

## Case Report

# Malignant Trigeminal Nerve Sheath Tumor and Anaplastic Astrocytoma Collision Tumor with High Proliferative Activity and Tumor Suppressor P53 Expression

Maher Kurdi,<sup>1</sup> Hosam Al-Ardati,<sup>2</sup> and Saleh S. Baeesa<sup>3</sup>

<sup>1</sup> Department of Pathology, Faculty of Medicine, King Abdulaziz University, Jeddah 21589, Saudi Arabia

<sup>2</sup> Department of Pathology, King Faisal Specialist Hospital, Jeddah 21499, Saudi Arabia

<sup>3</sup> Division of Neurosurgery, Faculty of Medicine, King Abdulaziz University, P.O. Box 80215, Jeddah 21589, Saudi Arabia

Correspondence should be addressed to Saleh S. Baeesa; [sbaeesa@kau.edu.sa](mailto:sbaeesa@kau.edu.sa)

Received 15 June 2014; Accepted 30 September 2014; Published 15 October 2014

Academic Editor: Paolo Perrini

Copyright © 2014 Maher Kurdi et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

**Background.** The synchronous development of two primary brain tumors of distinct cell of origin in close proximity or in contact with each other is extremely rare. We present the first case of collision tumor with two histological distinct tumors. **Case Presentation.** A 54-year-old woman presented with progressive atypical left facial pain and numbness for 8 months. MRI of the brain showed left middle cranial fossa heterogeneous mass extending into the infratemporal fossa. At surgery, a distinct but intermingled intra- and extradural tumor was demonstrated which was completely removed through left orbitozygomatic-temporal craniotomy. Histopathological examination showed that the tumor had two distinct components: malignant nerve sheath tumor of the trigeminal nerve and temporal lobe anaplastic astrocytoma. Proliferative activity and expressed tumor protein 53 (TP53) gene mutations were demonstrated in both tumors. **Conclusions.** We describe the first case of malignant trigeminal nerve sheath tumor (MTNST) and anaplastic astrocytoma in collision and discuss the possible hypothesis of this rare occurrence. We propose that MTNST, with TP53 mutation, have participated in the formation of anaplastic astrocytoma, or vice versa.

## 1. Introduction

Collision tumors are defined as two tumors with discrete histology appearing simultaneously and in proximity to each other at the same anatomic location. Such occurrence in the brain is relatively rare and few case reports of primary collision brain tumors were published in the literature, which are summarized in Table 1. The mechanism of this rare entity remains unclear, but some hypotheses for collision tumors were proposed.

Pituitary adenoma and craniopharyngioma in collision is the commonest association, which was recently reviewed by Jin et al., of 14 reported cases [1]. Meningioma is the second frequently reported tumor to collide with another tumor of different cell type, mostly astrocytoma [2–7]. The association of cranial nerve sheath tumor of the trigeminal and acoustic nerves has been reported to collide with epidermoid tumors in the posterior fossa in 3 cases [8–10].

We describe the first report of malignant nerve sheath tumor of the trigeminal nerve in collision with anaplastic astrocytoma of temporal lobe and discuss the possible theory of this rare association.

## 2. Case Presentation

A 54-year-old woman presented with 8-month history of progressive atypical left facial pain and numbness. She had no previous illness, and her elder brother died few years ago from parietal glioblastoma multiforme. General physical examination was unremarkable; there were no cutaneous stigmata of neurofibromatosis. The neurological examination demonstrated facial hypoesthesia in the distribution of the second and third divisions of the trigeminal nerve. The rest of cranial nerves and neurological examination were within normal.

TABLE 1: Reported primary brain collision tumors in the literature.

Author (year) reference	Histological type of collision tumor
Tajika et al. (1989) [11]	Intrasellar gangliocytoma and pituitary adenoma
Kitaoka et al. (1986) [8]	Posterior fossa epidermoid tumor and trigeminal neuroma
Vaquero et al. (1990) [2]	
Dario et al. (1995) [3]	
Hakan et al. (1998) [4]	
Mitsos et al. (2009) [6]	Meningioma and astrocytoma (including glioblastoma)
Prayson et al. (2002) [5]	
Khalatbari et al. (2011) [7]	
Suh et al. (2003) [22]	Suprasellar chordoid glioma and Rathke's cleft cyst
Johnson et al. (2001) [23]	Oligodendrogloma and ganglioglioma
Perry et al. (2001) [24]	Oligodendrogloma and pleomorphic xanthoastrocytoma
Muzumdar et al. (2001) [25]	Pontine glioma and epidermoid tumor
Vajtai et al. (1997) [26]	Pleomorphic xanthoastrocytoma and ganglioglioma
Goodman et al. (1991) [9]	Acoustic schwannoma and epidermoid cyst
Kleinpeter and Koos (1994) [10]	
Basil et al. (2011) [28]	Primary CNS B-cell lymphoma and anaplastic astrocytoma
Jin et al. (2013) [1] (review of 14 cases)	Pituitary adenoma and craniopharyngioma
Woo et al. (2014) [29]	Central neurocytoma and epidermoid tumor
Current case	Trigeminal nerve sheath tumor and anaplastic astrocytoma

Magnetic resonance imaging (MRI) of the brain revealed a  $40 \times 25 \times 40$  mm isointense lesion that enhanced heterogeneously following intravenous Gadolinium administration enhancing lesion in the anterior part of left middle cranial fossa involving the anterior part of the temporal lobe and extends to the infratemporal fossa through foramen ovale (Figures 1, 2, and 3). The tumor had intra-axial enhanced solid and cystic unenhanced components in the left anterior temporal lobe with surrounded vasogenic edema. The radiological findings were likely consistent with trigeminal schwannoma. Surgery was performed via temporal extradural and intradural approach, with neuronavigation guidance, through left orbitozygomatic-temporal craniotomy. The tumor was seen extradurally easily separable from the dura. It was noticed that it is smaller than the expected size from the MRI. The dura was then opened and a striking intra-axial soft tumor was noted in the superior and middle temporal gyri. Complete microsurgical resection, with ultrasonic aspirator, of the intradural portion of the tumor was performed through anterior temporal lobectomy and the dura was closed. The extradural portion was exposed with drilling of middle fossa

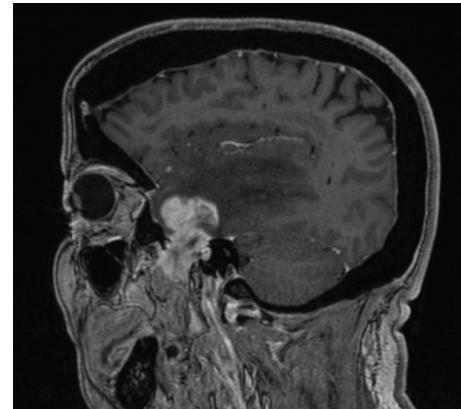


FIGURE 1: Preoperative enhanced parasagittal T1-WI MRI demonstrates extra-axial heterogeneously dumbbell-shaped enhancing tumor in the left middle fossa extending into infratemporal fossa.

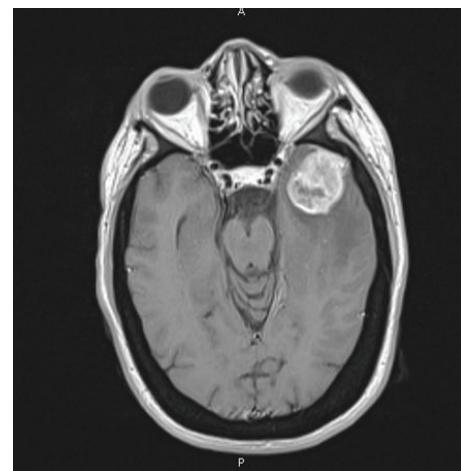


FIGURE 2: Axial T1-WI MRI demonstrating mass effect and infiltration to the temporal lobe with vasogenic edema.

floor into the infratemporal fossa and enlarging foramen ovale laterally. The tumor was encapsulated and removed completely, with ultrasonic aspirator, and few of the involved trigeminal nerve fascicles were sectioned.

Microscopically, the tumor showed two components. The first component of temporal lobe specimen revealed a mitotically active malignant glial neoplasm, with no endothelial proliferations or necrosis (Figure 4). These morphological features were consistent with anaplastic astrocytoma (WHO grade III). Immunohistochemistry study revealed a strong glial fibrillary acidic protein (GFAP) and P53 positivity (Figure 5). Ki-67 proliferative index showed a mild to moderate (5–10% per 10 HPF) proliferation (Figure 6). The second component from the extradural specimen revealed a malignant spindle cell neoplasm arranged in a fascicular pattern and embedded in a loosely textured background, with apparent numerous mitosis and tumor necrosis (Figure 7). Immunohistochemically, the spindle cells were strongly positive for vimentin and S-100 proteins, and apparent P53 expression (Figure 8). Ki-67 proliferative index

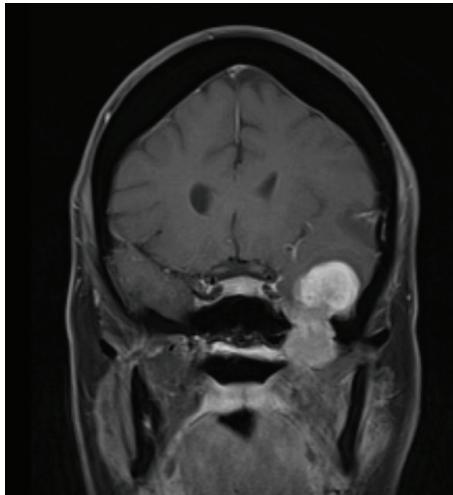


FIGURE 3: Coronal T1-WI MRI demonstrating middle cranial fossa tumor extending to the infratemporal region.

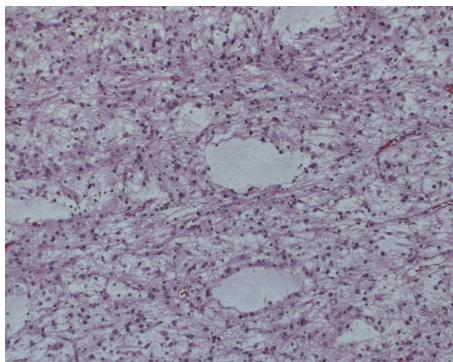


FIGURE 4: Microphotograph shows anaplastic astrocytoma with numerous mitoses (Hematoxylin & Eosin, original magnification  $\times 20$ ).

showed a mild to moderate (5–10% per 10 HPF) proliferation (Figure 9). The final diagnosis was consistent with two coexisting intermingled anaplastic astrocytomas and malignant trigeminal nerve sheath tumor (MTNST).

The patient had uneventful postoperative period, with significant improvement of facial pain. Postoperative brain MRI scans demonstrated a complete resection of both tumors (Figures 10 and 11). After counseling, the patient decided not to receive any further adjuvant therapy. She was readmitted 8 months later for palliative care due to progressive cognitive function decline. Brain MRI scans revealed left temporal leptomeningeal enhancement at resection cavity at the temporal and infratemporal regions, as well as new heterogeneous enhancing lesion at anterior part of corpus callosum; the latter is likely from the anaplastic astrocytoma component (Figure 12). She passed away 9 months from surgery from tumor progression causing raised intracranial pressure and brain herniation.

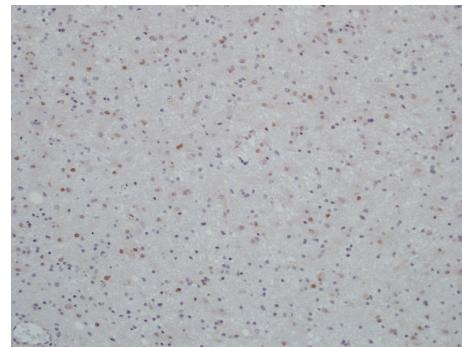


FIGURE 5: Microphotograph demonstrating significant P53 immunopositivity of anaplastic astrocytoma.

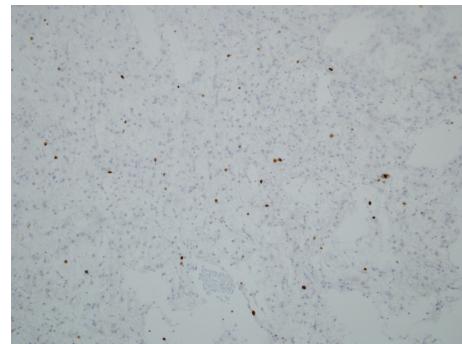


FIGURE 6: Ki 67 proliferative index of 10% per 10 HPF in the anaplastic astrocytoma.

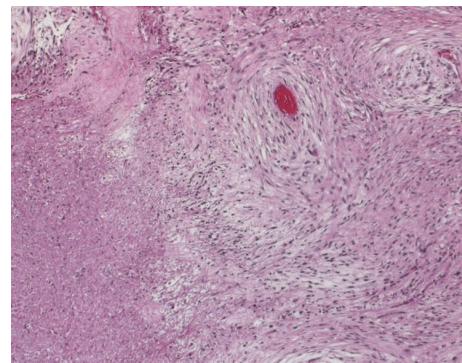


FIGURE 7: Microphotograph shows MTNST with extensive atypia, mitosis, and necrosis (Hematoxylin & Eosin, original magnification  $\times 20$ ).

### 3. Discussion

Collision tumor is described as two tumors with discrete histology occurring simultaneously and in proximity to each other at the same location. Such intracranial occurrence is rare with few reported cases in the literature (Table 1). The mechanism of this entity remains unclear, but some hypotheses were proposed. The observation that a significant number of the reported cases had their tumor localization in juxtaposition raises the possibility that one tumor may act

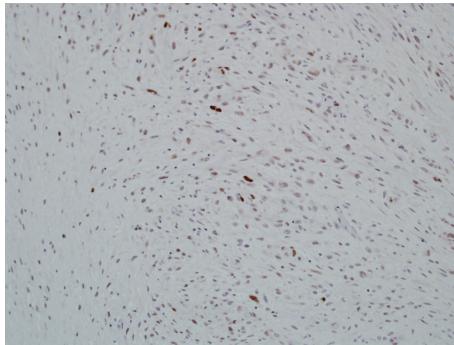


FIGURE 8: *P53* immunopositivity of MTNST was apparent.

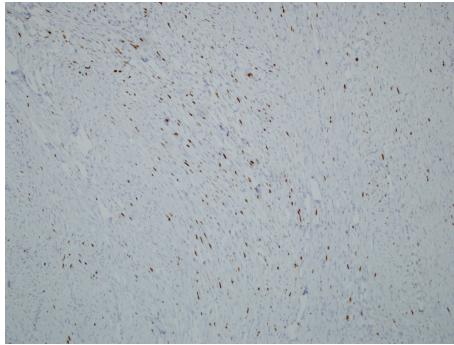


FIGURE 9: Ki 67 proliferative index of 10% per 10 HPF in MTNST.

as an irritating agent for the local proliferation and growth of the other [11]. Surgical trauma, ionizing radiation, and genetic factors may influence tumor development [4]. This theory was suggested in cases where the tumors are adjacent to each other. However, it may not explain why this collision occurred in our rare case making the pathogenesis more complex and multifactorial. Most of reported cases in the literature had reported collision of gliomas and meningiomas [2–7]. Glioma may develop due to neoplastic transformation of the reactive glial cells surrounding a meningioma [5]. This process may be mediated by locally acting oncogenic factors. The most suspected substance is platelet-derived growth factor subunit alpha-R (PDGF-alpha-R), which is the main receptor in astrocytoma [12]. Astrocytoma growth is probably stimulated by PDGF in an autocrine mechanism. It is possible to develop a meningioma as secondary malignant neoplasm due to transformation of the arachnoid cells in response to the growth of a subjacent glioma or after radiation therapy [4].

In our case, we present two different tumors: MTNST and anaplastic astrocytoma presented as collision. MPNSTs are rare malignancies with a reported frequency in the general population of 0.001% [13]. They arise in two principal forms, sporadic (50–70%) and in association with neurofibromatosis type 1 (30–50%) [14]. Unlike other MTNSTs, those involving the trigeminal nerve are not often associated with neurofibromatosis and seem to arise de novo or, rarely, through malignant transformation of preexisting benign Schwannoma [15].



FIGURE 10: Postoperative (24 hr) follow-up T1-WI parasagittal MRI demonstrates complete resection of tumor from the infratemporal region.



FIGURE 11: Postoperative (24 hr) follow-up T1-WI axial MRI demonstrates complete resection of tumor from the middle region.

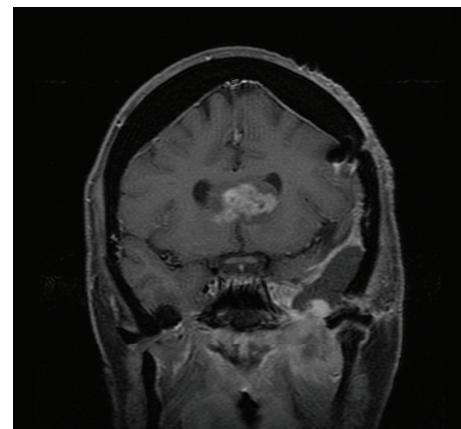


FIGURE 12: Postoperative (8-month) follow-up T1-WI axial MRI demonstrates recurrent local tumor, likely from anaplastic astrocytoma component, and distant spread to the anterior part of corpus callosum.

Trigeminal nerve tumors can occur in the posterior fossa, the middle fossa, or extend into multiple cranial fossae. There are 20 cases of MTNSTs reported in literatures since 1978 in which one of them was associated with neurofibromatosis while some cases had extracranial component, and none of them was associated with another different brain tumor [13–18]. Our case is unusual; the patient had MTNST with no history of neurofibromatosis, tumor extended extracranially into the infratemporal region through foramen ovale, and it was intermingled with anaplastic astrocytoma of temporal lobe, which has not, to our knowledge, has been reported as a collision tumor.

Schwannoma classically appears on MRI hypointense in T1 images and hyperintense on T2 images, with marked enhancement after gadolinium administration. The schwannoma in our patient was described as an extra-axial lesion in the left middle temporal fossa, continuous in a dumbbell-shaped fashion to infratemporal region. It was hypointense in T1- and hyperintense in T2- weighted images and enhanced significantly after Gadolinium administration. There was an intermingled cystic component in the left anterior temporal lobe region with surrounded vasogenic edema intermingled with the tumor.

Malignant peripheral nerve sheath tumors (MPNST) histologically consists of a mixture of plump spindle cells with large hyperchromatic pleomorphic nuclei [19]. Numerous mitotic figures, necrosis and epineurial invasion, may help to confirm the diagnosis. Our patient showed identical histopathological features of MPNST in the first tumour specimen. We performed immunohistochemical studies for P53, which revealed marked expression in more than 50% of tumor cells of both malignant neoplasms in our case. Tumor suppressor P53 is a protein, encoded by TP53 gene, is crucial in multicellular organisms, where it regulates the cell cycle, and, thus, functions as a tumor suppressor, inducing apoptosis and preventing cancer. When P53 immunostain is positive, it means that the tumour may have TP53 gene mutation. This component might be derived from a single precursor cell that undergoes divergent differentiation in the evolution of the tumor. However, the observed overexpression of the gene product, possibly the reflection of the TP53 gene mutation, suggests a role for a P53 in the proliferation of glial cells from anaplastic glioma and vice versa. There was one reported case in the literature of a P53 expression in MPNST and neurofibroma in which the possible role of the P53 in the progression of neurofibroma to MPNST was suggested [20].

Total tumor excision is the preferred treatment option in these cases, and radiosurgery is usually given as adjuvant therapy for malignant or residual or recurrent benign tumors [19]. MTNST carries a poor prognosis having a local recurrence rate of 54% and a 5-year survival rate of 34% [21]. Ki 67 proliferative index is a strong predictor factor in MTNST. Moderate to high Ki 67 proliferative index predicts a reduced survival rate. Our case showed mild to moderate proliferative activity of 10% in both tumors.

The patient had an uneventful recovery of her symptoms within 2 months from surgery. She refused to receive any adjuvant therapy due to her brother's death from glioblastoma. She presented with acute confusion, 9 months after

surgery, and MRI showed local recurrence from both tumors and distant recurrence at the corpus callosum, which was believed from the anaplastic astrocytoma. She died from progressive raised intracranial pressure due to severe tumoral edema. Autopsy examination was not performed in respect to family decision.

#### 4. Conclusion

We herein for the first time report MTNST and anaplastic astrocytoma in collision with similar proliferative activity and TP53 mutation which may have induced the malignant features of the first and may have played part of the proliferation of the latter, or vice versa.

#### Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

#### References

- [1] G. Jin, S. Hao, J. Xie, R. Mi, and F. Liu, "Collision tumors of the sella: coexistence of pituitary adenoma and craniopharyngioma in the sellar region," *World Journal of Surgical Oncology*, vol. 11, article 178, 2013.
- [2] J. Vaquero, S. Coca, R. Martínez, and C. Jiménez, "Convexity meningioma and glioblastoma in collision," *Surgical Neurology*, vol. 33, no. 2, pp. 139–141, 1990.
- [3] A. Dario, A. Marra, M. Cerati, C. Scamoni, and A. Dorizzi, "Intracranial meningioma and astrocytoma in the same patient. Case report and review of the literature," *Journal of Neurosurgical Sciences*, vol. 39, no. 1, pp. 27–35, 1995.
- [4] T. Hakan, S. Armagan, F. V. Aker, and L. Celik, "Meningioma and glioblastoma adjacent in the brain," *Turkish Neurosurgery*, vol. 8, no. 1-2, pp. 57–60, 1998.
- [5] R. A. Prayson, S. Chowdhary, S. Woodhouse, M. Hanson, and S. Nair, "Collision of a syncytial meningioma and malignant astrocytoma," *Annals of Diagnostic Pathology*, vol. 6, no. 1, pp. 44–48, 2002.
- [6] A. P. Mitsos, E. A. Kostantinou, and T. G. Fotis, "Sphenoid wing meningioma and glioblastoma multiforme in collision: a case report with review of the literature," *Polish Journal Neurology Neurosurgery*, vol. 43, no. 5, pp. 479–483, 2009.
- [7] M. Khalatbari, H. Borghei-Razavi, N. Shayanfar, A. H. Behzadi, and A. Sepehrnia, "Collision tumor of meningioma and malignant astrocytoma," *Pediatric Neurosurgery*, vol. 46, no. 5, pp. 357–361, 2011.
- [8] K. Kitaoka, H. Abe, K. Tashiro, T. Kawamoto, and K. Miyasaka, "The coexistence of basal epidermoid tumor and trigeminal neurinoma within the posterior fossa," *No Shinkei Geka*, vol. 14, no. 10, pp. 1243–1248, 1986.
- [9] R. R. Goodman, R. A. A. Torres, and J. G. McMurtry III, "Acoustic Schwannoma and epidermoid cyst occurring as a single cerebellopontine angle mass," *Neurosurgery*, vol. 28, no. 3, pp. 433–436, 1991.
- [10] G. Kleinpeter and W. Koos, "Another case of acoustic schwannoma and epidermoid cyst occurring as a single cerebellopontine angle mass: possibly not so rare?" *Surgical Neurology*, vol. 41, no. 4, pp. 310–312, 1994.

- [11] Y. Tajika, O. Kubo, M. Takeshita, T. Tajika, T. Shimizu, and K. Kitamura, "An intracranial collision tumor composed of intrasellar gangliocytoma and pituitary adenoma," *No Shinkei Geka*, vol. 17, no. 12, pp. 1181–1186, 1989.
- [12] T. Tokunaga, M. Shigemori, M. Hirohata, Y. Sugita, J. Miyagi, and S. Kuramoto, "Multiple primary brain tumors of different histological types. Report of two cases," *Neurology Medicine Surgery*, vol. 31, no. 3, pp. 141–145, 1991.
- [13] J. A. Rodríguez, T. R. Hedges III, C. B. Heilman, M. B. Strominger, and N. M. Laver, "Painful sixth cranial nerve palsy caused by a malignant trigeminal nerve sheath tumor," *Journal of Neuro-Ophthalmology*, vol. 27, no. 1, pp. 29–31, 2007.
- [14] J. A. Stone, H. Cooper, M. Castillo, and S. K. Mukherji, "Malignant schwannoma of the trigeminal nerve: case report," *American Journal of Neuroradiology*, vol. 22, no. 3, pp. 505–507, 2001.
- [15] Y. Horie, S. Akagi, K. Taguchi et al., "Malignant schwannoma arising in the intracranial trigeminal nerve: a report of an autopsy case and a review of the literature," *Acta Pathologica Japonica*, vol. 40, no. 3, pp. 219–225, 1990.
- [16] F. B. Maroun, M. Sadler, G. P. Murray et al., "Primary malignant tumours of the trigeminal nerve," *Canadian Journal of Neurological Sciences*, vol. 13, no. 2, pp. 146–148, 1986.
- [17] S. Chibbaro, P. Herman, M. Povlka, and B. George, "Malignant trigeminal schwannoma extending into the anterior skull base," *Acta Neurochirurgica*, vol. 150, no. 6, pp. 599–604, 2008.
- [18] A. Akhaddar, B. El Mostarchid, I. Zrara et al., "Intracranial trigeminal neuroma involving the infratemporal fossa: case report and review of the literature," *Neurosurgery*, vol. 50, no. 3, pp. 633–638, 2002.
- [19] L. Zhang, Y. Yang, S. Xu, J. Wang, Y. Liu, and S. Zhu, "Trigeminal schwannomas: a report of 42 cases and review of the relevant surgical approaches," *Clinical Neurology and Neurosurgery*, vol. 111, no. 3, pp. 261–269, 2009.
- [20] K. C. Halling, B. W. Scheithauer, A. C. Halling et al., "p53 Expression in neurofibroma and malignant peripheral nerve sheath tumor: an immunohistochemical study of sporadic and NF1-associated tumors," *American Journal of Clinical Pathology*, vol. 106, no. 3, pp. 282–288, 1996.
- [21] M. Samii, M. M. Migliori, M. Tatagiba, and R. Babu, "Surgical treatment of trigeminal schwannomas," *Journal of Neurosurgery*, vol. 82, no. 5, pp. 711–718, 1995.
- [22] Y.-L. Suh, N. R. Kim, J.-H. Kim, and S.-H. Park, "Suprasellar chordoid glioma combined with Rathke's cleft cyst," *Pathology International*, vol. 53, no. 11, pp. 780–785, 2003.
- [23] M. D. Johnson, M. T. Jennings, and S. A. Toms, "Oligodendroglial ganglioglioma with anaplastic features arising from the thalamus," *Pediatric Neurosurgery*, vol. 34, no. 6, pp. 301–305, 2001.
- [24] A. Perry, B. W. Scheithauer, D. M. Szczesniak, J. L. D. Atkinson, J. T. Wald, and J. E. Hammak, "Combined oligodendrogloma/pleomorphic xanthoastrocytoma: a probable collision tumor: case report," *Neurosurgery*, vol. 48, no. 6, pp. 1358–1361, 2001.
- [25] D. P. Muzumdar, A. Goel, and K. I. Desai, "Pontine glioma and cerebellopontine angle epidermoid tumour occurring as collision tumours," *British Journal of Neurosurgery*, vol. 15, no. 1, pp. 68–71, 2001.
- [26] I. Vajtai, Z. Varga, and A. Aguzzi, "Pleomorphic xanthoastrocytoma with gangliogliomatous component," *Pathology Research and Practice*, vol. 193, no. 9, pp. 617–621, 1997.
- [27] A. J. Evans, I. Fayaz, M. D. Cusimano, N. Laperriere, and J. M. Bilbao, "Combined pleomorphic xanthoastrocytoma-ganglioglioma of the cerebellum," *Archives of Pathology and Laboratory Medicine*, vol. 124, no. 11, pp. 1707–1709, 2000.
- [28] I. Basil, K. Ru, C. Pu, J. Silverman, and K. Jasnosz, "A collision tumor: primary central nervous system B-cell lymphoma and anaplastic astrocytoma," *Laboratory Medicine*, vol. 42, no. 6, pp. 324–328, 2011.
- [29] P. Y. M. Woo, H. H. Cheung, C. H. K. Mak et al., "Central neurocytoma and epidermoid tumor occurring as collision tumors: a rare association," *Open Journal of Modern Neurosurgery*, vol. 4, pp. 31–35, 2014.

