Relapsing Long-Lasting Garcin Syndrome Revealing Skull Base Diffuse B Cell Lymphoma: The Diagnosis through the “Hartel’s Route”

Barbara Casolla¹ Serena Candela¹ Antonio Ciacciarelli¹ Ludovico Ciolli¹ Andrea Romano¹
Michele Acqui¹ Maria Christina Cox² Giuliano Sette¹ Francesco Orzi¹

¹ Department of NESMOS (Neurosciences Mental Health and Sensory Organs), School of Medicine and Psychology, “Sant’Andrea” Hospital, “Sapienza” University of Rome, Rome, Italy

² Department of Hematology, “Sant’Andrea” Hospital, “Sapienza” University of Rome, 00189, Rome, Italy

Address for correspondence Barbara Casolla, MD, Department of NESMOS (Neurosciences Mental Health and Sensory Organs), School of Medicine and Psychology, “Sant’Andrea” Hospital, “Sapienza” University of Rome, Via di Grottarossa 1035-1039, 00189, Rome, Italy (e-mail: barbara.casolla@gmail.com).

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Abstract

The Garcin syndrome is a rare condition characterized by multiple unilateral cranial nerve palsy, without neither long-tract involvement nor intracranial hypertension. Non-Hodgkin lymphoma is a systemic malignant disease that localizes in a minority of cases in the central nervous system. We report a case of Garcin syndrome that revealed a diffuse large B cell lymphoma (DLBCL) located in the skull base and in the right kidney. We reached the diagnosis by mean of a nonstandard, mini-invasive, transforamen *ovale* biopsy of the intracranial lesion (Hartel’s route).

Keywords

- lymphoma
- multicranial neuropathy
- Garcin syndrome
- Hartel’s route biopsy
- neuroimaging

The nature of the renal mass was determined *ex juvantibus*. The patient responded to the polichemotherapy with a complete regression of the intracranial lesion and of the renal mass evaluated by computed tomography and total body positron emission tomography scans. We, therefore, confirmed the DLBCL location in the right kidney. Over 4 years of follow-up, the patient has showed a complete remission of the disease. In this report, we emphasize the importance of biopsy in case of Garcin syndrome.

Introduction

The non-Hodgkin’s lymphoma (NHL) is extranodal and localized in 40% of the cases.¹ In 10% of these cases, it nests in the head and neck,² especially in the clivus, cavernous sinus, or lateral skull. Symptoms result from mass effect.³ Early presentation includes ophthalmoplegia, secondary to abducens palsy. Early involvement of multiple cranial nerve is rare.^{4,5}

We herewith report the case of a patient with subacute Garcin syndrome, caused by diffuse large B cell lymphoma (DLBCL). In 1926, Raymond Garcin described the condition of progressive, unilateral, multiple cranial nerve palsy, without neither long-tract involvement nor intracranial hypertension and with osteoclastic involvement of the skull base on computed tomography (CT).⁶

Case Report

A healthy 69-year-old man suffered from two episodes, within a 9-month span, of hypoglossal palsy associated with mild dysphagia. In both cases, the palsy remitted under steroids treatment. Brain magnetic resonance imaging (MRI) was unremarkable. An acute, progressive involvement of the left side V to XII cranial nerves occurred 6 months after the second hypoglossal palsy. The patient was, therefore, referred to our Neurology Unit. On admission, routine blood tests were normal. Brain MRI showed pathological tissue, spreading from oropharynx to the pontocerebellar angle and compressing the root entry zone of the lower cranial nerves. Temporal, occipital (clivus), and sphenoid bones were partially eroded and the lesion showed pronounced enhancement after gadolinium

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(**Fig. 1**). A lumbar puncture revealed 16 cells/ μ L (20% T lymphocytes, no B cells), normal glucose, and protein cerebrospinal fluid contents. Total body CT scan showed a right renal solid mass (29 $\times$ 28 mm). Histology of the intracranial lesion, from a mini-invasive, transforamen ovale biopsy lesion (Hartel's route, **Box 1**), allowed the diagnosis of DLBCL (CD45, CD79a, and CD20 positive with high MIB-1 index, > 90%). Immunohistochemistry was negative for S100, CK, VIM, CD10, and PgR markers.

The patient underwent polichemotherapy (R-CHOP-21 for six cycles associated with high dose methotrexate for three cycles and intrathecal therapy with methotrexate and aracytin). Following the first cycle, brain MRI showed a significant reduction of both mass volume and contrast enhancement. Total body 18 F-FDG positron emission tomography, performed at the end of chemotherapy, was negative. The 2 months' follow-up total body CT scan demonstrated volumetric reduction of the renal mass (14 $\times$ 25 mm vs. 29 $\times$ 28 mm). Additional scans confirmed progressive reduction of the kidney mass lesion, which was not any more visible, by ultrasound imaging, at the 4-year follow-up. At the

same time, the neuroimaging was also negative and the cranial nerves dysfunction completely resolved.

Discussion

This case reports a few unusual features of the NHL of the skull base. In addition to the rare presentation as Garcin syndrome,^{4,5} the renal localization added uncertainty in the diagnosis. The kidney lesion presented with radiological characteristics of a coincident primary renal tumor. It was the response of the renal mass to chemotherapy that allowed the diagnosis *ex juvantibus* of renal DLBCL. Moreover, the intracranial lesion was characterized by atypically long duration, as signs and symptoms of NHL of the skull base typically do not last more than 4 months.³ Presumably, the long duration was caused by the antilymphoma activity of the steroid treatment.

In most cases, Garcin syndrome is due to extensive malignant tumors of the ear, nose, and throat regions, including paranasal sinuses tumors.^{4,7} The syndrome may also be associated with neurogenic tumors, such as trigeminal schwannoma, invasive meningioma, and other histologic

Fig. 1 Magnetic resonance imaging (MRI) T1-weighted fat-saturated sequences with gadolinium showing: the intracranial lymphoma infiltrating intrapontine and intracisternal portion of left trigeminal nerve up to the Meckel cave (A, curve arrow); left Dorello canal (A, circle); left internal acoustic canal with contrast enhancement of the dura mater (B, arrow); left hypoglossal canal (C, circle); and craniocaudal extension of the tumor (D, arrows). Computed tomography (CT) images showing erosion of the clivus and petrous ridge (E) and microsurgical route through the foramen ovale (F, arrow).

subtypes such as chondrosarcoma, chordoma, and pituitary adenoma.³

Neuroimaging helps clinicians in resolving diagnosis uncertainties. In our case, the occurrence of brain MRI lesion together with the presence of the renal mass raised the hypothesis of intracranial metastasis.⁸ The biopsy, performed through the "Hartel's route" (► **Box 1**), was determinant to disclose the diagnosis of DLBCL. The early diagnosis of an unusual presentation of NHL allowed a prompt treatment and a good long-term outcome, even in a patient presenting with an advanced stage and central nervous system involvement.

BOX 1: Hartel's Route

In 1912, Hartel described an anterior approach to the foramen ovale, passing between the mandible and the pterional wing.⁹ This access allows both biopsying of the cavernous sinus tumor and endoscopic approach to the Gasserian ganglion. Nowadays, the "Hartel's route" is not a standard procedure, as it is at risk to damage life-threatening anatomical structures. In the trajectory, the needle approaches the parotid duct. A lesion on the Stensen duct may result in postoperative hemodialorrhea. Several branches of the maxillary nerve may also be injured, especially the lingual and inferior alveolar nerves and the buccal nerve. Other nerves (buccal, lingual, inferior alveolar, auriculotemporal, zygomatic, glossopharyngeal), as well as vascular structures (internal maxillary artery, middle meningeal artery, internal carotid artery, the internal jugular vein, and the pterygoid venous plexus), are on the needle trajectory.

The approach, however, has several advantages. For instance, the foramen ovale is visualized better than by means of standard procedures,¹⁰ with the relevant advantage of visually adjusting the trajectory to anatomical variants.

Conflict of Interest

None.

Acknowledgments

None.

References

- 1 Armitage JO, Weisenburger DD. New approach to classifying non-Hodgkin's lymphomas: clinical features of the major histologic subtypes. Non-Hodgkin's Lymphoma Classification Project. *J Clin Oncol* 1998;16(08):2780–2795
- 2 Møller MB, Pedersen NT, Christensen BE. Diffuse large B-cell lymphoma: clinical implications of extranodal versus nodal presentation—a population-based study of 1575 cases. *Br J Haematol* 2004;124(02):151–159
- 3 Wang L, Lin S, Zhang J, Wang C. Primary non-Hodgkin's lymphoma of the skull base: a case report and literature review. *Clin Neurol Neurosurg* 2013;115(02):237–240
- 4 Letournel F, Lejeune P, Josselin N, Barthelaix A, Dubas F. Malignant non-Hodgkin lymphoma presenting with Garcin's syndrome [in French]. *Rev Neurol (Paris)* 2004;160(10):952–955
- 5 Nakamura A, Toyoda K, Shozawa Y, Saito-Arai Y, Shimizu T, Matsumura K. Primary non-Hodgkin lymphoma of the skull base presenting with Garcin syndrome: MRI manifestations. *J Neuroimaging* 2009;19(03):295–297
- 6 Guillaing R, Alajouanine T, Garcin R. Le syndrome paralitique unilatéral global des nerfs crâniens [in French]. *Bull Med Hop* 1926;50:456–460
- 7 Hakusui S, Fujishiro K, Takahashi A. An autopsied case of primary epipharyngeal rhabdomyosarcoma presenting Garcin syndrome. *Jpn J Med* 1991;30(04):379–382
- 8 Liu H, Hemminki K, Sundquist J. Renal cell carcinoma as first and second primary cancer: etiological clues from the Swedish Family-Cancer Database. *J Urol* 2011;185(06):2045–2049
- 9 Hartel F. Die Leitungsanästhesie und Injektionsbehandlung des Ganglion Gasserianum und der Trigeminusstämme [in French]. *Arch Clin Chir* 1912;100:193–29
- 10 Messerer M, Dubourg J, Saint-Pierre G, Jouanneau E, Sindou M. Percutaneous biopsy of lesions in the cavernous sinus region through the foramen ovale: diagnostic accuracy and limits in 50 patients. *J Neurosurg* 2012;116(02):390–398