Primary Intracranial Extraskelatal Mesenchymal Chondrosarcoma: Clinical Mimicry as Glomus Jugulare

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Keywords

Extraskelatal mesenchymal chondrosarcoma · Glomus jugulare · Radiosurgery · Gamma knife · Radiation induced malignancy

Abstract

Background: Extraskelatal mesenchymal chondrosarcoma (ESMCS) is an unusual pathologic variant of chondrosarcoma. There are no specific clinicoradiographic parameters to distinguish it from other intracranial pathologies. The diagnosis can be established only on the basis of histopathology, which may pose significant challenges in certain unusual locations. **Purpose:** In this case, we discuss the pitfalls in diagnosis, management, and major characteristics of ESMCS with a review of current literature. **Methods and Results:** A 47-year-old female patient presented with a jugular foramen tumor which was misdiagnosed as glomus jugulare tumor for which she received primary gamma knife radiosurgery at 2 instances. But unfortunately, the patient died because of the increase in size of the lesion associated with necrosis. Autopsy analysis revealed a highly cellular tumor, rich in sarcomatous cells, and well-differentiated cartilages consistent with ESMCS. **Conclusion:** A definite preoperative diagnosis

of ESMCS is crucial though difficult especially when located at complex sites like jugular foramen and clinicoradiological mimicry. The most crucial step in the management of ESMCS is accurate diagnosis with critical evaluation of clinical, radiological, and histopathological parameters and realization of highly variable clinical course of the disease.

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Introduction

Mesenchymal chondrosarcoma (MCS) is a malignant variant of chondrosarcoma that represents 10% of all chondrosarcomas. Unlike other variants, MCS is a fast growing tumor with frequent systemic metastases [1, 2]. Extraskelatal MCS (ESMCS) is an extremely rare variant of MCS with no evidence of any primary intracranial ESMCS till date [3, 4]. We describe our experience with the case of middle-aged female of primary ESMCS, managed as glomus jugulare tumor (GJT) by stereotactic gamma knife radiosurgery (GKRS). The diagnosis could be established only after autopsy of the patient. No ante-mortem confirmation could be done because of the rarity of the tumor, striking clinicoradiological mimicry

Fig. 1. **a** MRI (year 2001) showing contrast enhancing lesion in left jugular foramen with extension into CPA cistern; **b** T2 weighted image showing lesion extension into left CPA cistern and upper carotid space; **c, d** contrast MRI showing inferior extension;

e, f plain axial and coronal CT scan images showing bone destruction with salt and pepper appearance in left CPA region. CPA, cerebellopontine angle.

with GJT and patient's reluctance for any microsurgical intervention. In this paper, we discuss the pitfalls in management of this relatively unknown pathological entity.

Case Summary

History and examination: A 47-year-old female presented in 2001 with pulsatile tinnitus and left-sided hearing loss and involvement of lower cranial nerves for 3 years. Her systemic examination and laboratory investigations were unremarkable.

Radiological findings in 2001, MRI of brain revealed a well-defined dumbbell shaped intensely enhancing jugular foramen lesion of size $3.0 \times 2.9 \text{ cm}^2$ with trans-spatial component in the cerebellopontine angle (CPA) cistern and upper carotid space. Lesion was of variegated intensity on T1- and T2-weighted images with inhomogeneous contrast uptake and no perilesional edema. There was salt and pepper appearance with permeative destruction of

surrounding petrous bone (Fig. 1e, f). Her clinicoradiological profile was consistent with left-sided GJT (Table 1).

Treatment: In view of her reluctance for microsurgical excision, she was treated with primary GKRS at another center (2001). She received 16 Gy radiations with Leksell Gamma Knife B system (Elekta Instruments, Norcross, GA, USA). There was no clinical improvement at 6 months, after which she was lost to follow-up. A decade later, patient presented with complaints of recently worsened tinnitus, sticking of food bolus in the throat and nasal regurgitation. There was no medical record or radiology available for the decade long interval. Repeat MRI (2011) showed the same lesion with no gross change in size or character (Fig. 2a-c). Patient received dose-fractionated GKRS with Leksell Perfexion with marginal dose of 10, 8, and 8 Gy over consecutive 3 days.

Follow-up MRI demonstrated central necrosis in the lesion with relative increase in the size of cisternal component with associated mass effect (Fig. 2d). After 8 months, patient was received in unconscious state (Glasgow Coma Scale E2V2M4) and left hemiparesis. CT imaging of head revealed hypodensity in the left cerebellar hemisphere, with distortion of the brainstem and

Fig. 2. **a–c** Axial, sagittal, and coronal contrast MRI images (year 2011) showing residual lesion in left CPA cistern, jugular foramen and upper carotid space with inhomogeneous contrast uptake; **d** follow-up MRI showing ring enhancing lesion in left cerebellar hemisphere with minimal edema suggestive of radiation

necrosis; **e** plain axial CT scan showing left cerebellar edema with brainstem compression (year 2012); **f** axial CT scan with right ventriculo-peritoneal shunt in situ. CPA, cerebellopontine angle.

Table 1. Differential diagnosis of lesions at jugular foramen

Characteristics	Glomus jugulare tumor	Jugular foramen sarcoma	Jugular foramen meningioma	Jugular foramen cordoma/chondrosarcoma
Incidence in general population	1.2–3 per million population	Uncommon	Rare	Extremely rare
Age: middle aged female	Y	Y	Y	Y
Pulsatile tinnitus	Y	N	N	N
Conductive hearing loss	Y	N	N	N
Bruit over mastoid bone	Y	N	N	N
Destruction of surrounding bone (locally invasive)	Y	N	Y	Y
Enhanced on CEMR	Y	Y	Y	Y
CT-“salt-and-pepper” appearance	Y	N	N	N
Flow voids (highly vascular)	Y	N	N	N
Multicentric	Y	N	N	N
Metastasis	Y	N	N	N

Y, yes; N, no; CEMR, contrast enhanced magnetic resonance.

Fig. 3. a, b Autopsy specimen showing necrotic changes in left cerebellar hemisphere with brainstem compression; **c** radiation induced necrotic changes with micro-hemorrhages in midbrain and pons.

hydrocephalus (Fig. 2e). Patient had transient neurological improvement with CSF diversion (ventriculoperitoneal shunt; Fig. 2f). She gradually deteriorated and died on 8th postoperative day.

Autopsy findings (Fig. 3): Autopsy report was suggestive of gross cerebellar edema and features suggestive of central herniation.

Histopathology report (HPR; Fig. 4): HPR was suggestive of a bimorphic cellular population consisting of highly cellular areas of sarcomatous cells and well-differentiated cartilages. The fascicles were arranged at acute angle to each other in a “Herring bone” pattern. Tumor had indistinct margins showing infiltration into cerebellum and choroid plexus. Surprisingly, there was no pathologic evidence of any glomus tissue or radiation necrosis in the specimen. Immunohistochemically, the cartilaginous portion of the tumor showed strong S100 protein positivity.

Discussion

ESMCS is a rare neoplasm first described in clinical literature in 1959 by Lichenstein and Berstein [3, 4]. There are 2 histological variants, mesenchymal and myxoid, out of which former is rarer, more aggressive, and carries poorer prognosis. In about 30–40% cases, MCS have an extraskeletal origin [1, 3, 4]. The most common sites of origin are long limbs, orbital wall, and rarely spinal meninges. It has also been reported in axil-

lary and shoulder region as isolated case reports [1, 3, 4]. ESMCS is a very rare pathologic entity with no specific clinical or radiologic characteristics to distinguish them from other neoplastic pathologies. For similar reasons, ESMCS was never considered as a differential diagnosis in the present case. On the contrary, the diagnosis of GJT was suspected in view of strong clinico-radiologic appearance of the tumor at the traditional location for glomus (Table 1).

Non-arguably, GJT is primarily a clinical and radiologic diagnosis. Optimal control of GTs is a controversial topic till date. The location of lesion, preoperative symptoms, surgeons' experience, patient's age, and preferences are the guiding factors for treatment. Though surgery provides the best long-term tumor control and definitive diagnosis, it is compounded with significant complications [5, 6]. Literature supports stereotaxic radiosurgery (GKRS) as a primary treatment modality for GJT in elderly population [6–8].

Such a case is a diagnostic dilemma, if the lesion was a primary ESMCS or a radiation-induced sarcoma (RIS) in a GJT. The development of a secondary malignancy after conventional radiotherapy or GKRS is a well-known sinister complication. RISs are a very rare entity (incidence of 0.03–0.8%) and incidence of ESMCS secondary to ra-

Fig. 4. **a** Photomicrograph showing a cartilaginous tumor with primitive component (H&E $\times 100$); **b** primitive hyper chromatic cells showing brisk mitotic activity (H&E $\times 200$); **c** tumor cells infiltrating cerebellar cortex (H&E $\times 40$); **d** tumor cells infiltrating the area adjoining choroid plexus (H&E $\times 400$); **e** diffuse nuclear

immune positivity for S-100 in the cartilaginous cells (H&E $\times 400$) and **f** for CD99 (H&E $\times 200$); **g-i** tumor cells were immune negative for respectively GFAP, CD34, and cytokeratin. GFAP, glial fibrillary acidic protein.

diation is not described till date [1, 3]. Most of the available literature reports RIS in patients with vestibular schwannoma predominantly in neurofibromatosis type 2 or after-fractionated external beam radiotherapy [8, 9], but none after stereotactic radiosurgery. This case partially fulfills the Murray et al. [8] revision of Cahan's criteria of radiation-induced neoplasia [10]: (a) tumor must occur in the radiation field; (b) it cannot be present before irradiation; (c) any primary tumor must differ histologically from the induced tumor; (d) a latency period in the order of months to years; and (e) sarcoma must have arisen in the area included within 5% isodose line. Latent period can vary from 3 to 10 years.

The natural history of ESMC is quite variable with 5 and 10 years survival rates of 56.4 and 27.3%, respectively [1, 3, 4]. Patient should be assessed with a systemic evaluation by skeletal survey and chest X-ray to rule out any lung metastasis. The current management protocol is gross surgical resection with wide optimal margin. There is no proven role of any adjuvant chemo-radiotherapy [1, 3, 4].

In view of its rarity and absence of any characteristic clinicoradiological parameters, diagnosis of ESMCS can be established only on the basis of histopathologic appearance. In this particular case, lack of any pathologic evidence of glomus cells and the presence of cartilaginous tissue in the specimen raises the possibility of "pri-

mary ESMC in situ.” MCS has a characteristic bimorphic cellular population. It consists of both highly cellular areas composed of only cancer cells and other composed of well-differentiated cartilages. Both the populations can be mixed and there may be distinct areas of 2 populations. To identify the lesion as MCS, a pathologist needs to evaluate a population of these 2 appearances on the biopsy specimen. The key is to have an adequate sampling showing both parts of the tumor [1, 3, 4].

Because of the rarity of the tumor, there are no definite treatment guidelines for management of ESMCS. There is no exact correlation between the histological appearance and biological behavior of the tumor, but all should be considered high-grade lesions in view of presence of small round cells.

The most important striking point is probably the difficulty in diagnosing and formulating an effective management plan when such a lesion is encountered in clinical practice. The problem multiplies manifold when it is located in complex locations like jugular foramen as in this case. This is because one has to choose between a surgical vs. non-surgical management, and this is particularly challenging as the pathologies range from much benign tumors like glomus to malignant tumors like ESMCS. In addition, not many clinicians would prefer a pathological diagnosis by surgery or minimal invasive biopsy techniques especially when the differential diagnosis includes vascular tumors like glomus. Hence, a judicious compromise would be to depend upon the clinical and radiological parameters to reach a near conclusive diagnosis.

Conclusion

This case highlights how other jugular foramen tumors and rarely malignant lesions like MCS may mimic a classic clinicoradiologic diagnosis of GJT. It also highlights the pitfalls of using gamma knife without histopathological confirmation. The most crucial step in management of ESMCS is accurate diagnosis with critical evaluation of clinical, radiological, and histopathological parameters.

Acknowledgment

None.

Author Contribution

Rajesh Chhabra has done concept and design, manuscript review, and critical revision. Manjul Tripathi has done concept and design, manuscript preparation and editing, literature search, and revision. Devi Prasad Patra has done manuscript preparation and editing, literature search, and revision. Narendra Kumar and Bishan Radotra have done manuscript editing, critical review. Kanchan Kumar Mukherjee has done concept and design, manuscript editing, critical review, and administrative support.

Disclosure Statement

The authors declare no conflict of interest. This manuscript complied with ICMJE. This study received no funding or sponsorship of any form.

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