**Case Report**

**Brainstem intraparenchymal schwannoma: A case report and literature review**

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**ABSTRACT**

**Background:** Intracranial intraparenchymal schwannomas (IS) are rare tumors that have mainly been described in case reports. Here, we report on a case of a brainstem IS and included a comprehensive literature review.

**Case Description:** A 74-year-old man presented with progressive gait disturbances. CT- and MRI-imaging revealed a contrast-enhancing mass accompanied by a cyst in the dorsolateral pons. Hemangioblastoma was suspected and surgery was advised. During surgery, gross total resection of a non-invasive tumor was performed. Postoperative recovery was uneventful. Based on histopathological examination, the intraparenchymal brainstem tumor was diagnosed as schwannoma.

**Conclusion:** Our extensive review illustrates that ISs are benign tumors that most often present in relatively young patients. Malignant cases have been described but form an extremely rare entity. Preoperative diagnosis based on radiological features is difficult but should be considered when peritumoral edema, calcifications, and cysts are noted. In benign cases, gross total resection of the lesion is curative. To adequately select this treatment and adjust the surgical strategy accordingly, it is important to include IS in the preoperative differential diagnosis when the abovementioned radiological features are present.

**Keywords:** Brainstem, Case report, Intraparenchymal, Review, Schwannoma, Tumor

**INTRODUCTION**

Schwannomas are tumors that originate from Schwann cells, which form the myelin sheath of peripheral nerves.[¹] Intracranial schwannomas comprise around 8% of all primary brain tumors, with the vast majority arising from the cranial nerves.[²,³] Less than 1% of intracranial schwannomas are located within the brain parenchyma.[¹,⁴] The first case of intraparenchymal schwannoma (IS) was described by Gibson et al. in 1966.[⁵] Their histogenesis remains speculative, and radiological and histopathological diagnosis can be extremely difficult. Here, we present a case of a brainstem IS and included a comprehensive review on IS to shed light on the clinical, radiological, and histopathological characteristics.
CASE REPORT

A 74-year-old man with no reported prior medical condition presented with progressive gait disturbances and hearing loss that had developed over a few months. Neurological examination revealed sensory asymmetry in the left upper and middle trigeminal branch areas, broad-based gait, diplopia, dysphagia, and dysarthric speech. Imaging studies showed a cystic tumor in the left dorsolateral pons [Figure 1]. A pontine hemangioblastoma was suspected and surgery was recommended.

A left-sided suboccipital retrosigmoid craniotomy was performed [Video 1]. Intra-operative monitoring of trigeminal, facial, and vestibulocochlear nerve was used. An opaque aspect of the dorsolateral pons was noted and punctured, relieving a yellowish fluid. The solid mass consisted of flakey grey-yellowish tissue that was not invasive into the surrounding brain. Intraoperatively, the tumor resembled a pilocytic astrocytoma more than a hemangioblastoma. Gross total resection was performed.

Postoperatively, all symptoms had alleviated and hearing had subjectively returned to normal. The direct postoperative MRI showed a small dorsomedial remnant. Radiological follow-up after 1 year was agreed upon.

Histological assessment of the tumor sections showed clusters of spindle cells surrounded by fascicles and palisades in addition to thick-walled vessels [Figure 2a]. Some paucicellular areas were present, but no typical cystic spaces. Additional immunohistochemical examination exhibited positivity for S-100 protein, pericellular collagen IV basement membrane staining, and in some areas scattered few neurofilament (NF2F11) positive intratumoral axons [Figure 2b-d]. GFAP glial marker was negative, and MIB-1 proliferative activity was only 2%. The final histopathological diagnosis was IS Grade I. No clinical signs nor family history of neurofibromatosis (NF) was reported.

DISCUSSION

ISs are rare intracranial intra-axial tumors. We have found 150 cases reporting on histopathological confirmed IS [Table 1]. Intraventricular or schwannomas with dural attachment were excluded from our review as they form a different entity with an extra-axial origin. Based on our literature review, we will discuss characteristics of the clinical presentation, histogenesis, radiological features, histopathological findings, treatment, and prognosis of IS.

Clinical characteristics

ISs present at a relatively young age, with a majority occurring before the age of 30 and a slight male predominance [Table 2]. Around 65% of these tumors were located supratentorially and 35% infratentorially. The frontal lobe was most frequently affected [Table 3]. Only six cases of patients older than 70 years have been reported. Furthermore, we found only nine cases with pontine IS. This makes our case on a 74-year-old with a pontine IS unique.
Kovalainen, et al.: Brainstem intraparenchymal schwannoma: A case report and literature review

The mass lesion and cyst wall may indicate the relative rarity of ISs is in this latter theory explained by the intraparenchymal Schwann cells originate from the perivascular nerve plexus of parenchymal arterioles. Various theories have been proposed to explain the origin of IS. Menkü et al. differentiated these theories into developmental and non-developmental theories. Various theories have been proposed to explain the origin of IS. Menkü et al. differentiated these theories into developmental and non-developmental theories. According to the developmental theory, a distorted embryogenesis forms the source of aberrant foci of Schwann cells in the brain parenchyma. These foci may originate from transformation of developed mesenchymal pial cells into Schwann cells, differentiation of multipotential mesenchymal elements into Schwann cells, ectopic migration of neural crest cells forming foci of Schwann cells, or misplaced myelinated nerve fibers. The non-developmental theory suggests that the intraparenchymal Schwann cells originate from the perivascular nerve plexus of parenchymal arterioles. The relative rarity of ISs is in this latter theory explained by considering the relative amounts of peripheral as opposed to parenchymal myelinated peripheral nerve plexus.

In our case, one could suggest a relation of the tumor with Schwann cells of the trigeminal nerve. However, the radiological findings suggested an intraparenchymal origin of the tumor as there was no border between the brainstem and the tumor. In addition, the tumor was located within the brainstem parenchyma as observed intraoperatively. If the tumor was related to trigeminal nerve Schwann cells, one would have expected a capsule between the Schwannoma and the brainstem which was not apparent in this case. Since the intraparenchymal myelin covering of the trigeminal nerve is dependent on astrocytes, and not Schwann cells, it is unlikely that the tumor is directly related to the trigeminal nerve.

**Radiological features**

Diagnosis of IS based on preoperative radiological examinations is difficult. Our review revealed that a wide variety of differential diagnoses were suspected preoperatively and IS was not considered in any of these cases (Table 1). CT-images of the brain may show a hypodense and sometimes hyperdense mass with occasional cysts, calcifications, and peritumoral edema. The mass lesion and cyst wall may enhance following contrast administration. ISs usually appear hypointense and hyperintense on T1-weighted and T2-weighted MRI sequences, respectively. (The solid portion and cyst wall usually show homogeneous enhancement with gadolinium.) It is noteworthy that peritumoral edema, cyst formation and calcifications are commonly reported characteristics of IS, yet they lack specificity.

In contrast, cranial nerve Schwannomas are radiologically characterized by a heterogeneous hyperintensity in T2-weighted images, with deformation of adjacent parenchyma, neural cisterns and bony foramina, and have a clear relation to a cranial nerve. Moreover, cranial nerve Schwannomas usually have a well delineated margin from the brainstem parenchyma and cause minimal peritumoral edema.

**Histopathological findings**

Histological evaluation of IS shows a typical biphasic tissue pattern of Antoni type A and B areas. It remains however difficult to differentiate IS from other tumors without immunohistochemical examination. As there are no schwannoma-specific immunohistochemical markers to date, several markers should be included to differentiate schwannomas from other tumors. Schwannomas show a strong diffuse reactivity to S-100 protein and vimentin filament. There is usually no reactivity for GFAP, EMA, CD34 on endothelial cells or α-SMA, excluding glial tumors, meningiomas, solitary fibrous tumors, and smooth muscle cell tumors, respectively. The combination of histological analysis and immunohistochemical reactivity findings is required to make a definite diagnosis of IS. Malignant IS,
| Authors and year                      | Sex | Age | Symptoms                                      | Site of lesion                     | Radiological diagnosis  | Treatment                  | Histological diagnosis       | IHC confirmed di... |
|--------------------------------------|-----|-----|-----------------------------------------------|------------------------------------|------------------------|---------------------------|-----------------------------|--------------------------|
| Gibson et al., 1966                  | M   | 6   | Seizures                                      | Temporal                           | N.A.                    | CR                        | Ye s (EM: fibrillary basement membranes) | No                        |
| New, 1972                            | M   | 8   | Seizures, headache, vomiting                  | Parietal                           | Glioma                  | CR                        | Ye s                        | No                       |
| Ghatak et al., 1975                  | F   | 63  | Seizures, hemiparesis                          | Parietal                           | N.A.                    | Resection                 | N.A.                        | N.A.                     |
| Pialat et al. 1975                   |     |     |                                               | Frontal                            | N.A.                    | N.A.                      | N.A.                        | N.A.                     |
| Van Rensburg et al., 1975            | M   | 21  | Seizures, headache                            | Temporal                           | Glioma or calcified hamartoma | CR                        | Ye s                        | No                       |
| Hahn and Netsky., 1977               | M   | 26  | Headache, visual impairment                   | Frontal                            | N.A.                    | STR                       | Ye s                        | No                       |
| Komminoth et al., 1977               | M   | 15  | Cerebellar signs, headache                     | Cerebellar                         | N.A.                    | STR                       | Ye s                        | N.A.                     |
| Russel and Rubinstein, 1979          | M   | 26  | N.A.                                          | Frontal                            | N.A.                    | N.A.                      | N.A.                        | N.A.                     |
| Prakash et al., 1980                 | F   | 14  | Abducent and facial nerve palsy, tinnitus     | Pons                               | N.A.                    | STR                       | Ye s (GFAP -)               | No (EM: fibrillary basement membranes) |
| Vassilouthis and Richardson, 1980    | M   | 17  | Behavioral problems, headache, vomiting, confusion | Frontal                           | Meningioma              | CR                        | Ye s                        | No                       |
| Kasantikul et al., 1981              | M   | 23  | Schizophrenia                                  | Parietal                           | Metastasis              | GTR                       | Ye s                        | No (EM: fibrillary basement membranes) |
|                                       | M   | 21  | Seizures                                      | Temporal                           | N.A.                    | Temporal lobectomy        | Ye s                        | No (EM: fibrillary basement membranes) |
| Auer et al., 1982                     | M   | 15  | SAH                                           | Frontal                            | N.A.                    | STR                       | Ye s                        | No (EM: fibrillary basement membranes) |
| Shalit et al., 1982                   | F   | 29  | Headache, visual impairment, syncope           | Parieto-occipital                  | Astrocytoma             | Resection                 | Ye s                        | No                       |
| Doi et al., 1983                      | M   | 23  | Headache, vomiting, vertigo                    | 2 cerebellar and 4 cerebral lesions | CR (cerebellar lesions) | CR                        | Yes, malignant             | N.A. (NF1)               |
| Bruner et al., 1984                   | M   | 18  | Syncope                                        | Frontal                            | N.A.                    | GTR                       | Ye s                        | No                       |
| Bruni et al., 1984                    | M   | 39  | Seizures                                      | Frontal                            | N.A.                    | CR                        | Ye s                        | No                       |
| Gökay et al., 1984                    | F   | 16  | Seizures, hemiparesis                          | Frontotemporal                     | N.A.                    | STR, later CR             | Ye s (EM: fibrillary basement membranes) | No (EM: fibrillary basement membranes) |
| (Contd...)                            |     |     |                                               |                                    |                        |                           |                             |                          |
| Authors and year            | Sex and Age | Symptoms                                                                 | Site of lesion            | Radiological diagnosis | Treatment                                                                 | Histological diagnosis | IHC confirmed diagnosis | Additional findings       |
|-----------------------------|-------------|---------------------------------------------------------------------------|---------------------------|------------------------|---------------------------------------------------------------------------|-------------------------|--------------------------|--------------------------|
| Rodriquez-Salazar et al., 1984 | F, 10       | Seizures                                                                 | Frontal                   | N.A.                   | Frontal lobectomy                                                         | Yes                     | No (EM: fibrillary basement membranes) |                          |
| Kuhn et al., 1985 [abstract only] | E, 42       | N.A.                                                                     | Cerebellar                | N.A.                   | N.A.                                                                      | N.A.                   | N.A.                     |                          |
| Stefanko et al., 1986       | M, 15       | Headache, vomiting                                                       | Parieto-occipital         | N.A.                   | CR and RT, later re-resection                                             | Yes, malignant          | Yes (S-100 +)            | Recurrence, died 9 months postop |
| Sarkar et al., 1987         | M, 24       | Headache, vomiting, diplopia, visual impairment, gait disturbance         | Cerebellar                | N.A.                   | CR                                                                        | Yes                     | Yes (S-100 +, GFAP -)       |                          |
| Solomon et al., 1987        | M, 69       | Hemiparesis                                                              | Medulla oblongata and cervical medulla | N.A.                   | GTR                                                                       | Yes                     | No (S-100 -)              |                          |
| Aryanpur and Long., 1988    | E, 50       | Headache, vomiting, diplopia, facial numbness                            | Medulla oblongata         | Cystic glioma          | CR                                                                        | Yes                     | Yes (S-100 +, GFAP -)       |                          |
| Ben Rhouma et al., 1988 [abstract only] | E, 13       | ICP complaints                                                           | N.A.                     | N.A.                   | N.A.                                                                      | Yes                     | N.A.                     | Recurrence               |
| Cervoni et al., 1988 [abstract only] | E, 61       | Hemiparesis                                                              | Parieto-occipital         | N.A.                   | CR                                                                        | Yes                     | N.A.                     | NF1                      |
| Ng and South, 1988          | F, 42       | Headache                                                                 | Temporal                  | N.A.                   | N.A.                                                                      | N.A.                   | N.A.                     |                          |
| Schwartz and Sotrel, 1988   | M, 48       | Headache, sensory complaints                                             | Cerebellar                | N.A.                   | CR                                                                        | Yes                     | N.A.                     |                          |
| Benazza et al., 1989 [abstract only] | M, 8        | N.A.                                                                     | Cerebellar                | N.A.                   | N.A.                                                                      | N.A.                   | N.A.                     |                          |
| Ladoucœur et al., 1989      | E, 46       | Visual impairment, dysarthria, dysphagia                                 | Pons                      | N.A.                   | STR                                                                       | Yes                     | Yes (S-100 +, GFAP -)       |                          |
| Wilberger, 1989             | E, 62       | Headache                                                                 | Intrasellar               | Pituitary tumor        | Transsphenoidal STR followed by transcranial GTR                          | Yes                     | No                       | Second surgery for residual tumor |
| Redekop et al., 1990        | M, 7        | Ophthalmoplegia and facial nerve palsy                                   | Pons / 4th ventricle      | Glioma, ependymoma     | STR                                                                       | Yes                     | Yes (S-100 +, Vimentin +, GFAP -) |                          |
| Tran-Dinh et al., 1991 [abstract only] | E, 64       | N.A.                                                                     | Cerebellar and brainstem  | N.A.                   | Resection                                                                | N.A.                   | N.A.                     |                          |
| Authors and year          | Sex and Age | Symptoms                      | Site of lesion | Radiological diagnosis | Treatment | Histological diagnosis | IHC confirmed diagnosis | Additional findings       |
|---------------------------|-------------|-------------------------------|----------------|------------------------|-----------|------------------------|-------------------------|--------------------------|
| Bando et al., 1992        | F, 55       | Visual impairment, anosmia    | Frontal        | N.A.                   | CR        | Yes                    | Yes (S-100 +)            | Re-resection             |
| Ezura et al., 1992        | F, 13       | Seizures                      | Frontal        | N.A.                   | CR        | Yes                    | Yes (S-100 +, Vimentin +, GFAP -, EMA -) |                         |
| Frim et al., 1992         | F, 11       | Seizures                      | Temporal       | N.A.                   | GTR       | Yes                    | Yes (S-100 +, Vimentin +) |                         |
| Ghosh and Chandy, 1992    | M, 27       | Seizures, hemiparesis         | Frontal        | N.A.                   | CR        | Yes                    | Yes (S-100 +, Vimentin +) |                         |
| Casadei et al., 1993      | M, 16       | Asymptomatic                  | Temporal       | N.A.                   | CR        | Yes                    | Yes (S-100 +, GFAP -, EMA -) |                         |
|                           | M, 17       | Seizures                      | Temporal       | N.A.                   | STR       | Yes                    | Yes (S-100 +, GFAP -, EMA -) |                         |
|                           | M, 21       | Seizures                      | Parietal       | N.A.                   | CR        | Yes                    | Yes (S-100 +, GFAP -, EMA -) |                         |
|                           | F, 23       | Headache                      | Temporal       | N.A.                   | CR        | Yes                    | Yes (S-100 +, GFAP -, EMA -) |                         |
|                           | F, 49       | Headache                      | Temporal       | N.A.                   | CR        | Yes                    | Yes (S-100 +, GFAP -, EMA -) |                         |
|                           | F, 52       | Headache, hemiparesis         | Cerebellar     | N.A.                   | CR        | Yes                    | Yes (S-100 +, GFAP -, EMA -) |                         |
|                           | M, 55       | Headache                      | Cerebellar     | N.A.                   | CR        | Yes                    | Yes (S-100 +, GFAP -, EMA -) |                         |
|                           | F, 79       | Ataxia                        | Cerebellar     | N.A.                   | STR       | Yes                    | Yes (S-100 +, GFAP -, EMA -) |                         |
|                           | F, 84       | Mental change, hemiparesis    | Temporal       | N.A.                   | STR       | Yes                    | Yes (S-100 +, GFAP -, EMA -) |                         |
| Sharma and Newton, 1993   | M, 18       | Hemiparesis                   | Brainstem      | Glioma                 | RT followed by STR | Yes | Yes (S-100 +) | No improvement after RT |
| Sharma et al., 1993       | F, 73       | Gait disturbance, headache, vomiting | Brainstem | N.A. | GTR | Yes | Yes (S-100 +, GFAP -, EMA -) |                         |
| Singh et al., 1993        | F, 61       | Headache, vomiting, gait disturbance | Cerebellar | N.A. | GTR | Yes, malignant | Yes (S-100 +, GFAP -) | Recurrence, died 18 months postop |
| Weiner et al., 1993       | M, 61       | Facial nerve palsy and spasm, gait disturbance, headache | Brainstem | Glioma, epidermoid, arachnoid cyst | STR | Yes | No |                         |
|                           | F, 78       | Facial nerve spasm, diplopia  | Brainstem      | Ependymoma, glioma, plexus papilloma | STR | Yes | Yes (S-100 +, GFAP -) |                         |
| Authors and year | Sex and Age | Symptoms | Site of lesion | Radiological diagnosis | Treatment | Histological diagnosis | IHC confirmed diagnosis | Additional findings |
|-----------------|-------------|----------|----------------|------------------------|-----------|-----------------------|------------------------|---------------------|
| Deogaonkar et al., 1994 | F, 45 | Visual impairment | Frontal | Meningioma | CR | Yes | No | |
| Di Biasi et al., 1994 [abstract only] | M, 19 | N.A. | N.A. | Glioma | N.A. | Yes | N.A. | |
| Ranjan et al., 1995 | F, 65 | Vomiting, gait disturbance | Cerebellar | N.A. | CR | Yes | Yes (S-100 +) | Melanotic schwannoms |
| Blömer et al., 1996 | M, 8 | Hemiparesis | Frontal | N.A. | CR | Yes | Yes (S-100 +, GFAP +) | |
| Erongun et al., 1996 | F, 4 | Headache, vomiting | Parieto-occipital | Plexus papilloma | STR followed by CR | Yes | No | 2nd surgery for residual tumor |
| Sharma et al., 1996 | F, 19 | Hemiparesis | Occipital | N.A. | CR | Yes | Yes (S-100 +, GFAP -) | |
| | M, 8 | Seizures | Temporal | N.A. | CR | Yes | Yes (S-100 +, GFAP -) | NF2 |
| | F, 0.5 | Seizures, hemiparesis, vomiting | Temporal | N.A. | CR | Yes | Yes (S-100 +, GFAP -) | |
| | M, 21 | Seizures, headache, vomiting | Frontal | N.A. | CR | Yes | Yes (S-100 +, GFAP -) | |
| | M, 14 | Visual impairment, gait disturbance | Brainstem | N.A. | STR | Yes | Yes (S-100 +, GFAP -) | |
| | M, 45 | Headache, vomiting | Cerebellar | N.A. | CR | Yes | Yes (S-100 +, GFAP -) | |
| | M, 24 | Headache, vomiting, gait disturbance | Cerebellar | N.A. | CR | Yes | Yes (S-100 +, GFAP -) | |
| | M, 14 | Abducent and facial palsy | Pons | N.A. | CR | Yes | Yes (S-100 +, GFAP -) | |
| Tanabe et al., 1996 | F, 68 | Hemiparesis, diplopia | Pons | HGG | CR | Yes | Yes (S-100 +, GFAP -, EMA -) | |
| Haga et al., 1997 | F, 15 | Seizures | Parieto-occipital | HGG | CR | Yes | Yes (S-100 +, GFAP -) | |
| Tsuiki et al., 1997 | M, 17 | Seizures | Frontal | N.A. | CR | Yes | Yes (S-100 +, Vimentin +, EMA -, GFAP +) | |
| | F, 64 | Syncope | Cerebellar | N.A. | CR | Yes | Yes (S-100 +, Vimentin +, EMA -, GFAP -) | |
| | M, 21 | Seizures | Frontal | N.A. | CR | Yes | Yes (S-100 +, Vimentin +, EMA -, GFAP -) | |
### Table 1: (Continued)

| Authors and year                      | Sex and Age | Symptoms                                      | Site of lesion          | Radiological diagnosis | Treatment            | Histological diagnosis | IHC confirmed diagnosis | Additional findings                  |
|---------------------------------------|-------------|------------------------------------------------|-------------------------|------------------------|-----------------------|------------------------|-------------------------|--------------------------------------|
| Sharma et al., 1998 [abstract only]   | M, 15       | Posttraumatic incidental finding, headache, vomiting | Parietal, Cerebellar    | N.A.                   | Biopsy followed by CR CR | Yes                    | Yes (S-100 +, GFAP -) | No recurrence                        |
| Zagardo et al. 1998                   | F, 8        | N.A.                                           | Temporal               | N.A.                   | CR                    | Yes                    | Yes (S-100 +) | No recurrence                        |
| Bhatiwele and Gupta, 1999             | F, 29       | Hearing loss, facial numbness, gait disturbance | Multiple lesion: cerebellar, brainstem, cervical medulla | N.A.                   | STR                   | Yes                    | Yes (S-100 +, GFAP -) | No recurrence                        |
| Lee et al., 1999                      | M, 15       | Headache, vomiting                             | Parieto-occipital      | N.A.                   | CR                    | Yes                    | Yes (S-100 +, GFAP -) | No recurrence                        |
| Tanaka et al., 2000                   | M, 4        | Headache, vomiting                             | Thalamus               | N.A.                   | CR                    | Yes                    | Yes (S-100 +, GFAP -) | No recurrence                        |
| Andrade et al., 2002                  | M, 17       | Headache, vomiting, diplopia                   | Temporal               | N.A.                   | CR                    | Yes                    | Yes (S-100 +, GFAP -) | No recurrence                        |
| Bhatoe et al., 2003 [abstract only]   | F, 3         | Headache, vomiting                             | Parieto-occipital      | N.A.                   | STR                   | Yes                    | Yes (S-100 +, GFAP -) | Patient died 10 days postop due to hemorrhage |
| Chng et al., 2003 [abstract only]     | M, 48       | Seizures, ataxia, dysphagia, facial palsy and numbness | Medulla oblongata     | Cystic glioma          | RT followed by CR CR | Yes                    | Yes (Vimentin +, GFAP -) | No response to RT                    |
| Lin et al., 2003                      | M, 21       | Seizure                                        | N.A.                   | Pilocytic astrocytoma  | N.A.                  | Yes                    | N.A.                    | Died 29 months after biopsy          |
| Sarkar et al., 2003 [abstract only]   | F, 29       | Diplopia, headache, gait disturbance           | Mesencephalon Astrocytoma | N.A.                   | Biopsy, chemotherapy | Yes, malignant         | Yes (S-100 +, GFAP -) | Recurrence at 6 months, died 8 months postop |
| Beauchesne et al., 2004               | F, 7        | Headache, vomiting, visual impairment          | Cerebellar             | N.A.                   | GTR and RT            | Yes, malignant         | Yes (S-100 +, GFAP -) | Died 29 months after biopsy          |
Table 1: (Continued)

| Authors and year | Sex and Age | Symptoms | Site of lesion | Radiological diagnosis | Histological diagnosis | Treatment | Additional findings |
|------------------|-------------|----------|----------------|------------------------|------------------------|-----------|---------------------|
| Vaishya and Sharma, 2004 | M, 13 | Seizures, headache, vomiting, diplopia | Frontal | TBC lesion | Yes | No / N.A. | TB infection suspected |
| Takel et al., 2005 | F, 33 | Headache, hemiparesis | Frontoparietal | Meningioma | CR | CR | Ye s |
| Yako et al., 2005 | M, 14 | Headache, vomiting, anosmia | Frontal | Neuroblastoma, glioma, meningioma, metastasis | CR | CR | Ye s |
| Ahmad et al., 2006 | M, 21 | Seizures | Frontal | N.A. | CR | CR | Ye s |
| Bristol et al., 2006 | M, 8 | Seizures, ICP symptoms | Frontal | N.A. | CR | CR | Ye s |
| Bourgine et al., 2007 (abstract only) | F, 20 | Seizures | Frontal | N.A. | CR | CR | Ye s |
| DeCaen et al., 2007 | M, 57 | Seizures | Frontal | N.A. | CR | CR | Ye s |
| Cetekoglu et al., 2007 | M, 23 | Seizures | Frontal | N.A. | GTR | GTR | Ye s |
| Kozic et al., 2008 | M, 39 | Hemiparesis, ataxia, disadra, developmental delay | Frontotemporal | N.A. | Biopsy | Ye s |
| Oztnur et al., 2008 | F, 1 | Seizures | Pons | N.A. | STR | STR | Ye s |
| Ambekar et al., 2009 | M, 32 | Seizures, headache | Frontal | N.A. | GTR | GTR | Ye s |
| Ishihara et al., 2009 | M, 5 | Headache | Frontal | N.A. | Tuberculoma | GTR | Ye s |
| Menku et al., 2009 | M, 37 | Seizures | Frontal | N.A. | HGG, metastasis, lymphoma | CR | Ye s |
| Consales et al., 2010 | M, 5 | Headache, vomiting, diplopia, gait disturbance, hiccups | Frontal | N.A. | Parieto-occipital | CR | Ye s |
| Muzzafar et al., 2010 | M, 68 | Seizures | Brainstem | N.A. | GTR | GTR | Ye s |
| Authors and year       | Sex and Age | Symptoms                        | Site of lesion | Radiological diagnosis | Treatment | Histological diagnosis | IHC confirmed diagnosis | Additional findings |
|------------------------|-------------|---------------------------------|----------------|------------------------|-----------|------------------------|-------------------------|---------------------|
| Barnard et al., 2011   | F, 75       | Personality changes and dysphasia | Frontal        | N.A.                   | GTR + RT  | Yes, malignant         | Yes (S-100 +, GFAP -, EMA-, CD34 -, a-SMA -) |                     |
| Ellis et al., 2011     | F, 9        | Headaches                       | Frontal        | N.A.                   | STR       | Yes, malignant         | Yes (S-100 +)           |                     |
| Khursheed et al., 2011 | M, 16       | Seizures                        | Frontal        | N.A.                   | CR        | Yes                    | Yes (S-100 +)           |                     |
| Luan et al., 2011      | F, 39       | Seizures                        | Frontal        | N.A.                   | CR        | Yes                    | N.A.                    |                     |
| Srivastav et al., 2011 | M, 13       | Hemiparesis, headache           | Pons           | N.A.                   | STR       | Yes                    | Yes (S-100 +, Vimentin +, GFAP -) | NF                  |
| Umredkar et al., 2011  | F, 35       | Headaches, vomiting, ataxia     | Cerebellar     | Pylocytic astrocytoma, hemangioblastoma, metastasis | GTR       | Yes                    | Yes (S-100 +, Vimentin +, GFAP -) |                     |
| Guha et al., 2012      | F, 51       | Seizures                        | Temporal       | N.A.                   | CR        | Yes                    | Yes (S-100 +, GFAP -)   |                     |
| Kanakis et al., 2012   | M, 32       | Death due to sepsis             | Brainstem      | N.A.                   | N.A.      | Yes (S-100 +, Vimentin +) | Yes (S-100 +, Vimentin +, GFAP +, a-SMA -, CD-34 -) |                     |
| Khoo and Taki, 2012    | M, 60       | Vertigo                         | Frontal        | LGG                    | GTR       | Yes                    | Yes (S-100 +, GFAP -)   |                     |
| Paredes et al., 2012   | M, 19       | Seizures                        | Occipital      | SFT, Meningioma, PXA, DNET, Ganglioglioma | CR        | Yes                    | Yes (S-100 +, Vimentin +, EMA -) |                     |
|                       | F, 32       | Dizziness                       | Occipital      | HGG                    | CR        | Yes                    | Yes (S-100 +, Vimentin +, EMA -) |                     |
| Sharma et al., 2012    | M, 25       | Seizure, headache               | Parieto-occipital | PAC or PXA           | CR        | Yes                    | Yes (S-100 +, GFAP +)   |                     |
| Lee et al., 2013       | M, 25       | Seizures                        | Frontal        | PXA, ganglioglioma, DNET | CR        | Yes                    | Yes (S-100 +)           |                     |
| Li et al., 2013        | M, 19       | Seizures                        | Frontal        | Meningioma             | GTR       | Yes                    | Yes (S-100 +, Vimentin +, GFAP -, EMA -) |                     |
| Authors and year | Sex and Age | Symptoms                                | Site of lesion  | Radiological diagnosis | Treatment | Histological diagnosis | IHC confirmed diagnosis | Additional findings |
|------------------|-------------|-----------------------------------------|-----------------|------------------------|-----------|------------------------|-------------------------|----------------------|
| Luo et al., 2013 | M, 17       | Asymptomatic                            | Parietal        | N.A.                   | CR        | Yes                    | Yes (S-100 +, GFAP -) |                      |
|                  | F, 31       | Headache                                | Brainstem       | N.A.                   | CR        | Yes                    | Yes (S-100 +, GFAP -) |                      |
|                  | F, 44       | Headache, visual impairment, gait disturbance | Brainstem | N.A.                   | CR        | Yes                    | Yes (S-100 +, GFAP -) |                      |
|                  | M, 51       | Headache                                | Temporal        | N.A.                   | CR        | Yes                    | Yes (S-100 +, GFAP -) |                      |
|                  | F, 18       | Seizures                                | Frontal         | N.A.                   | CR        | Yes                    | Yes (S-100 +, GFAP -) |                      |
|                  | M, 72       | Hemiparesis, headache                   | Parieto-occipital | N.A.                  | CR        | Yes                    | Yes (S-100 +, GFAP -) |                       |
|                  | M, 38       | Headache, anosmia                       | Frontal         | N.A.                   | CR        | Yes                    | Yes (S-100 +, GFAP -) |                       |
|                  | M, 24       | Headache                                | Lateral ventricle | N.A.                 | CR        | Yes                    | Yes (S-100 +, GFAP -) |                       |
|                  | F, 43       | Headache                                | Occipitotemporal | N.A.                  | CR        | Yes                    | Yes (S-100 +, GFAP -) |                       |
|                  | M, 41       | Headache                                | Intrasellar     | N.A.                   | CR        | Yes                    | Yes (S-100 +, GFAP -) |                       |
|                  | F, 10       | Visual impairment                       | Frontal         | N.A.                   | CR        | Yes                    | Yes (S-100 +, GFAP -) |                       |
|                  | M, 34       | Asymptomatic                            | Occipital       | N.A.                   | CR        | Yes                    | Yes (S-100 +, GFAP -) |                       |
|                  | F, 55       | Anosmia                                 | Frontal         | N.A.                   | CR        | Yes                    | Yes (S-100 +, GFAP -) |                       |
|                  | M, 64       | Vomiting, gait disturbance              | Cerebellar      | N.A.                   | CR        | Yes                    | Yes (S-100 +, GFAP -) |                       |
|                  | M, 51       | Gait disturbance                        | Cerebellar      | N.A.                   | CR        | Yes                    | Yes (S-100 +, GFAP -) |                       |
|                  | M, 13       | Seizures                                | Frontal         | N.A.                   | CR        | Yes                    | Yes (S-100 +, GFAP -) |                       |
|                  | F, 31       | Seizures, anosmia                       | Frontal         | N.A.                   | CR        | Yes                    | Yes (S-100 +, GFAP -) |                       |
|                  | M, 35       | Visual impairment                       | Frontal         | N.A.                   | CR        | Yes                    | Yes (S-100 +, GFAP -) |                       |
### Table 1: (Continued)

| Authors and year | Sex and Age | Symptoms | Site of lesion | Radiological diagnosis | Treatment | Histological diagnosis | IHC confirmed diagnosis | Additional findings |
|------------------|-------------|----------|----------------|------------------------|-----------|------------------------|------------------------|---------------------|
| Ma et al., 2013  | F, 24       | Seizures | Frontal        | Meningioma             | GTR       | Yes                    | Yes (S-100 +, Vimentin +, GFAP -, EMA-) |
| Ramos et al., 2013| F, 17       | Headache, dizziness | Brainstem + CPA | N.A.                   | CR        | Yes                    | Yes (S-100 +, GFAP -) |
| Rotondo et al., 2013 | F, 45     | Depression, headache, visual impairment | Frontal | Meningioma | GTR       | Yes                    | No / N.A. |
| Shweikeh et al., 2013 | M, 18     | Headache, hemiparesis | Frontoparietal | Glioma | GTR and RT, followed by re-resection | Yes, malignant | Yes (S-100 +, Vimentin+, GFAP -) |
| Srinivas et al., 2013 | F, 16     | Seizures, headache | Frontoparietal | Glioma | GTR       | Yes                    | No / N.A. |
| Al Batly et al., 2014 | F, 49     | Headache, gait disturbance | Temporal | Glioma | STR       | Yes                    | Yes (S-100 +, GFAP -) |
| Gupta et al., 2016 | M, 17     | Headache, vomiting | Temporoparietal | HGG | GTR       | Yes                    | Yes (S-100 +) |
| Sharma et al., 2016 | F, 26     | Headache, hemiparesis, facial palsy, gait disturbance | Pons and medulla oblongata | LGG | GTR       | Yes                    | |
| Wilson et al., 2016 | M, 34     | N.A. | Temporal | Ganglioglioma, Oligodendroglioma, post infectious | CR       | Yes                    | Yes (S-100 +, EMA -, GFAP - CD34 +) |
| Zhang et al., 2016 | F, 40     | Paresis, numbness upper extremities, cervical pain | Medulla oblongata | Glioma | STR followed by GTR | Yes                    | Yes (S-100 +, Vimentin +, GFAP -) |
| Pearson et al., 2017 | F, 22     | Headache | Frontal | LGG, Pilocytic astrocytoma, ependymoma, neurocytoma | GTR       | Yes                    | Recurrence (STR due to adherence) |
| Gao et al., 2018  | F, 12      | Headache, vomiting, gait disturbance | Brainstem | N.A. | CR        | Yes                    | Yes (S-100 +, GFAP - , EMA-) |
| Khaleghi et al., 2018 | F, 44     | Headache, vomiting, diplopia | Frontal | Meningioma | GTR       | Yes                    | Yes (S-100 +, GFAP - , EMA-) |
| Ten et al., 2018  | M, 19      | Visual impairment, headache | Occipital | N.A. | CR        | Yes                    | No (EM: basement membrane attached to neoplastic cells) |
often called malignant intracerebral nerve sheath tumor (MINST), is extremely rare. Compared to benign IS, MINST are characterized by a high mitotic activity and Ki-labeling index.\(^9,18\) A variant of MINST is a triton tumor, which is characterized additionally by rhabdomyoblastic components.\(^3\)

**Treatment and prognosis**

Since IS are mostly benign lesions, gross total or complete resection of the tumor is usually curative. Therefore, surgical resection is the preferred treatment for symptomatic lesions.\(^7\) We calculated a recurrence rate of 5.3% following gross total or complete resection [Table 1]. All recurrences were related to malignant histopathology. In cases with subtotal resection, only four patients required reoperation because of residual tumor or recurrence.\(^4,6,21,22\) None of these recurrent cases were related to malignant pathology, suggesting that recurrence was the result of subtotal resection. Mortality rate among histopathological benign IS cases was 0% compared to 53% in malignant cases [Table 1].

Although rare, IS should be included in the differential diagnosis when typical radiological features are present. This is relevant as surgical approach and technique may be different in comparison to the many differential diagnoses that are included
in [Table 1]. For example, IS can be removed in a piecemeal intratumoral debulking fashion, whereas hemangioblastomas, being the preoperative suspected diagnosis in our case, requires an en bloc removal and entering the tumor could result in unnecessary blood loss. Similarly, in some cases, high grade glioma (of the brainstem) was the preoperative suspected diagnosis [Table 1] which may result in diagnostic biopsy surgery instead of surgical resection. Therefore, including IS in the differential diagnosis when typical radiological features are present is relevant for the surgical strategy.

The role of radiotherapy or chemotherapy as primary treatment of benign IS remains unknown. We found two cases in which radiotherapy was given as primary treatment. In both cases, radiotherapy failed to reduce tumor size and tumor-related symptoms after which surgery was performed. Radiotherapy and chemotherapy may play a role as adjuvant treatment in malignant IS cases.

CONCLUSION

ISs are rare benign tumors occurring mostly in young patients. Clinical presentation is usually related to tumor location or increased intracranial pressure. Gross total resection of the lesion is curative. To adjust the surgical strategy accordingly, ISs should be considered preoperatively when radiological features such as peritumoral edema, calcifications, and cysts are noted.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

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