagnosis, which is rare and results in significant mortality.
- Early diagnosis of multiple CNS lesions in JXG is essential for a good outcome, which can otherwise be fatal.

Keywords

Systemic juvenile xanthogranuloma · Langerhans cell histiocytosis · Central nervous system lesions · Fatality

Abstract

Introduction: Juvenile xanthogranuloma (JXG) is a disorder of histiocytic proliferation that affects young children and usually presents as spontaneously regressing cutaneous lesions. JXG with systemic involvement is a rare entity associated with significant morbidity and mortality. Intracranial solitary lesions are uncommon, and when comorbid with multiple lesions of the central nervous system in young chil-

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dren, it has an extremely worse prognosis. *Case Presentation:* We have reported here an unusual case of a 6-year-old boy who initially presented with the complaints of headache, vomiting, seizure, and speech disorder without cutaneous and other organ involvement and a neurological tendency to sleep. Acute hydrocephalus was detected in his brain CT. As an emergency intervention, ventriculo-peritoneal shunt operation was performed on the patient. His postoperative MRI revealed a disseminated intracranial disease involving the extensive dural, sellar-suprasellar region, the orbit, and the brain parenchyma. The patient accordingly underwent a pterional approach for open biopsy and for the mass tissue diagnosis. Histopathology reports were con-

Emre Bilgin Department of Neurosurgery, Adana City Training and Research Hospital AdanaKışla Mah. 4522 Sok. No. 1 Yüreğir, Dr. Mithat Özsan Bulvarı Kışla Adana (Turkey) dremreblgn@gmail.com sistent with JXG. Unfortunately, the patient succumbed to the disseminated disease within 2 months of the JXG diagnosis. **Conclusion:** JXG is a disorder that usually affects the skin. Intracranial lesion can be simple or have multiple involvement. This is a rare case of fatal disseminated multiple intracranial JXG without cutaneous and other organ manifestations. The presentation as a sellar-suprasellar, extensive dural, orbit, and parenchymal involvement at the time of diagnosis is unusual and rarely described in the literature.

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Introduction

Juvenile xanthogranuloma (JXG) is a rare, usually selflimiting, histiocytic disorder that affects young children. JXG most often presents with the cutaneous involvement of the head, neck, and trunk regions [1]. The median age at diagnosis is 2 years, with the male/female ratio of 1.5/1 in infancy [1]. This rare dendritic cell-related disorder mostly presents as spontaneously regressing nodular skin lesions [1].

Systemic involvement is rare and generally difficult to treat. The brain parenchymal lesions have been reported with JXG [1]. Cutaneous lesions are usually self-limiting and benign. Extracutaneous lesions, especially multiple intracranial systemic JXG, are often associated with a higher morbidity and fatality [2, 3]. Conservative therapy with steroids, surgery, radiation, and chemotherapy has also been attempted in multiple lesions [4].

Central nervous system (CNS)-JXG neoplasm often requires surgical resection or chemotherapy [5–8]. This neoplasm ranges from isolated CNS lesions to multifocal CNS lesions [9–11]. Disseminated CNS lesions in young children have been reported to have an extremely poor prognosis [5]. In children, both systemic JXG with CNS involvement and CNS-limited JXG appear to have poorer outcomes than pediatric JXG without CNS diseases [8].

Case Report

History

A 6-year-old boy was evaluated in the emergency service department with the complaints of headache, vomiting, seizure, and speech disorder, as well as a neurological tendency to sleep. His family reported complaints of fever and weakness for 2 months and that his consciousness had deteriorated in the past 1 week. Acute hydrocephalus was detected on brain CT (Fig. 1) of the patient. No abnormal values were recorded in his blood hemogram and biochemistry examinations. The color of the cerebrospinal fluid sample collected via lumbar puncture was clear. Ventriculo-

Diagnosis of Multiple CNS Lesions in JXG



Fig. 1. Preoperative CT.

peritoneal shunt operation was accordingly performed on the patient under emergency conditions, as no finding suggesting infection or malignancy was noted.

Multiple intracranial lesions were detected in the contrast-enhanced MRI (Fig. 2a–c) performed in the patient whose postoperative general condition improved and consciousness returned. A pterional approach for open biopsy and tissue diagnosis of the mass was selected for the patient. Open biopsy was performed from the sellar-suprasellar region lesions with the second cranial surgery performed 3 days after the shunt surgery.

Histopathological Analysis

Microscopic examination of the sellar-suprasellar lesion revealed leptomeningeal tissues with granulomatous infiltrate, foamy cells, and Touton giant cells. Xanthomatous cells infiltrating leptomeningeal tissue were noted (hematoxylin and eosin, ×100; Fig. 3a). The xanthomatous cells had large clear cytoplasm and small nuclei. Eosinophils and lymphocytes were noted in the stroma (HE, ×200; Fig. 3b). Histiocytic cells showed diffuse positive staining with CD68 antibody (immunohistochemistry, anti-CD68, ×100; Fig. 3c). The proliferation index of CD 68 (+), F13a (+), and Ki67 applied by immunohistochemistry yielded 1-2% results. S100 and CD1a showed negative staining. Biopsy revealed JXG, but no visible skin pathology was detected on physical examination. No lesions of JXG were observed in the abdominal- and thorax-enhanced CTs. Moreover, no abnormalities were noted in the samples from the skin, liver, spleen, and lungs. The blood examination results were normal. The patient consulted with a pediatric oncology clinic, and his medical treatment was accordingly initiated. Unfortunately, he succumbed to the disseminated disease within 2 months of the JXG diagnosis.

Discussion

JXG is one of the most common non-Langerhans cell histiocytosis (LCH) affecting children [3]. Its cutaneous presentation include benign, usually asymptomatic lesions primarily involving the head, neck, and trunk regions. Cutaneous JXG lesions are usually believed to be benign, and they regress spontaneously [3].

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Fig. 2. Contrast-enhanced MRI, T1-weighted image showing multiple enhancing intracranial lesions (axial (a), sagittal (**b**), and coronal (**c**)).



Fig. 3. a HE1: xanthomatous cells infiltrating leptomeningeal tissue (hematoxylin and eosin, ×100). b HE2: xanthomatous cells having large clear cytoplasm and small nuclei. Eosinophils and lymphocytes can be observed in the stroma (HE, ×200). c CD68: histiocytic cells show diffusely positive staining with CD68 antibody (immunohistochemistry, anti-CD68, ×100).

JXG usually affects the skin. The most frequent extracutaneous sites involved in JXG are the kidneys, lungs, spleen, liver, eyes, CNS, and musculoskeletal system. Intracranial involvement is unusual and has been described previously [12, 13]. There are only a few cases reports without cutaneous lesion until date [14].

Solitary intracranial lesions are more generally frequently detected than multiple lesions. Comprehensive dural, sellar-suprasellar region, orbit, and parenchymal involvement at time of diagnosis was noted in our case, which is extremely unusual. JXG appears in the CNS secondary to the skin or other organs involved [12]. No skin or other organ involvement was observed in the present case.

Intracranial lesions may be detected in the cerebral parenchyma, meninges, choroid plexus, or cranial nerves. Clinically, the affected children may be asymptomatic or may present with seizures, ataxia, weakness, or growth retardation. Intracranial involvement in JXG is associated with increased mortality and morbidity. The intracranial lesions possess a tendency to grow slowly and should be followed up [15].

Treatment for JXG can be nonsurgical or surgical. Cases with isolated symptomatic lesions may require surgery. The conservative management of this disease with steroid therapy can provide symptomatic relief, and radiotherapy has also been attempted for multiple lesions. Thus, CNS-JXG disease may be difficult to treat and has been associated with severe morbidity and mortality [16].

Orsey et al. [17] reported 26 patients with CNS-JXG, who were treated with surgery, a variety of chemotherapy, radiotherapy, or immunosuppressive therapies, or combinations of these modalities. The authors used pred-

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nisolone, vinblastine, methotrexate, and etoposide to treat JXG patients with diffuse involvement of the CNS who did not respond and subsequently died because of progression into clonal histiocytic neoplasm.

Dolken et al. [18] reported the successful treatment of a 7-month-old girl with systemic JXG and multiple lesions in the CNS with systemic prednisolone, vinblastine and etoposide, intrathecal methotrexate, and prednisolone, as well as the surgical removal of the larger CNS lesion. Although surgical excision appears to be curative in well-defined and accessible lesions, disseminated CNS lesions are not sufficient to be removed surgically and have been considered for systemic therapies using agents with activity against LCH, such as corticosteroids, cyclosporine, vinca alkaloids, etoposide, and methotrexate [18, 19]. Cases with systemic JXG show good outcomes with LCH-based chemotherapy because both LCH and JXG are dendritic cellrelated disorders [19]. The inclusion of a vinca alkaloid and steroid in the treatment is associated with better overall response rates in patients with systemic JXG [20].

Our patient showed JXG with disseminated CNS involvement and did not respond to medical treatment. He died due to the disseminated disease within 2 months of the JXG diagnosis. In summary, the present report describes a rare JXG patient with fatal multiple CNS lesions at the time of diagnosis without involvement of the skin or other organs.

Conclusion

JXG usually affects the skin. The most frequent extracutaneous sites that are involved include the kidneys, lungs, spleen, liver, eyes, CNS, and musculoskeletal sys-

References

- Zahir ST, Sharahjin NS, Vahedian H, Akhavan A. Juvenile xanthogranuloma presenting as a large neck mass and ocular complications: a diagnostic and therapeutic dilemma. BMJ Case Rep. 2014;2014:bcr2013202683.
- 2 Meshkini A, Shahzadi S, Zali A, Tajeddini A, Mirzayan J, Hamdi A. Systemic juvenile xanthogranuloma with multiple central nervous system lesions. J Cancer Res Ther. 2012;8(2): 311–3.
- 3 Lalitha P, Reddy MCh, Reddy KJ. Extensive intracranial juvenile xanthogranulomas. AJNR Am J Neuroradiol. 2011;32(7):E132–3.
- 4 Liang S, Liu YH, Fang K. Juvenile xanthogranuloma with ocular involvement. Pediatr Dermatol. 2009;26(2):232–4.
- 5 Dehner LP. Juvenile xanthogranulomas in the first two decades of life: a clinicopathologic study of 174 cases with cutaneous and extracutaneous manifestations. Am J Surg Pathol. 2003;27(5):579–93.
- 6 Janssen D, Harms D. Juvenile xanthogranuloma in childhood and adolescence: a clinicopathologic study of 129 patients from the Kiel pediatric tumor registry. Am J Surg Pathol. 2005;29:21–8.
- 7 Tamir I, Davir R, Fellig Y, Weintraub M, Constantini S, Spektor S. Solitary juvenile xanthogranuloma mimicking intracranial tumor in children. J Clin Neurosci. 2013;20(1):183–8.

tem. Solitary intracranial lesions are generally more frequently detected than multiple lesions. The observations of extensive dural, sellar-suprasellar region, orbit, and parenchymal involvement noted in our case patient at the time of diagnosis were extremely uncommon. No skin or other organs (such as the liver, spleen, and lungs) were involved, as in the present case.

Statement of Ethics

The parents of the subject provided written informed consent for the publication of data and images. At no point has the identity of the subject been revealed.

Conflict of Interest Statement

The authors declare no conflicts of interest.

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Author Contributions

Dr. Emre Bilgin, corresponding author, has contributed to the conceptualization of article, analyzing the data and articles related to the case, revising the manuscript writing and making it relevant for the readers and fellow researchers, final approval of the submitted manuscript material, and ensuring the accuracy and integrity of the submitted data. Dr. Ali İhsan Ökten has contributed to the design of the manuscript, the search for articles related to the case, drafting the work required for the manuscript, and the final structure of the submitted manuscript.

- 8 Wang B, Jin H, Zhao Y, Ma J. The clinical diagnosis and management options for intracranial juvenile xanthogranuloma in children: based on four cases and another 39 patients in the literature. Acta Neurochir. 2016; 158(7):1289–97.
- 9 Bostrom J, Janssen G, Messing-Junger M, Felsberg JU, Neuen-Jacob E, Engelbrecht V, et al. Multiple intracranial juvenile xanthogranulomas. Case report J Neurosurg. 2000; 93:335–41.
- 10 Ernemann U, Skalej M, Hermisson M, Platten M, Jaffe R, Voigt K. Primary cerebral non-Langerhans cell histiocytosis: MRI and differential diagnosis. Neuroradiology. 2002;44(9): 759–63.

- 11 Fulkerson DH, Luerssen TG, Hattab EM, Kim DL, Smith JL. Long-term follow-up of solitary intracerebral juvenile xanthogranuloma. Case report and review of the literature. Pediatr Neurosurg. 2008;44(6):480–5.
- 12 Sun LP, Jin HM, Yang B, Wu XR. Intracranial solitary juvenile xanthogranuloma in an infant. World J Pediatr. 2009;5(1):71–3.
- 13 Chidambaram B, Santosh V. Giant orbital and intracranial xanthogranuloma: a short report. Neurol India. 2001;49(2):208–10.
- 14 Pimentel J, Fernandes A, Távora L, Miguéns J, Lobo Antunes J. Benign isolated fi brohistiocytic tumor arising from the central nervous system. Considerations about two cases. Clin Neuropathol. 2002;21:93–8.
- 15 Kasliwal MK, Suri A, Rishi A, Suri V, Sharma BS, Sarkar C. Symptomatic bilateral cerebellar mass lesions: an unusual presentation of intracranial xanthogranuloma. J Clin Neurosci. 2008;15(12):1401–4.
- 16 Ernemann U, Skalej M, Hermisson M, Platten M, Jaffe R, Voigt K. Primary cerebral non-Langerhans cell histiocytosis: MRI and differential diagnosis. Neuroradiology. 2002;44(9): 759–63.
- 17 Orsey A, Paessler M, Lange BJ, Nichols KE. Central nervous system juvenile xanthogranuloma with malignant transformation. Pediatr Blood Cancer. 2008;50(4):927–30.
- 18 Dolken R, Weigel S, Schroder H, Hartwig M, Harms D, Beck JF. Treatment of severe disseminated juvenile systemic xanthogranuloma with multiple lesions in the central nervous system. J Pediatr Hematol Oncol. 2006; 28:95–7.
- 19 Nakatani T, Morimoto A, Kato R, Tokuda S, Sugimoto T, Tokiwa K, et al. Successful treatment of congenital systemic juvenile xanthogranuloma with Langerhans cell histiocytosis-based chemotherapy. J Pediatr Hematol Oncol. 2004;26(6):371–4.
- 20 Stover DG, Alapati S, Regueira O, Turner C, Whitlock JA. Treatment of juvenile xanthogranuloma. Pediatr Blood Cancer. 2008; 51(1):130–3.