

Available online at [www.sciencedirect.com](http://www.sciencedirect.com)

ScienceDirect

journal homepage: <http://www.elsevier.com/locate/pjnns>

## Case report

## Langerhans cell histiocytosis in the jugular foramen

Cui Daming<sup>1</sup>, Xue Yajun<sup>1</sup>, Shen Zhaoli, Shen Rui, Lou Meiqing\*

Department of Neurosurgery, Shanghai Tenth People's Hospital, Tongji University, Shanghai, China

## ARTICLE INFO

## Article history:

Received 28 July 2013

Accepted 23 December 2013

Available online 23 January 2014

## Keywords:

Langerhans cell histiocytosis

Jugular foramen

Birbeck granules

## ABSTRACT

Langerhans cell histiocytosis (LCH) is a rare disease of neoplastic proliferation of monocyte-macrophage system. Although LCH can affect almost any organ, solitary involvement of jugular foramen is extremely rare and can present a diagnostic dilemma because of its rarity at this location. Here, we present the case of an adult patient with LCH affecting the jugular foramen, and review the relevant literature.

© 2014 Polish Neurological Society. Published by Elsevier Urban & Partner Sp. z o.o. All rights reserved.

## 1. Introduction

Langerhans cell histiocytosis (LCH), previously referred to as histiocytosis X, is a rare disorder characterized by clonal proliferation and excess accumulation of pathologic Langerhans cells causing local or systemic effects [1,2]. The exact etiology of LCH is still unknown. Clinical syndromes within this entity include eosinophilic granuloma, Hand-Schüller-Christian disease, and Abt-Letterer-Siwe disease [2]. Langerhans cell histiocytosis typically occurs in childhood and adolescence as solitary osteolytic lesions. The most frequent sites of the bony lesions are the skull, femur, mandible, pelvis and spine [3]. A variety of treatment modalities have been reported [4,5]. Here, we present an adult female patient with LCH of the jugular foramen.

## 2. Case report

## 2.1. History

A 23-year-old female patient presented with a 6-week history of occipital pain. There was no history of trauma or neoplasm.

More recently, the patient complained of progressive stiffness and weakness of neck, which impaired her range of neck motion and caused torticollis. She must use cervical gear to complete the daily activities. In the month prior to her admission, her occipital pain increased with hoarseness of voice and difficulty swallowing.

## 2.2. Examination

Neurologic examination was remarkable for marked impairment of cervical flexion, extension and rotation. The left palate was mildly weak with diminution of the gag reflex. Exceptionally, physical examination revealed a 3-cm, firm, and regular lesion with normal overlying skin in the left mastoid process.

## 2.3. Investigation

Magnetic resonance imaging (MRI) demonstrated a homogeneous, 5.5 cm × 3.5 cm solid mass involving the left jugular foramen and lateral mass of atlas. The mass showed low signal intensity on both T1- and T2-weighted images, and intense heterogeneous enhancement following intrave-

\* Corresponding author at: Department of Neurosurgery, Shanghai Tenth People's Hospital, Tongji University, Shanghai 200072, China. Tel.: +86 21 66307370; fax: +86 21 66307370.

E-mail address: [kalantes@126.com](mailto:kalantes@126.com) (L. Meiqing).

<sup>1</sup> These authors contributed equally to this work.

nous gadolinium administration. Magnetic resonance venography revealed occlusion of transverse and sigmoid sinus. Computed tomography showed an irregular osteolytic lesion of jugular foramen extending downwards lateral mass of atlas (Fig. 1). The remainder of the examination was unremarkable.

#### 2.4. Surgery

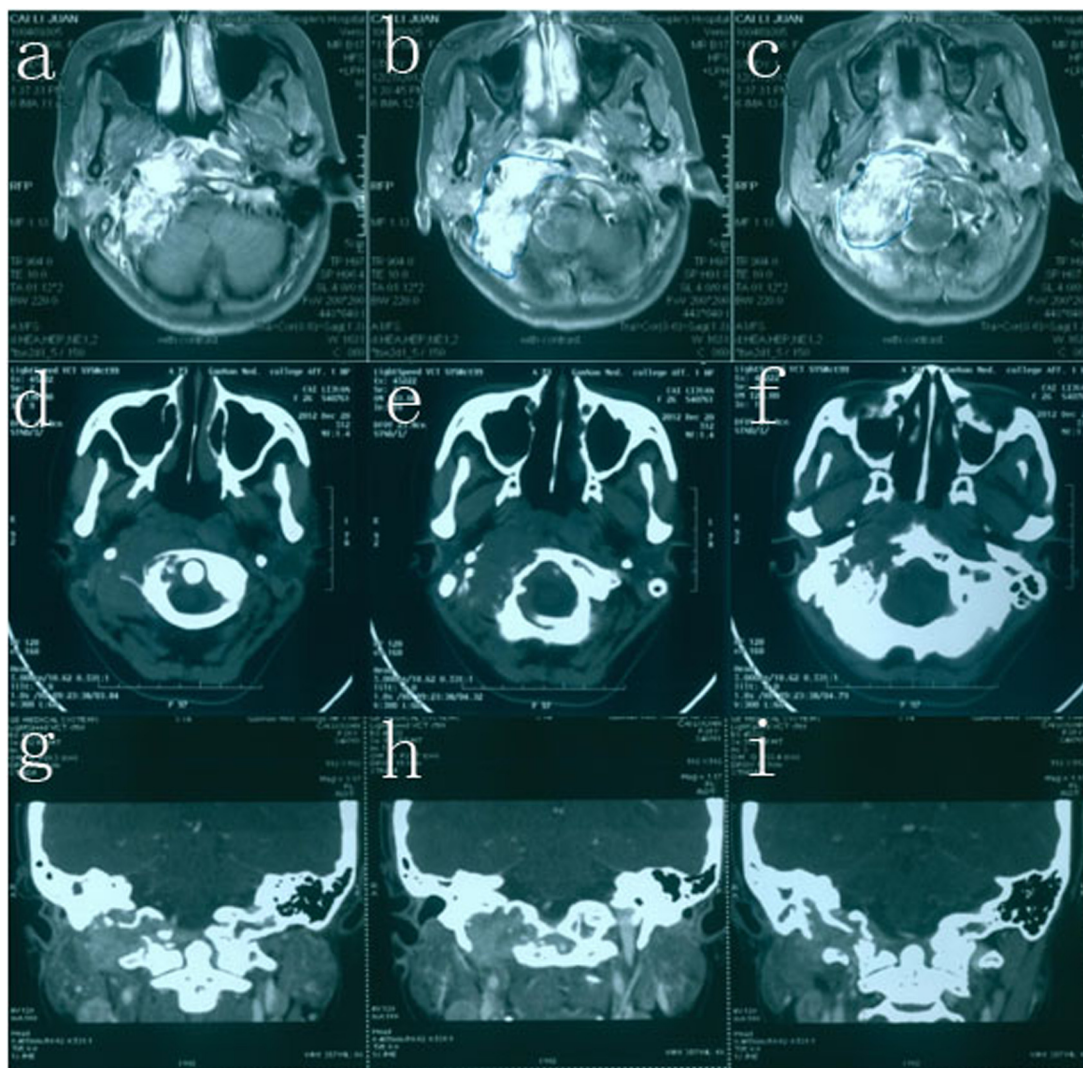
A left far lateral approach was utilized to excise the lesion. A surgical corridor was created by separating suboccipital muscles and paravertebral muscle, drilling the left partial occipital condyle. Exposure of the tumor demonstrated a gray, yellow mass in the jugular foramen and lateral mass of atlas. The lesion was easily separated, blood supply was moderate, and finally tumor was partially resected. In order to restore stability of the cervical spine, occipitocervical fusion was performed.

#### 2.5. Histology

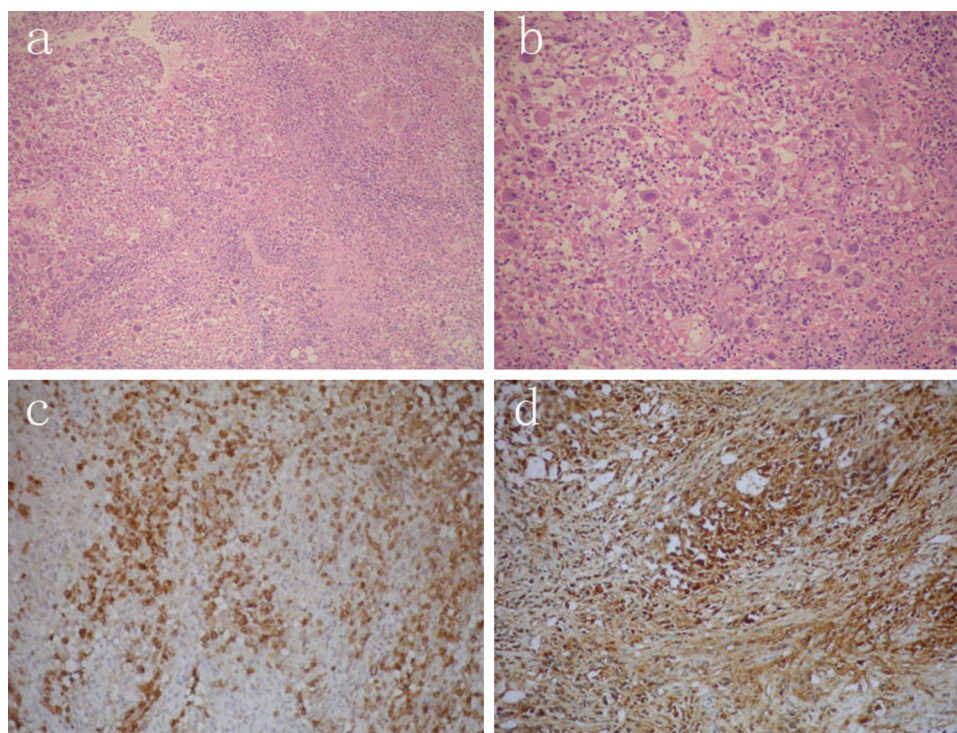
Gross examination of the surgical specimen revealed multiple, irregular fragments of pale and tan soft tissue measuring in aggregate 3 cm × 2.1 cm × 1.7 cm. Histological sections revealed a granulomatous reaction pattern, with extensive aggregates of histiocytes proliferation, which showed broad cytoplasm cells and a kidney-shape nucleus, along with clusters of eosinophils. Immunohistochemical stain by CD1a antibody and S-100 immunoperoxidase stain were positive only in the histiocytic cells. Because of the immunorexpression of S-100 and CD1a by lesional cells, the diagnosis of LCH was made (Fig. 2).

#### 2.6. Postoperative course

The patient tolerated surgery well, without neurological deficit and with good recovery. In the first month, MRI demonstrated



**Fig. 1** – Post-gadolinium axial T1-weighted MR images (a–c) show an intensive heterogeneously enhancing mass affecting the left jugular foramen with extension to the lateral mass of atlas. CT images (d–i) show bone destruction of the left jugular foramen and lateral mass of atlas.



**Fig. 2 – Histologic examination shows tissue fragments composed of an eosinophil-rich infiltrate admixed with histiocytes (a). The histiocytes are characterized by grooved, reniform nuclei (b). Histiocytic elements show diffuse, intense nuclear and cytoplasmic reactivity for CD1a (c) and for S-100 protein (d).**

no change in the size of the tumor. Two months after resection, she received radiotherapy in a total dose of 10 Gy administered over five consecutive days to affected area. After 6 months of follow-up, the patient denied recurrence of occipital pain and neck stiffness, and resumed her routine activities and started working (Fig. 3). Now, the patient continues to undergo serial MRIs to monitor the residual tumor.

### 3. Discussion

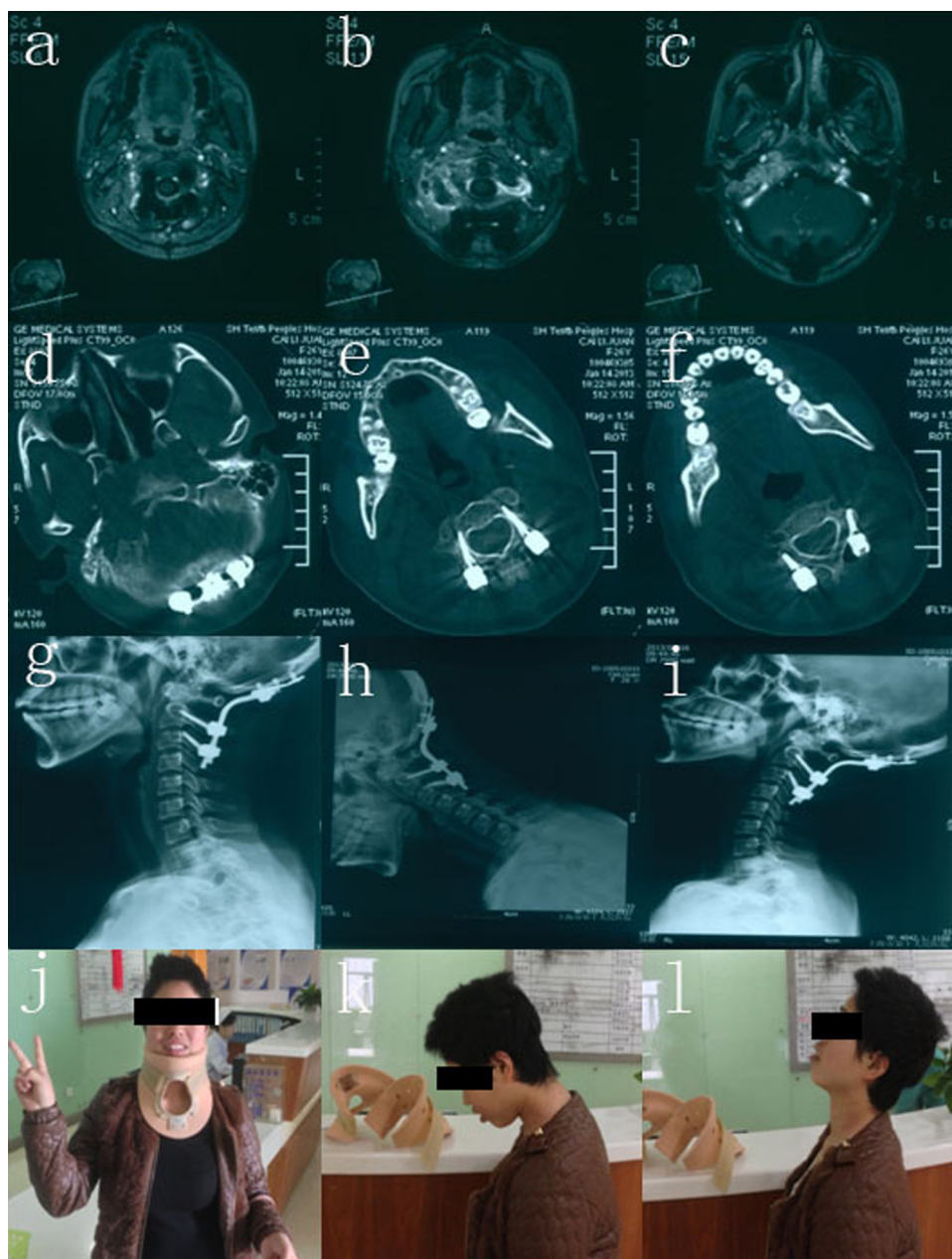
The first clinical description of LCH was published in 1865 by Smith [6]. He described a case of a 4-year-old child who died of whooping cough and was found at autopsy to have erythematous changes on the skin and a few osteolytic foci in the calvaria. Three years later, Paul Langerhans described epithelial cells with long, dendrite-like processes. Langerhans suggested that they might originate from bone marrow and be a part of the immunological system [7]. There is now strong evidence that proliferation of these cells was not only the cause of Dr. Smith's patient's disorder, but was also one of LCH. Langerhans cells are antigen-presenting histiocytes which have a dendritic morphology by which their surface area increases many folds in order to maximize the chance of successful antigen presentation to specific subsets of T-cells [1,2]. Lichtenstein named Langerhans histiocytosis as histiocytosis X in 1953 [8]. The letter "X" emphasized the unknown etiology of diseases such as eosinophilic granuloma, Hand-Schüller-Christian or Abt-Letterer-Siwe disease. In 1987, the

Writing Group of the Histiocyte Society replaced the name "histiocytosis X" with the current term "Langerhans cell histiocytosis" [9].

Langerhans cell histiocytosis is encountered mostly in the pediatric population. The annual incidence in the pediatric age range has been estimated at 2–5 per million per year. Most cases are diagnosed before the age of 20 years, male slightly more than females [10–12]. Hand-Schüller-Christian disease involves multiple skeletal and extraskeletal lesions. Ten to thirty percent of patients have the originally described exophthalmos, polyuria, and skull lesions. Abt-Letterer-Siwe disease is marked by widespread visceral involvement and may have marked constitutional symptoms. It usually occurs in infancy and often proves fatal as a result of multisystem failure. Eosinophilic granuloma is classified as a unifocal bony lesion, usually found in the calvaria, vertebral bodies, and long bones, and rarely in the skull base [2,13,14].

In the skull base, petrous ridge of the temporal bone is the most common site of LCH described [15]. Exceptionally, clivus, sphenoid bone, petrous apex, infratemporal fossa involvement have been documented in a few cases [12,14,16]. In our patient, the unifocal osseous lesion extending from the left jugular foramen to lateral mass of atlas has not previously been reported.

The etiology of LCH is unknown. It is still debated whether the proliferation of LCH is of neoplastic or reactive origin [2,11]. The clinical presentation of LCH involving skull base is widely varied and is entirely dependent on the location, size and extent of the lesion. These patients most commonly present



**Fig. 3 – Axial post-gadolinium T1-weighted images (a–c) show reduction in size of the lesion. CT images show (d–f) occipital fusion device, C2 pedicle screws, and C3 lateral mass screws in good position. Flexion–extension radiographs of cervical spine (g–i). The patient is in a very good condition, and resumes her normal life 6 months after the operation (j–l).**

with cranial nerve paralysis and local pain [3,11,12,14–16]. Our patient was mainly symptomatic with hoarseness of voice and difficulty swallowing. Physical examination showed limitation of cervical movement, local pain and swelling.

Imaging features of LCH lack specificity. Magnetic resonance imaging appearance of LCH affecting skull base includes abnormal signal with homogeneously or heterogeneously enhancing destructive soft tissue mass. It is hyperintense on T2- and hypointense on T1-weighted images. Due to the increased cellularity of the lesion, diffusion restriction is often found [15,17]. Computed tomography in thin slices is a very useful method in the

diagnosis of this disease. It is more suitable for the observation of local bone destruction [17]. Even so, the other radiological differential diagnosis including chordoma, neurinoma and glomus jugulare tumor must be considered in jugular foramen region.

Clear diagnosis of LCH depends on histopathological tests. Langerhans cell histiocytosis can be readily recognized on or suggested by hematoxylin and eosin examination, where a mixture of inflammatory cells is present, including macrophages, lymphocytes, plasma and Langerhans cells. The latter is characterized by slight eccentric, ovoid, reniform or convoluted nuclei. Immunohistochemistry confirms positive

stains of S-100 and CD1a. Apart from that, Birbeck granules demonstrated by electron microscopy are also characteristic changes of LCH in the cytoplasm [18,19].

The treatment of patients with LCH varied widely according to the extent of the disease. Surgery, radiotherapy, and chemotherapy may be utilized separately or in combination [11]. Surgical treatment is primarily advocated for isolated lesions. Some studies, moreover, considered that non-radical removal might result in higher incidence of relapses and extensive surgery with healthy bone margin resection is a better choice. Unless the lesion is totally curettage, to avoid recurrence, adjuvant radiotherapy must be carried out after surgery [20]. Treatment of extensive diseases (Hand-Schüller-Christian disease and Abt-Letterer-Siwe disease) is much more complex. Corticosteroids, methotrexate, vinblastine, growth hormones, interferon alpha, cytosine arabinoside and low-dose radiotherapy in combination or alone has shown some modest success [21,22].

It has been 6 months since our patient's surgery. She is in a very good condition, resumes her normal life, and continues to undergo serial MRIs to monitor the residual tumor.

### Conflict of interest

None declared.

### Acknowledgement and financial support

The study was supported by the National Natural Science Funds (no. 81201979).

### Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; Uniform Requirements for manuscripts submitted to Biomedical journals.

### REFERENCES

- [1] Laman JD, Leenen PJ, Annels NE, Hogendoorn PC, Egeler RM. Langerhans-cell histiocytosis 'insight into DC biology'. *Trends Immunol* 2003;24:190-6.
- [2] Hoover KB, Rosenthal DI, Mankin H. Langerhans cell histiocytosis. *Skeletal Radiol* 2007;36:95-104.
- [3] Zhong WQ, Jiang L, Ma QJ, Liu ZJ, Liu XG, Mei F, et al. Langerhans cell histiocytosis of the atlas in an adult. *Eur Spine J* 2010;19:19-22.
- [4] Cantu MA, Lupo PJ, Bilgi M, Hicks MJ, Allen CE, McClain KL. Optimal therapy for adults with Langerhans cell histiocytosis bone lesions. *PLoS ONE* 2012;7:e43257.
- [5] Allen CE, McClain KL. Langerhans cell histiocytosis: a review of past, current and future therapies. *Drugs Today (Barc)* 2007;43:627-43.
- [6] Smith T. Skull cap showing congenital deficiency of bone. *Trans Pathol Soc Lond* 1865;16:224-5.
- [7] Langerhans P. Über die Nerven der menschlichen Haut. *Arch Pathol Anat* 1868;44:325-37.
- [8] Lichtenstein L. Histiocytosis X: integration of eosinophilic granuloma of bone, Letterer-Siwe disease, and Schüller-Christian disease as related manifestations of a single nosologic entity. *Am Med Assoc Arch Pathol* 1953;56:84-102.
- [9] Chu A, D'Angio GK, Favara B, Ladisch S, Nezelof C, Prichard J. Report and recommendations of the workshop on the childhood histiocytoses: concepts and controversies. *Med Pediatr Oncol* 1986;14:116-7.
- [10] Nicholson HS, Egeler RM, Nesbit ME. The epidemiology of Langerhans cell histiocytosis. *Hematol Oncol Clin North Am* 1998;12:379-84.
- [11] Vezina JP, Audit N, Fradet G. Cerebrospinal fluid otorrhoea: a rare presentation of Langerhans' cell histiocytosis of the temporal bone. *J Laryngol Otol* 2010;124:545-8.
- [12] Krishna H, Behari S, Pal L, Chhabra AK, Banerji D, Chhabra DK, et al. Solitary Langerhans-cell histiocytosis of the clivus and sphenoid sinus with parasellar and petrous extensions: case report and a review of literature. *Surg Neurol* 2004;62:447-54.
- [13] Paulus W, Perry A. Histiocytic tumours. In: Louis DN, Ohgaki H, Wiestler OD, et al., editors. *WHO classification of tumours of the central nervous system*. 4th ed. Lyon: IARC Press; 2007. p. 193-6.
- [14] Lederman CR, Lederman ME. Unifocal Langerhans' cell histiocytosis in the clivus of a child with abducens palsy and diplopia. *J AAPOS* 1998;2:378-9.
- [15] Ahmed M, Sureka J, Koshy CG, Chacko BR, Chacko G. Langerhans cell histiocytosis of the clivus: an unusual cause of a destructive central skull base mass in a child. *Neurol India* 2012;60:346-8.
- [16] Binning MJ, Brochmeyer DL. Novel multidisciplinary approach for treatment of langerhans cell histiocytosis of the skull base. *Skull Base* 2008;18:53-8.
- [17] Prayer D, Grois N, Prosch H, Gadner H, Barkovich AJ. MR imaging presentation of intracranial disease associated with langerhans cell histiocytosis. *AJNR Am J Neuroradiol* 2004;25:880-91.
- [18] Le BH, Truex RC. 29 year-old male with seizure and syncope. *Brain Pathol* 2013;23:363-4.
- [19] Favara BE. Langerhans' cell histiocytosis pathobiology and pathogenesis. *Semin Oncol* 1991;18:3-7.
- [20] Mosiewicz A, Rola R, Jarosz B, Trojanowska A, Trojanowski T. Langerhans cell histiocytosis of the parietal bone with epidural and extracranial expansion - case report and a review of the literature. *Neurol Neurochir Pol* 2010;44:196-203.
- [21] Steen AE, Steen KH, Bauer R, Bieber T. Successful treatment of cutaneous Langerhans cell histiocytosis with low-dose methotrexate. *Br J Dermatol* 2001;145:137-40.
- [22] Culic S, Jakobson A, Culic V, Kuzmić I, Šćukanec-Spoljar M, Primorac D. Etoposide as the basic and interferon-alpha as the maintenance therapy for Langerhans cell histiocytosis: a RTC. *Pediatr Hematol Oncol* 2001;18:291-4.