Hemangioblastomas of the Posterior Cranial Fossa in Adults: Demographics, Clinical, Morphologic, Pathologic, Surgical Features, and Outcomes. A Systematic Review

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■ BACKGROUND: **Posterior cranial fossa (PCF) hemangioblastomas are benign, highly vascularized, and well-differentiated tumors with well-described histopathologic features. Although relatively rare, this tumor is the most prevalent primary tumor of the cerebellum in adults.**

■ OBJECTIVE: **Because the demographics of patients with such a tumor (as well as the clinical, morphologic, pathologic, surgical features, and outcomes) are not fully understood, we systematized characteristic patient and tumor features.**

■ METHODS: **We undertook a systematic review of the English-language literature in PubMed for PCF hemangioblastomas in adults published in the past 31 years. We analyzed geographic distribution and year of publication of articles; demographic data of patients; presenting symptoms and clinical signs; tumor location and morphology; histopathologic features, extent of tumor resection, perioperative blood loss, and postoperative complications; length of hospital stay; and outcomes.**

■ RESULTS: **We reviewed 207 articles describing 1759 infratentorial hemangioblastomas in a cohort of 1515 adult patients. We found female predominance in patients with Von Hippel-Lindau disease (VHLD) compared with male predominance in the general patient group. Symptoms of intracranial hypertension were more common in the VHLD group compared with the general group of patients. The cerebellar location was more common in the VHLD group and solid (parenchymatous) tumor was the most common type. Most patients underwent total resection but rate of resection did not differ between the general and VHLD groups. Most patients had a favorable outcome.**

■ CONCLUSIONS: **The literature of adult PCF hemangioblastomas is limited and general surgical experience with such tumors is scarce because of their rarity. Rates of postoperative complications and mortality remain higher than expected. However, prognosis and surgical outcomes are generally favorable. Nevertheless, surgery of adult PCF hemangioblastomas is a demanding and challenging task.**

INTRODUCTION

Hemangioblastomas are relatively rare tumors of the central nervous system representing 1.5%–2.5% of all intracranial tumors and 7%–8% of all posterior cranial fossa (PCF) tumors.[1,2] They mainly arise in the cerebellar hemispheres (76%), making them the most common primary neoplasm of the cerebellum in adults.[3] These tumors are believed to appear more often in males than in females and are most common in the fifth and sixth decades of life.[3] Single tumors may appear sporadically in the general population, but multiple tumors almost always occur earlier in life and in patients with Von Hippel-Lindau disease (VHLD) (33%).[3-7]

Many of the details of these tumors are not well known. These details include precise demographics, sex and geographic distribution of patients, rate of different morphologic types, and ratio of sporadic versus VHLD cases. Also not well known are the rates of

Key words
- Adult hemangioblastoma
- Histopathology
- Morphology
- Outcome
- Posterior fossa
- Surgery
- Symptoms
- Systematic review

Abbreviations and Acronyms
ICP: Intracranial pressure
PCF: Posterior cranial fossa
VHLD: Von Hippel-Lindau disease

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Citation: World Neurosurg. (2017). https://doi.org/10.1016/j.wneu.2017.11.173

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

resection, intraoperative blood loss for different tumor types, rate of different tumor locations within the PCF, proteins used for diagnostic staining, postoperative complications and their rates, mortality, and clinical outcomes. Whether a difference in these parameters exists between sporadic and VHLD cases is also unknown.

We reviewed all reports of PCF hemangioblastomas published in the past 31 years to investigate all these parameters. We also examined possible demographic disparity among patients of different origin and gender, as well as between those having sporadic tumors and VHLD tumors, comparing differences in tumor location and surgical outcomes. A systematic review of case reports and patient series was undertaken to summarize, synthesize, and better understand the literature results.

METHODS

Because no review protocol for the management of PCF adult hemangioblastoma exists, we performed a systematic review of all available literature over a span of 31 years (January 1, 1985–December 31, 2015). We used a PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) structured checklist for our study.[6,7]

Eligibility Criteria

We searched the PubMed/Medline database to identify all English-language articles that focused on the PCF hemangioblastomas.

Information Sources

We included case reports and series in the review, and excluded articles describing hemangioblastomas outside the PCF, as well as series that included pediatric cases (<18 years old).

Search Strategy, Selection of Studies, Data Collection Process, and Data Items

Case reports and series were analyzed according to the year, country, and continent of publication. The articles included were analyzed for 9 parameters of interest: geographic distribution and year of publication of articles; demographic data, including age and gender of patients; presenting symptoms and clinical signs; tumor location and morphology; histopathologic diagnosis; the extent of surgical resection and perioperative blood loss; postoperative complications; length of hospital stay; and outcomes.

The age and gender of patients were analyzed and the medians, ranges, means, and standard deviations were calculated, as well as the presenting symptoms and clinical signs.

Tumor location within the PCF was identified as follows: cerebellum; brainstem; cerebellopontine angle; the fourth ventricle; craniocervical junction; and unspecified. Tumor morphology was analyzed and the immunohistochemical markers used for staining were noted.

The surgical parameters analyzed were the following: the extent of tumor resection; intraoperative blood loss; postoperative complications; and length of hospital stay. The extent of resection was listed as total, subtotal/near total, partial, or not operated on. Postoperative complications were categorized into intracranial; infections; those involving cranial nerves; gastrointestinal; cardiopulmonary; and other unspecified complications.

Outcomes were categorized as the following: favorable (no postoperative neurologic deficits and no postoperative complications); fair (mild postoperative neurologic deficit or postoperative complications); poor (debilitating postoperative complications or grave neurologic deficits); and death. The mortality was calculated from the articles that provided such information. All parameters were analyzed and compared between the patients with sporadic hemangioblastomas and those with VHLD.

Risk of Bias

The risk of any bias in interpretation of individual studies reviewed was avoided by using 2 authors who independently analyzed the data at the study results and outcomes levels. The same strategy was used to avoid the risk of bias that may affect the cumulative data across the studies reviewed and possible reporting of overlapping patients' results.

Synthesis of Results

A methodical synthesis of the results collected was performed to summarize evidence and reach the conclusions.

RESULTS

General Information on Study Characteristics

A total of 207 articles were identified, screened, assessed for eligibility, and included in qualitative synthesis. Of these 207 articles, 54 (26%) were series[3-5,8-58] and 153 (73.9%) were case reports.[1,2,59-209] The median number of patients in each series was 14 (interquartile range, 7.75–33.25). The number of articles reporting adult PFC hemangioblastomas per year of publication is shown in Figure 1.

Any overlapping of patients' results as well as major differences in surgical strategy and outcomes occurring over the years were not observed.

Geographic Distribution

Most of the articles (20.7%) were published in the United States,[5,9,18,21,22,30,37,39,52,53,63,69,70,72,73,84,86,87,97,99,104,105,115,117,130,136,137,141,142,147,153,157,162,163,173,180,181,184,190,198,203,207] followed by Japan (18.8%),[1,23,25,31,32,38,43,46,47,50,93,102,103,107,109,113,116,120,121,125,126,135,139,143,144,146,150,152,154,169,175,177,185,189,192,193,204] China (10.1%),[2,13,14,35,37,51,54,55,57,58,76,82,149,178,183,187,197,200,202,205,208] and the United Kingdom, with (8.2%)[3,12,26,27,49,56,61,77,78,85,96,101,148,174,176,182,209] (Figure 2).

The continental distribution of articles is shown in Figure 3. The continental distribution of patients was most common in Asia (49.1%), Europe (30.9%), and North America (16.8%).

Demographics

The total number of patients in articles included in the review was 1515. Of these patients, 805 (53.1%) were male and 682 (45.0%) were female. Four articles[42,69,170,206] did not provide information about patients' gender. Individual age information was available in 187 articles (90.3%), which accounted for 542 patients (35.8%). The median age of those patients was 40 years (range, 15–95 years; interquartile range, 31–54 years). The mean age was 42.72 years, with a standard deviation of 15.62 years.

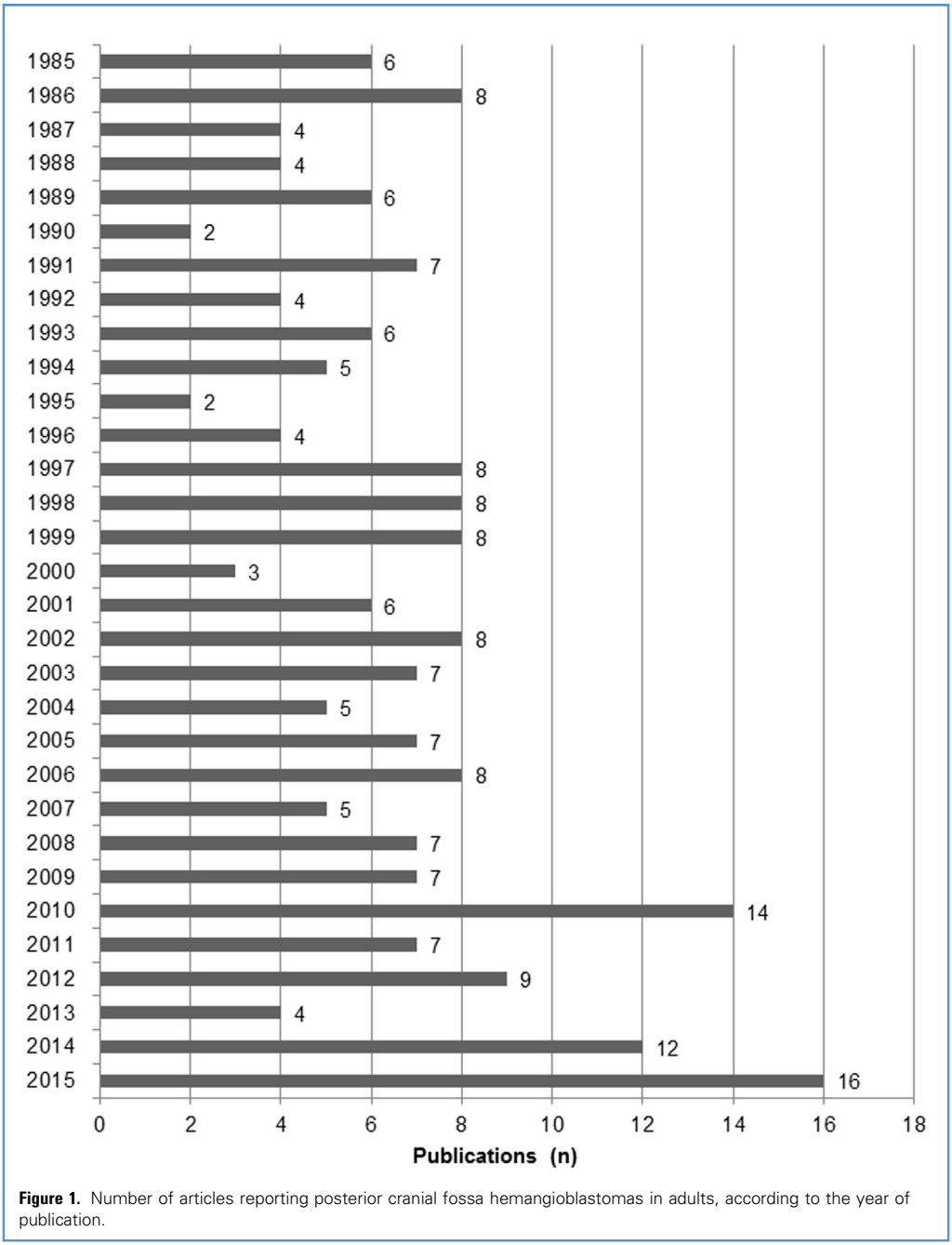

Figure 1. Number of articles reporting posterior cranial fossa hemangioblastomas in adults, according to the year of publication.

Of the 1515 patients, information about VHLD was available for 882 (58.2%) in 112 (54.1%) of the reviewed articles.[3,5,9,11,12,17,19-26,28,29,33,34,37,38,40-43,46,47,49,51,54,58,59-61,63-66,68,70-72,75-77,80,82,85,87,90,95,97,98,101-103,105,107,110,112,114,116-118,122-126,128,132,134,136,139,140,145,148,149,152,153,155-160,162,164,165,171,173,176,177,179,180,184-187,192,194,196,201,202,205,207,209] A total of 379 patients were affected by the disease (43.0%), whereas 503 (57.0%) were unaffected. Of 379 patients with VHLD, individual age and gender were available for 140 and 305 patients, respectively. A total of 138 patients (45.2%) with VHLD were male and 167 (54.8%) were female. Age and gender for patients with sporadic hemangioblastomas were available for 173 and 203 patients, respectively. A total of 112 (55.2%) were male and 91 (44.8%) were female.

Presenting Symptoms and Clinical Signs

Presenting symptoms and clinical signs were available for 1010 patients (66.6%).[1,2,5,9-13,15,16,18-20,23-26,29,34,36,37,41,44,46,48-53,55,57,58,59-65,67,68,71-81,83-103,105-129,131-139,141-183,185-201,203-209] The most common presenting symptoms and clinical signs were related to increased intracranial pressure (ICP) (50.4%), followed by

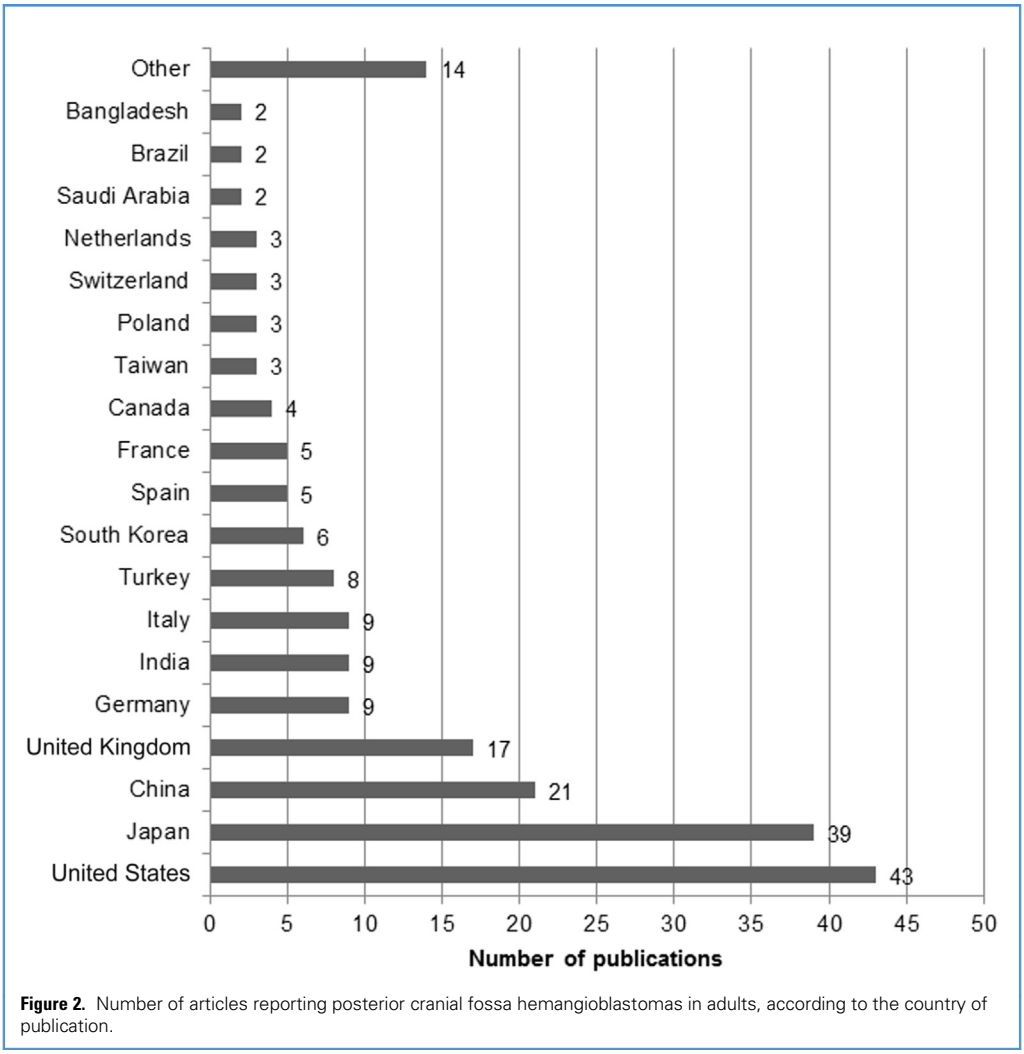

Figure 2. Number of articles reporting posterior cranial fossa hemangioblastomas in adults, according to the country of publication.

cerebellar signs (33.4%). All other presenting signs and symptoms accounted for the remaining 16.2%.

Of 882 patients with VHLD information, presenting clinical signs and symptoms were noted in 398 (45.1%). The distribution of symptoms between patients with VHLD and those with sporadic hemangioblastomas is shown in Figure 4. Polycythemia was reported in only 41 articles, which accounted for 75 patients with polycythemia and 165 patients without it. No further analysis of this finding was available.

Data about the tumor location were available in 204 articles (98.5%).[1-5,8-31,33-103,105-156,158-209] Of the 1759 tumors, most ($n = 1230$) were located in the cerebellum, accounting for 70% (Figure 5). The second most common location was the brainstem (24.3%), followed by the fourth ventricle (1.8%), the cerebellopontine angle (1.8%), and the craniocervical junction (1.6%). In 9 cases (0.5%), the exact tumor location within the posterior fossa was not specified. Both the patients' VHLD status and tumor location data were available for 760 cases (43.2%). Distribution of tumor location within the PCF between patients diagnosed with VHLD and those with sporadic tumors showed no major differences between groups (Figure 6).

Tumor morphology data were available in 153 articles (73.9%), which accounted for 1014 tumors.[1,3,8,10,13,17-20,22-27,29,30,33,34,36-38,41,43,44,46,47,49-52,54-60,62,63,65,67-76,78-85,87-89,93-100,102,103,106,108-110,112,114-120,122-124,126-129,131,132,134,136,138-142,145-155,157-159,161-165,168-173,176-179,181,183,184,186-188,190-206,208,209] Morphologically, 4 types of hemangioblastomas were described: solid hemangioblastomas were the most common (47.7%), followed by cystic (26.3%) and cystic with a mural nodule (21.3%), whereas tumors described as being both solid and cystic were the least common (4.7%) (Figure 7). Of 1014 tumors with described morphologic types, only 289 cases (28.5%) had information about both the tumor morphology and the patients' VHLD status (Figure 8).

There were only 2 cases describing multiple lesions in patients without VHLD. One article[40] reported the case of a 52-year-old man who had presented with 6 lesions. The second article[156] reported the case of a 40-year-old woman who had multiple lesions. All other articles that provided information on the patients' VHLD status reported cases of multiple lesions exclusively in patients who were VHLD positive.

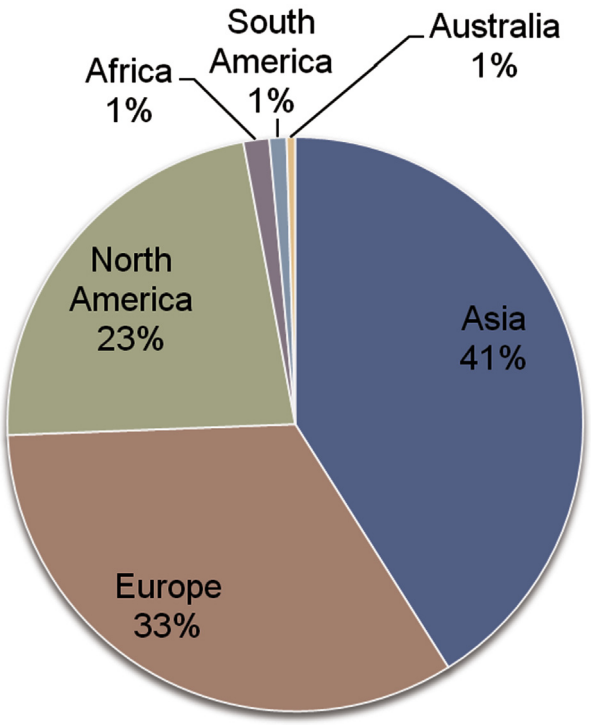

Figure 3. Distribution of articles describing posterior cranial fossa hemangioblastomas in adults, according to the continent of publication.

Histopathology and Immunohistochemistry

A total of 142 articles (68.6%) offered information about the histopathologic diagnosis of hemangioblastoma.[1,2,4,5,10,12,13,17-20,22,23,27,29,30,31,37,38,40,43,45,49,50,53,56,58,59,61-63,65-67,70-72,74,77-82,84-89,94-100,102,103,107-114,117,119-121,123-128,130,131,134,137,138,140-147,149-152,154-156,159,161,163-172,174-181,183,184,187,189-193,195-206,208,209]

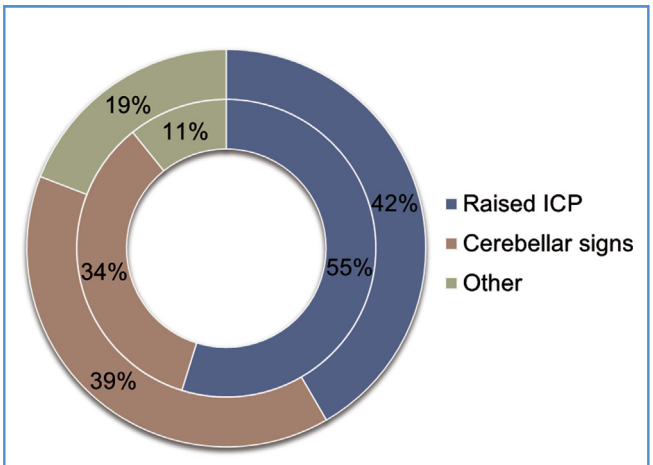

Figure 4. Distribution of main symptoms between patients diagnosed with Von Hippel-Lindau disease (*inner circle*) and those with sporadic tumors (*outer circle*): tumor location and morphology. ICP, intracranial pressure.

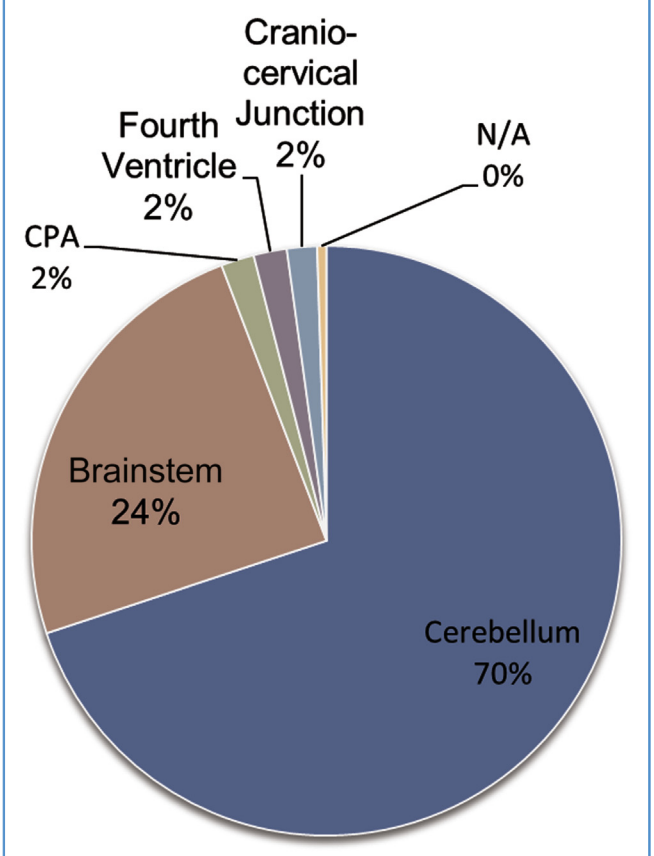

Figure 5. Distribution of hemangioblastomas within the posterior cranial fossa. CPA, cerebellopontine angle; N/A, not applicable.

In addition to histopathology, information about immunohistochemical staining was available in 40 articles (19.3%).[2,17,22,37,45,53,59,61,65,66,70-72,76,77,78,80,82,88,97,102,107,110,123,134,136,142,149,156,159,164,165,170,177,184,189,199,202,204,205] The 8 most common proteins

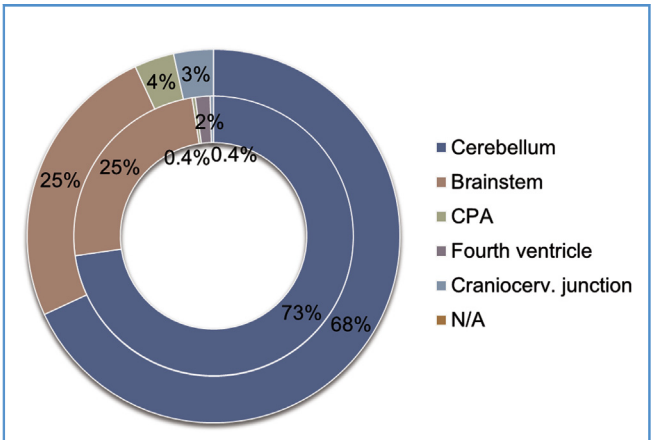

Figure 6. Distribution of tumor location within the posterior cranial fossa between patients diagnosed with Von Hippel-Lindau disease (*inner circle*) and those with sporadic tumors (*outer circle*). CPA, cerebellopontine angle; Craniocerv., craniocervical; N/A, not applicable.

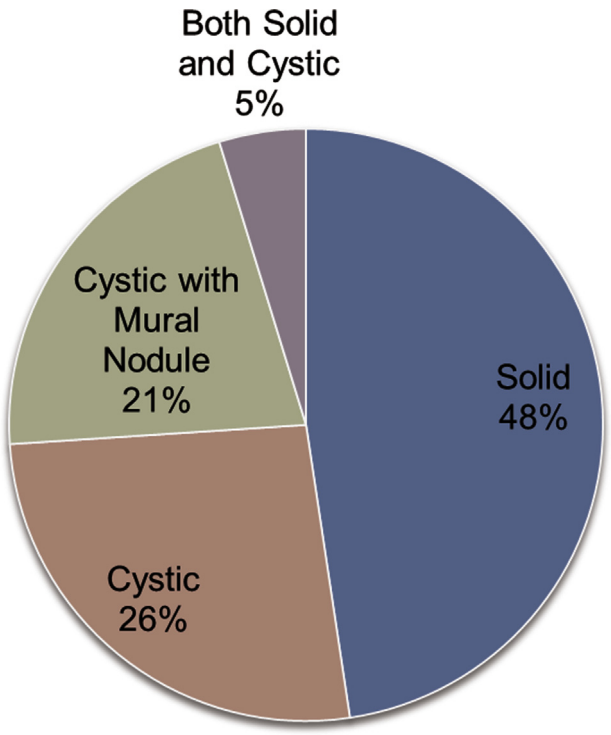

Figure 7. Distribution of morphologic types of hemangioblastomas.

stained are listed in **Table 1**. The Ki-67 protein was mentioned in 9 articles (4.4%).[37,61,66,72,76,97,189,202,205]

Extent of Tumor Resection and Blood Loss

A total of 164 articles (79.2%) provided information about the extent of tumor resection, accounting for a total of 1167

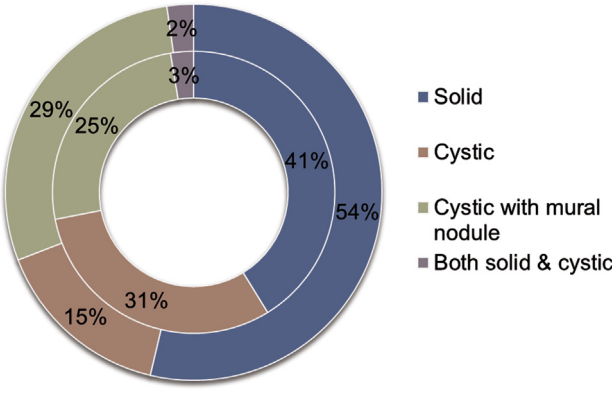

Figure 8. Distribution of morphologic types of hemangioblastomas between patients diagnosed with Von Hippel-Lindau disease (*inner circle*) and those with sporadic tumors (*outer circle*).

Table 1. The Most Common Proteins Stained During Immunohistochemical Analysis of Resected Tumor Tissue Samples

Protein	N	Positive Staining (%)
S-100	21	80.9
Glial fibrillary acidic protein	20	50
Vimentin	16	100
Neuron-specific enolase	15	93.3
Epithelial membrane antigen	14	27.3
CD 34	11	81.8
Cytokeratin	10	30
Reticulin	8	87.5
CD 56	7	85.7
Inhibin	5	80
CD 10	5	20
Vascular endothelial growth factor	3	100

hemangioblastomas.[1,4,8,10,11,13,15,16,18,19,23,25-27,29,32,34-38,40,42,44-46,48-50,51,53-63,65-67,69-72,74-76,78-81,83-89,91-94,96,99,100,103,107-109,111-127,129-131,133-141,143-155,157-164,166-181,183-190,192-209] Most hemangioblastomas were totally resected (88.5%), with subtotal/near total resection (2.3%) and partial resection (3.6%) a rarity. Tumors were not operated on in 5.6% of cases (**Figure 9**).

With regard to the extent of resection, information about patients' VHLD status was available for 27.3% of patients among the

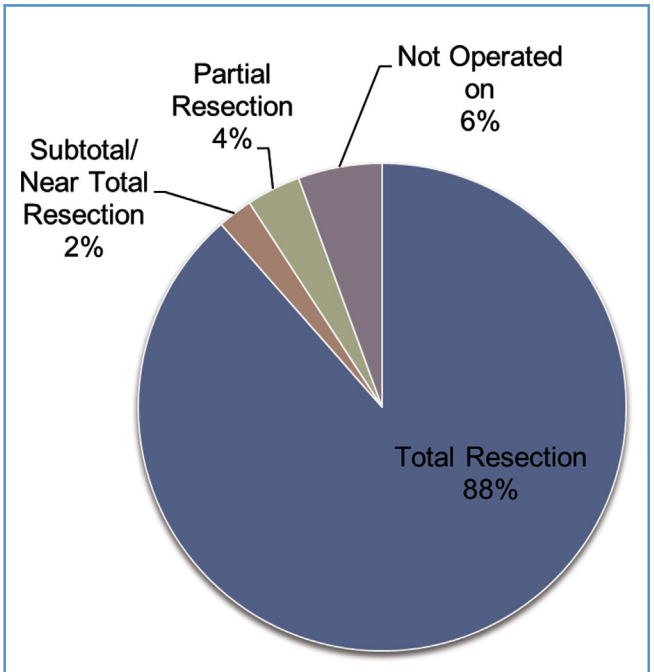

Figure 9. Distribution of the extent of hemangioblastoma resection.

1167 hemangioblastomas. Data for intraoperative blood loss were available in only 7.3% of articles.[8,14,18,31,35,46,50,52,57,85,93,120,122,146,192] The mean blood loss reported was 675.85 ± 470.29 mL.

Postoperative Complications

Postoperative complications were reported in 54.1% of the 207 reviewed articles, which accounted for 610 patients (40.3%).[4,5,8-10,13,16,18,19,23,26,27,32,34-36,39-42,44,46,48-50,52-58,62,65,67,69,71,72,74,77,80,81,83-86,88,89,92-94,96,98,103,105,108,109,113-115,118,122,123,127,131,133,135,136,138,139,142-144,146-152,155,156,158-164,166,167,169,170,172,173,175,176,178-180,182,186,187,189,192,195,196,198,199,201,203-206] The most common complications were intracranial (31.5%), followed by infections (27.7%) and complications affecting cranial nerve function (11.4%) (Figure 10). The most common intracranial complications were postoperative hemorrhage, hydrocephalus, and pseudomeningocele, whereas meningitis and pneumonia were the most common infections.

The types and rates of reported complications was steady yearly during all 3 decades (1985–1995, 1996–2005, and 2006–2015). For example, the reported intracranial complications were 40% and 39%, respectively, for the first and third decades.

Because there was only a small sample of patients with information about both their VHLD status and postoperative complications, we did not analyze the differences in types of complications between sporadic and VHLD cases.

Outcome and Mortality

Outcomes were described in 154 articles (74.4%), which accounted for 1106 patients (73.0%).[1,2,4,5,8,10,12-16,18,23,24,26,27,29,34,36-38,41,42,44,46,48,49,51,52,54-58,60-63,65,67,69-75,77,78,80,81,83-90,92-97,100-103,105-108,110-115,120,122,123,127,129,131,133,135-162,164-170,172-183,190,191,194-196,198-201,203-209]

A favorable outcome was the most common result (73.9%), followed by fair outcome (11.1%), and poor outcome (4.7%). Postoperative mortality was reported in 80.7% articles.[1,2,4,5,8,10-16,18,19,23,24,26,27,29,34-42,44,46,48-63,65,67,69-75,77,78,80,81,83-98,100-103,105-114,116,118-120,122-124,126,127,129,131,133,135-162,164-170,172-183,185-190,192,195,196,198-201,203-209] The overall mortality was 10.3% (Figure 11). There were no major differences in outcome between sporadic and VHLD cases.

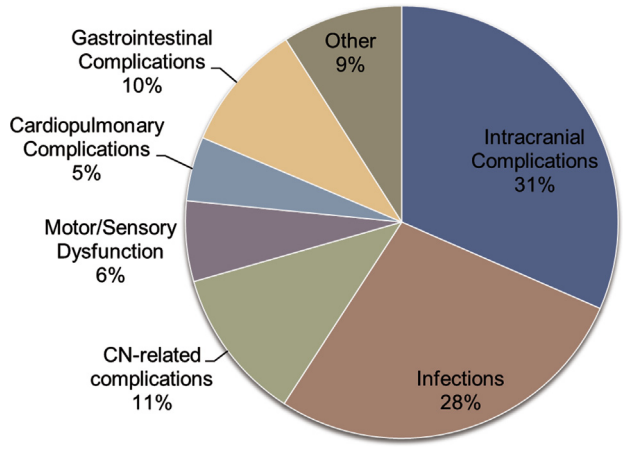

Figure 10. Distribution of postoperative complications. CN, central nervous system.

We observed causes of death within 3 groups: those directly related to surgery, those in the early postoperative period (<15 days postoperatively), and those in the later postoperative period (>15 days postoperatively). The most common cause of death directly related to surgery was postoperative hematoma. The most common causes of death in the early postoperative period, generally, were infections (most commonly pneumonias), followed by gastrointestinal bleeds and complications caused by altered states of consciousness. Death occurred most commonly in the later postoperative period (>15 days). As mentioned earlier, just more than 80% of articles mentioned patient mortality. When taking into account that mortality was 10%, the number of causes of death was not large enough to give further assessment in percentages, especially because numerous articles only stated their mortality and did not provide specific information on cause of death.

DISCUSSION

To the best of our knowledge, our study is the only one of such scope and magnitude that has systematically surveyed and summarized the literature concerned with PCF hemangioblastomas in adults. Therefore, we believe that it is an important critical analysis of this rare and challenging entity.

General Information on Study Characteristics and Demographics

Our research identified 207 articles describing 1759 adult PCF hemangioblastomas in 1515 patients over the last 31 years. Overall, the sporadic cases were more prevalent than those of VHLD (57% vs. 43%). Single tumors may be sporadic, but multiple tumors almost always occur in patients with VHLD.

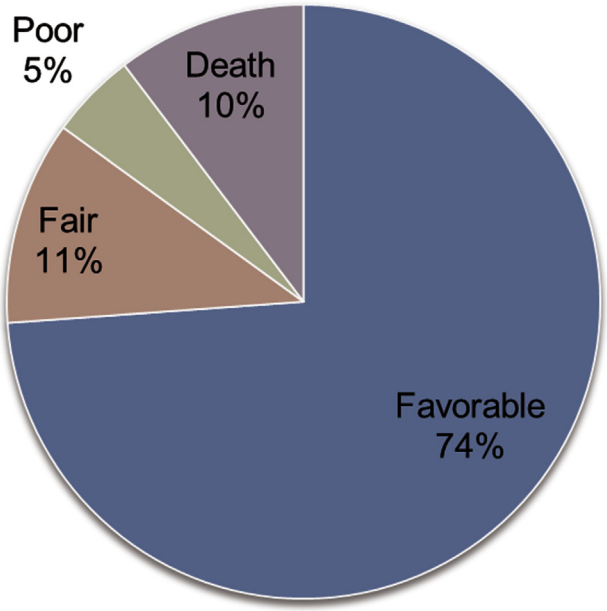

Figure 11. Distribution of patients according to outcome.

Most of the articles included in this review were published during the past 10 years (Figure 1), most commonly in the United States, followed by Japan, China, and the United Kingdom (Figure 2). When the continental distribution reflected the number of patients, patients from Asia (49.1%), Europe (30.9%), and North America (16.8%) were strongly predominant. However, it would be highly speculative to hypothesize that the rate of hemangioblastomas is highest in Asians, followed by whites. This finding clearly needs further investigation by adequate demographic research.

Case reports accounted for 73.9% of all articles. Furthermore, the median number of patients per series was 14. These 2 facts emphasize that the general experience in treatment of patients with PCF hemangioblastomas is not abundant even in subspecialized centers. In additionally, we did not observe any overlapping of patients' results after analyzing the data.

Although heterogeneity of study designs was found in the included publications and the availability of mostly small series and case reports, all analyzed parameters were available in most publications; for example, outcomes in 74%, extent of tumor resection in 79%, histopathology in 69%, presenting signs and symptoms in 67%, VHLD data in 58%, and complications in 54% of articles.

The mean age of patients was 42.7 years, with a slight male predominance (53.1%). Previous data support our findings and emphasize that hemangioblastomas appear more often in males than in females, most commonly in the fifth and sixth decades of life.[3] Nonetheless, the notation of female predominance among patients with VHLD is an original and novel observation of this study previously unrecorded in the literature.

Presenting Symptoms and Clinical Signs

Presenting symptoms and clinical signs were mainly related to tumor size and/or cyst-associated mass effect, if a cystic component was present, most commonly, increased ICP (50.4%). Increased ICP was more common in patients with VHLD (55%) than in the sporadic group (42%) (Figure 4), as was the rate of purely cystic tumors (31%–15%) (Figure 8), as well as with multiple tumors. Thus, one may speculate that cystic tumors having a larger volume and producing a greater mass effect, together with multiple tumors effect, are probably responsible for the increased ICP, which occurred more frequently in patients with VHLD than in the sporadic group.

Tumor Location and Morphology

Most tumors were located in the cerebellum (Figure 9) and the cerebellar location was slightly more frequent in patients with VHLD than in the sporadic group (Figures 5 and 6). Nonetheless, almost one third of PCF hemangioblastomas were of extracerebellar location.

Solid hemangioblastomas were the most common, followed by the cystic type (Figure 7). Some investigators advocated a typical morphologic spectrum of 60% mostly cystic and 40% mostly solid tumors, but this view is clearly disputed by our review, which showed an opposite ratio between solid and cystic tumors. The solid tumor type was most frequently represented in both sporadic and VHLD groups. This is a novel observation not recorded previously in the literature.

Histology and Immunohistochemistry

In most of the articles reviewed (55.6%), the tumors were histopathologically confirmed. Information about the immunohistochemical analysis was available in only a few articles (19.3%). This finding clearly points out the importance of including the detailed histologic features and immunostaining information in future reports. The most frequent positive staining, in decreasing order of frequency, was for vimentin, vascular endothelial growth factor, neuron-specific enolase, reticulin, CD 56, S-100, and inhibin, which all stained at more than 80% (Table 1).

Extent of Tumor Resection and Intraoperative Blood Loss

It has been stated that the complete tumor resection remains the most effective treatment for hemangioblastomas with minimal morbidity and mortality. Our study clearly affirms the first part of this statement and clearly disputes the second. Most hemangioblastomas disclosed by our research were totally resected (88.5%), with subtotal/near total (2.3%) and partial resection (3.6%) being a rarity (Figure 9). Although marked improvements in management and technique have occurred over the last 3 decades, we did not record any major differences in surgical strategy over the years. Although it is well known that hemangioblastomas are highly vascularized tumors, the available blood loss data were too restrictive to be analyzed.

Postoperative Complications

Postoperative complications were reported in more than half (54.1%) of the reviewed articles. The most common complications were intracranial (31.5%), consisting of postoperative hemorrhage and hydrocephalus and pseudomeningocele formation (Figure 10). We did not record any major changes in type, rates, and trends of complications over the years. Rate and ration of complications were similar in the first and third decade of the 31 years review span. This important and novel finding indicates that many patients can be expected to have some complication postoperatively. Accordingly, the same proportion of patients seemed to be prone to repeated surgery to avoid permanent neurologic deficits. Because almost half of the articles (45.9%) did not report complications, that number may be even higher. Thus, the surgeon should discuss this possibility with prospective patients. It is reasonable to speculate that patients with solid tumors may be more likely to have complications because of the bleeding propensity of that type of hemangioblastoma.

Outcomes and Mortality

It has been stated that after complete tumor removal, the prognosis and surgical outcomes are generally good. A favorable outcome was the most commonly recorded (Figure 11), and there were no major differences in outcomes between patients with VHLD and those having sporadic tumors.

Some previous reports recorded a mortality of 2% after complete tumor resection. However, we calculated an overall postoperative mortality of 10.3%, which was a significantly greater number than previously recorded in the literature. This is an important finding. Consequently, surgical management of adult PCF seems to be demanding.

Summary of Evidence and Limitations

There are no evidence-based guidelines for surgical management of posterior fossa hemangioblastomas in adults.

The limitations of this review are the heterogeneity of study designs found in the included publications, and the availability of only small series and case reports. Accordingly, postoperative complications incidence was high but almost certainly underreported. Furthermore, some characteristics, such as intraoperative blood loss and the length of hospital stay, had too few details and number of samples to be conclusive.

CONCLUSIONS

There is a female predominance of PCF hemangioblastomas among patients with VHLD as opposed to male predominance in the sporadic group. The solid type of tumor is the most common type generally. The increased ICP symptoms are more common in patients with VHLD compared with the sporadic group (possibly because of a higher rate of cystic and multiple tumors in this group) and the cerebellar location is more common in the VHLD group.

Most patients undergo total tumor resection; the rate of resection does not differ between sporadic and VHLD groups and radical tumor resection rate is high (88.5%). However, the rate of postoperative complications (at least 40%) as well as postoperative mortality (10.3%) still seem to be high.

The literature of adult PCF hemangioblastomas is limited and general surgical experience with such tumors is scarce because of their rarity.

Prognosis and surgical outcomes are generally favorable. Nevertheless, surgery of adult PCF hemangioblastomas is a demanding and challenging task.

ACKNOWLEDGEMENTS

The authors wish to thank Julie Yamamoto, M.A., for her assistance with the English language editing and manuscript preparation and to Andrew J. Gienapp, B.A., for copyediting, preparation of the manuscript and figures for publishing, and publication assistance.

REFERENCES

1. Amano T, Tokunaga S, Shono T, Mizoguchi M, Matsumoto K, Yoshida F, et al. Cerebellar hemangioblastoma manifesting as hearing disturbance. *Neurol Med Chir (Tokyo)*. 2009;49:418-420.
2. Qiao PF, Niu GM, Han XD. Hemangioblastoma originating from the right cerebellopontine angle. *Neurosciences (Riyadh)*. 2011;16:372-374.
3. Slater A, Moore NR, Huson SM. The natural history of cerebellar hemangioblastomas in von Hippel-Lindau disease. *AJNR Am J Neuroradiol*. 2003;24:1570-1574.
4. Ahyai A, Woerner U, Markakis E. Surgical treatment of intramedullary tumors (spinal cord and medulla oblongata). Analysis of 16 cases. *Neurosurg Rev*. 1990;13:45-52.
5. Jagannathan J, Lonser RR, Smith R, DeVroom HL, Oldfield EH. Surgical management of cerebellar hemangioblastomas in patients with von Hippel-Lindau disease. *J Neurosurg*. 2008;108:210-222.
6. Klimo P Jr, Thompson CJ, Ragel BT, Boop FA. Methodology and reporting of meta-analyses in the neurosurgical literature. *Response J Neurosurg*. 2014;120:794-795.
7. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ*. 2009;339:b2535.
8. Amer M, Shadad M, Zyton H. The impact of preoperative endovascular embolization on surgical outcome of cerebellar cystic hemangioblastoma. *Egypt J Neurosurg*. 2015;30:271-276.
9. Asthagiri AR, Mehta GU, Zach L, Li X, Butman JA, Camphausen KA, et al. Prospective evaluation of radiosurgery for hemangioblastomas in von Hippel-Lindau disease. *Neuro Oncol*. 2010;12:80-86.
10. Brundl E, Schodel P, Ullrich OW, Brawanski A, Schebesch KM. Surgical resection of sporadic and hereditary hemangioblastoma: Our 10-year experience and a literature review. *Surg Neurol Int*. 2014;5:138.
11. Catapano D, Muscarella LA, Guarnieri V, Zelante L, D'Angelo VA, D'Agruma L. Hemangioblastomas of central nervous system: molecular genetic analysis and clinical management. *Neurosurgery*. 2005;56:1215-1221 [discussion: 1221].
12. Chakraborti PR, Chakrabarti KB, Doughty D, Plowman PN. Stereotactic multiple are radiotherapy. IV—Haemangioblastoma. *Br J Neurosurg*. 1997;11:110-115.
13. Chen LF, Yang Y, Yu XG, Bu B, Xu BN, Zhou DB. Operative management of brainstem hemangioblastomas. *J Clin Neurosci*. 2013;20:1727-1733.
14. Chen W, Zhang G, Lin C, Yang Y, Cai D, Huang M, et al. Clinical use of a neuronavigation system in hemangioblastoma resection of posterior cranial fossa. *Minim Invasive Ther Allied Technol*. 2012;21:234-240.
15. Constans JP, Meder F, Maiuri F, Donzelli R, Spaziante R, de Divitiis E. Posterior fossa hemangioblastomas. *Surg Neurol*. 1986;25:269-275.
16. Cornelius JF, Saint-Maurice JP, Bresson D, George B, Houdart E. Hemorrhage after particle embolization of hemangioblastomas: comparison of outcomes in spinal and cerebellar lesions. *J Neurosurg*. 2007;106:994-998.
17. Cuccurullo L, Prudente ME, Maffia S, Accardo M. An ultrastructural study of the histogenesis of haemangioblastoma. *Pathologica*. 2009;101:1-5.
18. Ding D, Starke RM, Evans AJ, Liu KC. Direct transcranial puncture for Onyx embolization of a cerebellar hemangioblastoma. *J Clin Neurosci*. 2014;21:1040-1043.
19. Dwarakanath S, Suri A, Sharma BS, Mehta VS. Intracranial hemangioblastomas: an institutional experience. *Neurol India*. 2006;54:276-278.
20. Elster AD, Arthur DW. Intracranial hemangioblastomas: CT and MR findings. *J Comput Assist Tomogr*. 1988;12:736-739.
21. Eskridge JM, McAuliffe W, Harris B, Kim DK, Scott J, Winn HR. Preoperative endovascular embolization of craniospinal hemangioblastomas. *AJNR Am J Neuroradiol*. 1996;17:525-531.
22. Feldenzer JA, McKeever PE. Selective localization of gamma-enolase in stromal cells of cerebellar hemangioblastomas. *Acta Neuropathol*. 1987;72:281-285.
23. Fukuda M, Takao T, Hiraishi T, Yoshimura J, Yajima N, Saito A, et al. Clinical factors predicting outcomes after surgical resection for sporadic cerebellar hemangioblastomas. *World Neurosurg*. 2014;82:815-821.
24. Georg AE, Lunsford LD, Kondziolka D, Flickinger JC, Maitz A. Hemangioblastoma of the posterior fossa. The role of multimodality treatment. *Arq Neuropsiquiatr*. 1997;55:278-286.
25. Hojo M, Arakawa Y, Funaki T, Yoshida K, Kikuchi T, Takagi Y, et al. Usefulness of tumor blood flow imaging by intraoperative indocyanine green videoangiography in hemangioblastoma surgery. *World Neurosurg*. 2014;82:e495-e501.
26. Huson SM, Harper PS, Hourihan MD, Cole G, Weeks RD, Compston DA. Cerebellar haemangioblastoma and von Hippel-Lindau disease. *Brain*. 1986;109:1297-1310.
27. Julow J, Balint K, Gortvai P, Pasztor E. Posterior fossa haemangioblastomas. *Acta Neurochir (Wien)*. 1994;128:109-114.

28. Karabagli H, Genc A, Karabagli P, Abacioglu U, Seker A, Kilic T. Outcomes of gamma knife treatment for solid intracranial hemangioblastomas. *J Clin Neurosci*. 2010;17:706-710.

29. Kassardjian CD, Macdonald RL, Munoz DG. Hemangioblastomas in the elderly: epidemiology and clinical characteristics. *J Clin Neurosci*. 2014;21:1205-1208.

30. Kumar VA, Knopp EA, Zagzag D. Magnetic resonance dynamic susceptibility-weighted contrast-enhanced perfusion imaging in the diagnosis of posterior fossa hemangioblastomas and pilocytic astrocytomas: initial results. *J Comput Assist Tomogr*. 2010;34:825-829.

31. Kuroiwa T, Tanaka H, Ohta T, Tsutsumi A. Preoperative embolization of highly vascular brain tumors: clinical and histopathological findings. *Noshuyo Byori*. 1996;13:27-36.

32. Kurokawa Y, Uede T, Hashi K. Operative approach to mediosuperior cerebellar tumors: occipital interhemispheric transtentorial approach. *Surg Neurol*. 1999;51:421-425.

33. Lee SR, Sanches J, Mark AS, Dillon WP, Norman D, Newton TH. Posterior fossa hemangioblastomas: MR imaging. *Radiology*. 1989;171:463-468.

34. Liao CC, Huang YH. Clinical features and surgical outcomes of sporadic cerebellar hemangioblastomas. *Clin Neurol Neurosurg*. 2014;125:160-165.

35. Liu AH, Peng TM, Wu Z, Xiao XR, Jiang CH, Wu ZX, et al. Clinical effectiveness of preoperative embolization for cerebellar hemangioblastoma. *Asian Pac J Cancer Prev*. 2013;14:5179-5183.

36. Lodrini S, Lasio G, Cimino C, Pluchino F. Hemangioblastomas: clinical characteristics, surgical results and immunohistochemical studies. *J Neurosurg Sci*. 1991;35:179-185.

37. Ma D, Wang Y, Du G, Zhou L. Neurosurgical management of brainstem hemangioblastomas: a single-institution experience with 116 patients. *World Neurosurg*. 2015;84:1030-1038.

38. Miyagami M, Katayama Y. Long-term prognosis of hemangioblastomas of the central nervous system: clinical and immunohistochemical study in relation to recurrence. *Brain Tumor Pathol*. 2004;21:75-82.

39. Moss JM, Choi CY, Adler JR Jr, Soltys SG, Gibbs IC, Chang SD. Stereotactic radiosurgical treatment of cranial and spinal hemangioblastomas. *Neurosurgery*. 2009;65:79-85 [discussion: 85].

40. Park YS, Chang JH, Chang JW, Chung SS, Park YG. Gamma Knife surgery for multiple hemangioblastomas. *J Neurosurg*. 2005;102(suppl):97-101.

41. Pavesi G, Berlucchi S, Munari M, Manara R, Scienza R, Opocher G. Clinical and surgical features of lower brain stem hemangioblastomas in von Hippel-Lindau disease. *Acta Neurochir (Wien)*. 2010;152:287-292.

42. Pavesi G, Feletti A, Berlucchi S, Opocher G, Martella M, Murgia A, et al. Neurosurgical treatment of von Hippel-Lindau-associated hemangioblastomas: benefits, risks and outcome. *J Neurosurg Sci*. 2008;52:29-36.

43. Quadery FA, Okamoto K. Diffusion-weighted MRI of haemangioblastomas and other cerebellar tumours. *Neuroradiology*. 2003;45:212-219.

44. Rachinger J, Buslei R, Prell J, Strauss C. Solid haemangioblastomas of the CNS: a review of 17 consecutive cases. *Neurosurg Rev*. 2009;32:37-47 [discussion: 47-48].

45. Rosenlof K, Fyhrquist F, Gronhagen-Riska C, Bohling T, Haltia M. Erythropoietin and renin substrate in cerebellar haemangioblastoma. *Acta Med Scand*. 1985;218:481-485.

46. Sakamoto N, Ishikawa E, Nakai Y, Akutsu H, Yamamoto T, Nakai K, et al. Preoperative endovascular embolization for hemangioblastoma in the posterior fossa. *Neurol Med Chir (Tokyo)*. 2012;52:878-884.

47. Sora S, Ueki K, Saito N, Kawahara N, Shitara N, Kirino T. Incidence of von Hippel-Lindau disease in hemangioblastoma patients: the University of Tokyo Hospital experience from 1954-1998. *Acta Neurochir (Wien)*. 2001;143:893-896.

48. Spetzger U, Bertalanffy H, Huffmann B, Mayfrank L, Reul J, Gilsbach JM. Hemangioblastomas of the spinal cord and the brainstem: diagnostic and therapeutic features. *Neurosurg Rev*. 1996;19:147-151.

49. Symon L, Murota T, Pell M, Bordi L. Surgical management of haemangioblastoma of the posterior fossa. *Acta Neurochir (Wien)*. 1993;120:103-110.

50. Takeuchi S, Tanaka R, Fujii Y, Abe H, Ito Y. Surgical treatment of hemangioblastomas with presurgical endovascular embolization. *Neurol Med Chir (Tokyo)*. 2001;41:246-251 [discussion: 251-252].

51. Wan JQ, Cui H, Wang Y. Surgical management of large solid hemangioblastomas of the posterior fossa. *J Clin Neurosci*. 2011;18:39-42.

52. Weil RJ, Lonser RR, DeVroom HL, Wanebo JE, Oldfield EH. Surgical management of brainstem hemangioblastomas in patients with von Hippel-Lindau disease. *J Neurosurg*. 2003;98:95-105.

53. Wind JJ, Bakhtian KD, Sweet JA, Mehta GU, Thawani JP, Asthagiri AR, et al. Long-term outcome after resection of brainstem hemangioblastomas in von Hippel-Lindau disease. *J Neurosurg*. 2011;114:1312-1318.

54. Xu QW, Xu R, Du ZY, Gao X. Surgical treatment for hemangioblastomas in the medulla oblongata. *Acta Neurochir (Wien)*. 2010;152:1331-1335 [discussion: 1335].

55. Yin L, Zhang L, Hao S, Zhang J, Wu Z. Medullary hemangioblastoma: 34 patients at a single institution. *J Clin Neurosci*. 2014;21:250-255.

56. Young S, Richardson AE. Solid haemangioblastomas of the posterior fossa: radiological features and results of surgery. *J Neurol Neurosurg Psychiatry*. 1987;50:155-158.

57. Zhou L, Du G. Diagnosis and surgical treatment of posterior fossa solid hemangioblastomas. *Chin Med J*. 2000;113:129-132.

58. Zhou LF, Du G, Mao Y, Zhang R. Diagnosis and surgical treatment of brainstem hemangioblastomas. *Surg Neurol*. 2005;63:307-315 [discussion: 315-316].

59. Abd Hamid D, Abdullah J, Ariff A, Muhamad M, Madhavan M. Cerebellar hemangioblastoma in a patient with von hippel-lindau disease: a case report. *Malays J Med Sci*. 2000;7:43-48.

60. Abo-Al Hassan A, Ismail M, Panda SM. Preoperative endovascular embolization of a cerebellar haemangioblastoma. A case report. *Med Princ Pract*. 2006;15:459-462.

61. Adams SA, Hilton DA. Recurrent haemangioblastoma with glial differentiation. *Neuropathol Appl Neurobiol*. 2002;28:142-146.

62. Agrawal A, Kakani A, Vagh SJ, Hiwale KM, Kolte G. Cystic hemangioblastoma of the brainstem. *J Neurosci Rural Pract*. 2010;1:20-22.

63. Anson JA, Glick RP, Crowell RM. Use of gadolinium-enhanced magnetic resonance imaging in the diagnosis and management of posterior fossa hemangioblastomas. *Surg Neurol*. 1991;35:300-304.

64. Asserraji M, El Kharras A. From headache to kidney tumor; an example of von Hippel- Lindau disease. *J Renal Inj Prev*. 2015;4:104-106.

65. Aziz M, Alam K, Varshney M, Maheshwari V, Sherwani RK, Gaur K, et al. Cerebellar haemangioblastoma: a rare entity. *BMJ Case Rep*. 2011;2011. https://doi.org/10.1136/bcr.03.2011.3943.

66. Bakariş S, Yüksel M. Cerebellar hemangioblastoma. Four case reports and review of the literature. *Cukurova Med J*. 2015;40:184-192.

67. Bhatoe HS. Mutism, oropharyngeal apraxia and dysarthria after posterior fossa tumour excision. *Br J Neurosurg*. 1997;11:341-343.

68. Bilge T, Bilge S, Barut S, Cokneseli B. Familial hemangioblastoma and von Hippel-Lindau's disease: case report. *Acta Neurol Belg*. 1991;91:223-229.

69. Binning MJ, Siddiqui AH. Cerebellar hemangioblastoma supplied by persistent hypoglossal artery. *J Neurointerv Surg*. 2012;4:e3.

70. Bishop FS, Liu JK, Chin SS, Fults DW. Recurrent cerebellar hemangioblastoma with enhancing tumor in the cyst wall: case report. *Neurosurgery*. 2008;62:E1378-E1379 [discussion: E1379].

71. Bret P, Streichenberger N, Guyotat J. Metastasis of renal carcinoma to a cerebellar hemangioblastoma in a patient with von Hippel Lindau disease: a case report. *Br J Neurosurg*. 1999;13:413-416.

72. Bush ML, Pritchett C, Packer M, Ray-Chaudhury A, Jacob A. Hemangioblastoma of the

cerebellopontine angle. *Arch Otolaryngol Head Neck Surg*. 2010;136:734-738.

73. Chandler HC Jr, Friedman WA. Radiosurgical treatment of a hemangioblastoma: case report. *Neurosurgery*. 1994;34:353-355 [discussion: 355].

74. Chang DS, Howng SL, Hwang SL, Chai CY. Contralateral recurrent cerebellar hemangioblastoma—a case report. *Kaohsiung J Med Sci*. 1998;14:514-518.

75. Choudhury T, Jahan S, Kamal M, Hossain MM, Khan ZR. Von Hippel-Lindau disease in a pregnant lady. *Mymensingh Med J*. 2012;21:184-187.

76. Chu LZ, Guan ZZ, Liu J, Yang H, Qi XL, Dong MG, et al. Multifocal central nervous system hemangioblastoma: a case report and review of the literature. *Genet Mol Res*. 2014;13:7904-7911.

77. Clelland CA, Treip CS. Histological differentiation of metastatic renal carcinoma in the cerebellum from cerebellar haemangioblastoma in von Hippel-Lindau's disease. *J Neurol Neurosurg Psychiatry*. 1989;52:162-166.

78. Crockard HA, Barnard RO, Isaacson PG. Metastasis of carcinoma to hemangioblastoma cerebelli: case report. *Neurosurgery*. 1988;23:382-384.

79. de Jonge JC, Wilmink JT, Janevski BK. Cerebellar hemangioblastoma. *J Belge Radiol*. 1998;81:236.

80. de San Pedro JR, Rodriguez FA, Niguez BF, Sanchez JF, Lopez-Guerrero AL, Murcia MF, et al. Massive hemorrhage in hemangioblastomas Literature review. *Neurosurg Rev*. 2010;33:11-26.

81. Dimogerontas G, Konstantinidis E, Antoniadis I. Gustatory disturbance due to a cerebellar hemangioblastoma. *Br J Neurosurg*. 2008;22:110-112.

82. Ding XH, Zhou LF, Tan YZ, Zhao Y, Zhu JJ. Histologic and histogenetic investigations of intracranial hemangioblastomas. *Surg Neurol*. 2007;67:239-245 [discussion: 245].

83. Djindjian M. Successful removal of a brainstem hemangioblastoma. *Surg Neurol*. 1986;25:97-100.

84. Donovan DJ, Iskandar JI, Citrone MJ, Royer MC. Successful removal of a cerebellar hemangioblastoma in a combat support hospital. *Mil Med*. 2006;171:211-215.

85. Dow GR, Sim DW, O'Sullivan MG. Excision of large solid haemangioblastomas of the cerebellopontine angle by a skull base approach. *Br J Neurosurg*. 2002;16:168-171.

86. Ehrenpreis SJ, Kristt DA, Rigamonti D. Fourth ventricular hemangioblastoma associated with pheochromocytoma and renal medullary fibroma. *J Neuroophthalmol*. 1994;14:183-187.

87. Ene CI, Morton RP, Ferreira M Jr, Sekhar LN, Kim LJ. Spontaneous hemorrhage from central nervous system hemangioblastomas. *World Neurosurg*. 2015;83, 1180.e1113-1187.

88. Eom KS, Kim DW, Choi SS, Choi KH, Kim TY. Preoperative embolization of a cerebellar haemangioblastoma using Onyx: case report and literature revie. *Neurol Neurochir Pol*. 2011;45:292-296.

89. Erdogan B, Sen O, Aydin MV, Bagis T, Bavbek M. Cerebellar hemangioblastoma in pregnancy. A case report. *J Reprod Med*. 2002;47:864-866.

90. Ertas G, Altundag MB, Ucer AR, Cankal F, Altundag K. Treatment of recurrent cerebellar hemangioblastoma with external radiotherapy in a patient with von Hippel-Lindau disease: a case report and review of the literature. *J Neurooncol*. 2005;73:273-275.

91. Escalona-Zapata J, Gimenez-Roldan S, Benito C. Cerebellar hemangioblastoma and subependymoma: a case report of an unprecedented association. *Clin Neuropathol*. 1985;4:87-91.

92. Finestone HM, Teasell RW. Autonomic dysreflexia after brainstem tumor resection. A case report. *Am J Phys Med Rehabil*. 1993;72:395-397.

93. Fukushima T, Sakamoto S, Iwaasa M, Hayashi S, Yamamoto M, Utsunomiya H, et al. Intramedullary hemangioblastoma of the medulla oblongata—two case reports and review of the literature. *Neurol Med Chir (Tokyo)*. 1998;38:489-498.

94. Gaymard B, Jan M, Gouaze A, Ozoux P, Autret A, Bacq Y. Cerebellar hemangioblastoma and primary hyperparathyroidism. *Surg Neurol*. 1989;31:369-375.

95. Giannetti AV, Rocha MD, Rosseto RS, Pedrosa HA. Pure neuroendoscopic resection of cystic cerebellar tumors. *World Neurosurg*. 2015;84, 867.e867-811.

96. Gnanalingham KK, Apostolopoulos V, Chopra I, Mendoza N, Peterson D. Haemangioblastoma: a rare cause of a cerebellar mass in the elderly. *Br J Neurosurg*. 2003;17:461-464.

97. Gorman EF, Bag AK, Palmer CA. Man with posterior fossa tumors 15 years apart. *Brain Pathol*. 2012;22:117-120.

98. Grahovac G. Solid hemangioblastoma of vestibular nerve mimicking vestibular schwannoma. *Neurol Sci*. 2015;36:1537-1539.

99. Guzman R, Grady MS. An intracranial aneurysm on the feeding artery of a cerebellar hemangioblastoma. Case report. *J Neurosurg*. 1999;91:136-138.

100. Hakim A, Isaac R, Vaidya G, Alimchandani A, Mehta PJ, Soneji SL. Hemangioblastoma of the brain stem presenting as hypertension. *J Assoc Physicians India*. 1993;41:463-464.

101. Hallsworth D, Thompson J, Wilkinson D, Kerr RS, Russell R. Intracranial pressure monitoring and caesarean section in a patient with von Hippel-Lindau disease and symptomatic cerebellar haemangioblastomas. *Int J Obst Anesth*. 2015;24:73-77.

102. Hamazaki S, Nakashima H, Matsumoto K, Taguchi K, Okada S. Metastasis of renal cell carcinoma to central nervous system hemangioblastoma in two patients with von Hippel-Lindau disease. *Pathol Int*. 2001;51:948-953.

103. Hayashi S, Takeda N, Komura E. Symptomatic cerebellar hemorrhage from recurrent hemangioblastoma during delivery. Case report. *Neurol Med Chir (Tokyo)*. 2010;50:1105-1107.

104. Ho VB, Smirniotopoulos JG, Murphy FM, Rushing EJ. Radiologic-pathologic correlation: hemangioblastoma. *AJNR Am J Neuroradiol*. 1992;13:1343-1352.

105. Hocker S, Hoover JM, Puffer RC, Meyer FB. Orthostatic hypotension following resection of a dorsal medullary hemangioblastoma. *Neurocrit Care*. 2012;16:306-310.

106. Hwang KJ, Song SJ, Park K-C, Yoon SS, Ahn T-B. Solid cerebellar hemangioblastoma with peritumoral edema: 5-years follow up. *Investig Magn Reson Imag*. 2015;19:248-251.

107. Ichikawa T, Hamazaki S, Sakai N, Otsuki Y, Wataya T, Kambara H, et al. Mixed germ cell tumor and hemangioblastoma in the cerebellum: report of a rare coexistence. *Brain Tumor Pathol*. 2011;28:279-284.

108. Ideguchi M, Kajiwara K, Yoshikawa K, Kato S, Ishihara H, Fujii M, et al. Continuous hypertension and tachycardia after resection of a hemangioblastoma behind the dorsal medulla oblongata: relationship to sympathetic overactivity at the neurogenic vasomotor center. *J Neurosurg*. 2010;113:369-373.

109. Isobe T, Yamamoto T, Akutsu H, Anno I, Shiigai M, Zaboronok A, et al. Proton magnetic resonance spectroscopy findings of hemangioblastoma. *Jpn J Radiol*. 2010;28:318-321.

110. Jamjoom A, Kane N, Nicoll J. Metastasis of a renal carcinoma to a cerebellar haemangioblastoma in a case of von Hippel-Lindau disease. *Neurosurg Rev*. 1992;15:231-234.

111. Jankovic GM, Ristic MS, Pavlovic-Kentera V. Cerebellar hemangioblastoma with erythropoietin in cerebrospinal fluid. *Scand J Haematol*. 1986;36:511-514.

112. Joerger M, Koeberle D, Neumann HP, Gillessen S. Von Hippel-Lindau disease—a rare disease important to recognize. *Onkologie*. 2005;28:159-163.

113. Kai Y, Kuratsu J, Suginohara K, Marubayashi T, Ushio Y. Cerebellar mutism after posterior fossa surgery—two case reports. *Neurol Med Chir (Tokyo)*. 1997;37:929-933.

114. Kamitani H, Hirano N, Takigawa H, Yokota M, Miyata H, Ohama E, et al. Attenuation of vascularity by preoperative radiosurgery facilitates total removal of a hypervascular hemangioblastoma at the cerebello-pontine angle: case report. *Surg Neurol*. 2004;62:238-243 [discussion: 243-244].

115. Kasarskis EJ, Tibbs PA, Lee C. Cerebellar hemangioblastoma symptomatic during pregnancy. *Neurosurgery*. 1988;22:770-772.

116. Kawano T, Iwamoto K, Mori K, Matsuse E. Multicentric hemangioblastomas in the cerebellum. *Surg Neurol*. 1985;24:677-680.

117. Kepes JJ, Yarde WL. Renal cell carcinoma followed by a cerebellar mass. *Kansas Med*. 1994;95:15-17.

118. Kim H, Joo JD, Kim YH, Kim CY. Development of a small solid cerebellar haemangioblastoma into a large pseudocyst with a mural nodule in a patient without VHL; the importance of regular follow-up. *BMJ Case Rep*. 2014;2014. https://doi.org/10.1136/bcr-2014-207149.

119. Kobos J, Kuroszczyk J, Janczukowicz J. A rare case of haemangioblastoma of the medulla oblongata with atypical clinical course. *Neurol Psychiatr (Bucur)*. 1989;27:163-165.

120. Kohno K, Matsui S, Nishizaki A, Takeda S, Sadamoto K, Sakaki S. Successful total removal of intramedullary hemangioblastoma from the medulla oblongata. *Surg Neurol*. 1993;39:25-30.

121. Kojimahara M, Watanabe T. Ultrastructural study of hemangiomas. 3. Specific endothelial granules in the cerebellar hemangioblastoma. *J Submicrosc Cytol*. 1986;18:177-181.

122. Krishnan KG, Schackert G. Outcomes of surgical resection of large solitary hemangioblastomas of the craniocervical junction with limitations in preoperative angiographic intervention: report of three cases. *Zentralbl Neurochir*. 2006;67:137-143.

123. Kuhne M, Sidler D, Hofer S, Lugli A, Ludwig C. Challenging manifestations of malignancies. Case 1. Polycythemia and high serum erythropoietin level as a result of hemangioblastoma. *J Clin Oncol*. 2004;22:3639-3640.

124. Kumar D, Sheoran RK, Bansal SK, Arora OP, Patil S. Cerebellar haemangioblastoma with spontaneous subarachnoid haemorrhage: a rare presentation. *Clin Radiol*. 2009;64:1241-1243.

125. Kume H, Kameyama S, Tanaka Y, Kitamura T. Cerebellar hemangioblastoma as a late manifestation of sporadic von Hippel-Lindau disease. *J Urol*. 1999;161:911-912.

126. Kurosaki Y, Tanaka YO, Itai Y. Solid cerebellar hemangioblastoma with an evolving large cystic component. *Eur Radiol*. 1997;7:910-912.

127. Laborde G, Gilsbach J, Harders A. Successful treatment of a haemangioblastoma in a 95 year-old patient. Case report. *Acta Neurochir (Wien)*. 1991;110:193-194.

128. Lallu S, Naran S, Palmer D, Bethwaite P. Cyst fluid cytology of cerebellar hemangioblastoma: a case report. *Diagn Cytopathol*. 2008;36:341-343.

129. Lee JY, Cho BM, Oh SM, Park SH. Delayed diagnosis of cerebellar hemangioblastoma after intracerebellar hemorrhage. *Surg Neurol*. 2007;67:419-421.

130. Love GL, Harkin JC. Hemangioblastomas with cystic stromal cell nuclei. *Acta Neuropathol*. 1985;67:160-162.

131. Lu K, Lee TC, Chen WJ, Lui CC. Successful removal of a hemangioblastoma from the medulla oblongata: case report. *Changgeng Yi Xue Za Zhi*. 1998;21:503-508.

132. Mariani L, Seiler RW. Cerebellar haemangioblastoma and invasive macroprolactinoma: case report. *J Clin Neurosci*. 1999;6:75-77.

133. Martin Escribano P, Melchor Iniguez R, Alfaro Abreu J, Palomera Frade J, Martinez Cruz R. A case of dirhythmic breathing. *Chest*. 1990;97:1018-1020.

134. Martin SE, Al-Khatib SM, Turner MS, Douglas-Akinwande AC, Hattab EM. A 41-year-old woman with von Hippel-Lindau and a cerebellar lesion. *Brain Pathol*. 2010;20:511-514.

135. Matsumura A, Maki Y, Munekata K, Kobayashi E. Intracerebellar hemorrhage due to cerebellar hemangioblastoma. *Surg Neurol*. 1985;24:227-230.

136. McComb RD, Eastman PJ, Hahn FJ, Bennett DR. Cerebellar hemangioblastoma with prominent stromal astrocytosis: diagnostic and histogenetic considerations. *Clin Neuropathol*. 1987;6:149-154.

137. Medvedev YA, Matsko DE, Zubkov YN, Pak VA, Alexander LF. Coexistent hemangioblastoma and arteriovenous malformation of the cerebellum. Case report. *J Neurosurg*. 1991;75:121-125.

138. Menovsky T, Andre Grotenhuis J, Bartels RH. Aneurysm of the anterior inferior cerebellar artery (AICA) associated with high-flow lesion: report of two cases and review of literature. *J Clin Neurosci*. 2002;9:207-211.

139. Mizobuchi Y, Kageji T, Tadashi Y, Nagahiro S. Craniotomy for cerebellar hemangioblastoma excision in a patient with von Hippel-Lindau disease complicated by uncontrolled hypertension due to pheochromocytoma. *Int J Surg Case Rep*. 2015;17:96-99.

140. Mottolese C, Stan H, Giordano F, Frappaz D, Alexei D, Streichenberger N. Metastasis of clear-cell renal carcinoma to cerebellar hemangioblastoma in von Hippel Lindau disease: rare or not investigated? *Acta Neurochir (Wien)*. 2001;143:1059-1063.

141. Mullally WJ, Hall KE. Hypnic headache secondary to haemangioblastoma of the cerebellum. *Cephalalgia*. 2010;30:887-889.

142. Munyon C, Chowdhry SA, Cohen ML, Bambakidis NC, Hsu DP. N-butyl 2-cyanoacrylate (n-BCA) embolization of a cerebellar hemangioblastoma. *J Neurointerv Surg*. 2011;3:386-389.

143. Murai Y, Kobayashi S, Tateyama K, Teramoto A. Persistent primitive trigeminal artery aneurysm associated with cerebellar hemangioblastoma. Case report. *Neurol Med Chir (Tokyo)*. 2006;46:143-146.

144. Nagayama T, Kaji M, Hirano H, Niiro M, Kuratsu J. Intractable hiccups as a presenting symptom of cerebellar hemangioblastoma. Case report. *J Neurosurg*. 2004;100:1107-1110.

145. Naidoo K, Bhigjee AI. Multiple cerebellar haemangioblastomas symptomatic during pregnancy. *Br J Neurosurg*. 1998;12:281-284.

146. Nakamura N, Sekino H, Taguchi Y, Fuse T. Successful total extirpation of hemangioblastoma originating in the medulla oblongata. *Surg Neurol*. 1985;24:87-94.

147. Nathan L, Satin AJ, Twickler DM. Cerebellar hemangioblastoma complicating pregnancy. A case report. *J Reprod Med*. 1995;40:662-664.

148. Newman S, Wasserberg J. A case report of the management of multiple metachronous haemangioblastomas in a patient with von Hippel-Lindau disease. *Br J Neurosurg*. 2008;22:104-106.

149. Nie Q, Guo P, Shen L, Li X, Qiu Y. Early-stage hemangioblastoma presenting as a small lesion with significant edema in the cerebellum. *J Craniofac Surg*. 2015;26:e119-e121.

150. Nishizawa S, Yokoyama T, Hinokuma K, Uemura K. Unilateral sensori-neural hearing disturbance caused by intramedullary cerebellar tumors—three case reports. *Neurol Med Chir (Tokyo)*. 1997;37:701-707.

151. Novak Z. Endoscopic cure of cerebellar hemangioblastoma. *Bratisl Lek Listy*. 2004;105:8-10.

152. Ogiwara H, Ichi S, Ueki K, Suzuki I. Cerebellar hemangioblastoma associated with primary hyperparathyroidism—case report. *Neurol Med Chir (Tokyo)*. 2003;43:92-94.

153. Othmane IS, Shields C, Singh A, Shields J, Goldman W. Postpartum cerebellar herniation in von Hippel-Lindau syndrome. *Am J Ophthalmol*. 1999;128:387-389.

154. Oya S, Nejo T, Indo M, Matsui T. Pearls & Oysters: Anorexia and emaciation in patients with cerebellar hemangioblastoma. *Neurology*. 2014;83:1298-1300.

155. Ozturk S, Soyluk O, Gorcin S, Alisir S, Guven D, Turkmen A, et al. A rare post-transplant malignancy, cerebellar hemangioblastoma: a case report. *J Nephrol*. 2005;18:781-782.

156. Ozveren MF, Topsakal C, Erol FS, Kaplan M, Uchida K, Tanik C. Tentorial vascularization in solid hemangioblastoma—case report. *Neurol Med Chir (Tokyo)*. 2001;41:201-205.

157. Page KA, Wayson K, Steinberg GK, Adler JR Jr. Stereotaxic radiosurgical ablation: an alternative treatment for recurrent and multifocal hemangioblastomas. A report of four cases. *Surg Neurol*. 1993;40:424-428.

158. Pavesi G, Berlucchi S, Feletti A, Opocher G, Scienza R. Hemangioblastoma of the obex mimicking anorexia nervosa. *Neurology*. 2006;67:178-179.

159. Pereda Rios A, Pintado Recarte P, De Leon-Luis J, Fernandez-Garcia P, Iza B, Salinero Paniagua E, et al. Cerebellar hemangioblastoma as the cause of maternal obstructive hydrocephalus during the third trimester. *Eur J Obstet Gynecol Reprod Biol*. 2012;165:370-372.

160. Prontera A, Puzzolante A, Carpeggiani P, Pavesi G. Symptomatic anterior cerebral artery vasospasm after brainstem hemangioblastoma resection. A case report. *Neuroradiol J*. 2014;27:186-190.

161. Rahman A, Hoque SU, Bhandari PB, Alam S. Contiguous haemangioblastomas of the brain and spine in a patient of Von Hippel-Lindau disease. *BMJ Case Rep*. 2013;2013. https://doi.org/10.1136/bcr-2012-007989.

162. Rehman T, Ali R, Yonas H. Cerebellar haemangioblastoma: temporising treatment in a high risk pregnancy. *BMJ Case Rep*. 2009;2009. https://doi.org/10.1136/bcr.01.2009.1413.

163. Rey-Dios R, Cohen-Gadol AA. Intraoperative fluorescence for resection of hemangioblastomas. *Acta Neurochir (Wien)*. 2013;155:1287-1292.

164. Reynolds MR, Crilly SM, Sweeney KJ, Farrell M, Rawluk D. Metastatic pancreatic neuroendocrine tumor to the central nervous system in a patient with von Hippel-Lindau disease: A case report and literature review. *Br J Neurosurg*. 2015;29:291-293.

165. Rojiani AM, Elliott K, Dorovini-Zis K. Extensive replacement of spinal cord and brainstem by hemangioblastoma in a case of von Hippel-Lindau disease. *Clin Neuropathol*. 1991;10:297-302.

166. Romansky K, Arnaudova V, Nachev S. Hemangioblastoma during pregnancy. Case report. *Zentralbl Neurochir*. 1992;53:37-39.

167. Rosenthal G, Israel Z, Umansky F. Metastatic brain adenocarcinoma masquerading as recurrent haemangioblastoma. *Acta Neurochir (Wien)*. 1998;140:1207-1208.

168. Ryang YM, Oertel MF, Thron A, Gilsbach J, Rohde V. Rare intramedullary hemorrhage of a brainstem hemangioblastoma. *Zentralbl Neurochir*. 2007;68:29-33.

169. Sadanaga N, Kuwano H, Watanabe M, Mori M, Morioka T, Sugimachi K. Esophageal cancer and second primary brain tumor. *Oncol Rep*. 1998;5:1135-1136.

170. Sadiq S, Jamjoom ZB, Kyriacou KC. Haemangioblastoma. *J Pak Med Assoc*. 1989;39:113-115.

171. Sajadi A, de Tribolet N. Unusual locations of hemangioblastomas. Case illustration. *J Neurosurg*. 2002;97:727.

172. Samuel EJ, Natarajan N, Latha RM. Polycythemia with cerebellar hemangioblastoma. *Global J Med Res*. 2015;15:39-45.

173. Sanford RA, Smith RA. Hemangioblastoma of the cervicomedullary junction. Report of three cases. *J Neurosurg*. 1986;64:317-321.

174. Sawle GV, Sarkies NJ. Bilateral fourth nerve palsy due to cerebellar haemangioblastoma. *J R Soc Med*. 1989;82:111-112.

175. Seyama H, Kurita H, Noguchi A, Shiokawa Y, Saito I. Resolution of intractable hiccups caused by cerebellar hemangioblastoma. *Neurology*. 2001;57:2142.

176. Shekhar H, Myles L, Lee M. Von Hippel-Lindau disease: delayed presentation as a cerebellar haemangioblastoma in an elderly patient. *Br J Neurosurg*. 2009;23:97-98.

177. Shimoda Y, Ogawa Y, Endo H, Watanabe M, Tominaga T. Coexistence of sporadic cerebellar hemangioblastoma and pituitary null cell adenoma: simultaneous expression of von Hippel-Lindau gene product. Case report. *Neurol Med Chir (Tokyo)*. 2012;52:591-594.

178. So CC, Ho LC. Polycythemia secondary to cerebellar hemangioblastoma. *Am J Hematol*. 2002;71:346-347.

179. Sobottka SB, Frank S, Hampl M, Schackert HK, Schackert G. Multiple intracerebral haemangioblastomas in identical twins with von Hippel-Lindau disease—a clinical and molecular study. *Acta Neurochir (Wien)*. 1998;140:281-285.

180. Song DK, Lonser RR. Pathological satiety caused by brainstem hemangioblastoma. *J Neurosurg Pediatr*. 2008;2:397-401.

181. Standard SC, Ahuja A, Livingston K, Guterman LR, Hopkins LN. Endovascular embolization and surgical excision for the treatment of cerebellar and brain stem hemangioblastomas. *Surg Neurol*. 1994;41:405-410.

182. Summerfield DA. Psychiatric vulnerability and cerebellar haemangioblastoma. A case report. *Br J Psychiatr*. 1987;150:858-860.

183. Sun Z, Yuan D, Sun Y, Yan P, Zuo H. Surgical resection of cerebellar hemangioblastoma with enhanced wall thickness: A report of two cases. *Oncol Lett*. 2015;9:1597-1599.

184. Svensson AM, Pang Y, Moore NJ, Tindle BH. Cystic tumor of the cerebellum with megaloblastic erythropoiesis. Hemangioblastoma with megaloblastic hematopoiesis. *Arch Pathol Lab Med*. 2006;130:886-889.

185. Takayasu K, Yuhki K, Ohkura H, Tobisu K, Tajiri H, Nomura K, et al. Imaging diagnosis of von Hippel-Lindau disease: a case report. *Jpn J Clin Oncol*. 1988;18:261-267.

186. Tampieri D, Leblanc R, TerBrugge K. Preoperative embolization of brain and spinal hemangioblastomas. *Neurosurgery*. 1993;33:502-505 [discussion: 505].

187. Tang Z, Wang C, Shi J. A solitary hemangioblastoma located on the trochlear nerve. *J Clin Neurosci*. 2014;21:333-335.

188. Tognetti F, Galassi E, Servadei F, Gaist G. Haemangioblastomas of the brain stem. *Neurochirurgia*. 1986;29:230-234.

189. Tomono A, Hara S, Hirose T, Itoh T. A case of cerebellar hemangioblastoma with rhabdoid features. *Brain Tumor Pathol*. 2015;32:145-150.

190. Trimble M, Caro J, Talalla A, Brain M. Secondary erythrocytosis due to a cerebellar hemangioblastoma: demonstration of erythropoietin mRNA in the tumor. *Blood*. 1991;78:599-601.

191. Tripathy K, Gouda KP, Das R, Rath J, Mohanty R. Cerebellar haemangioblastoma mimicking renal cell carcinoma—a case report. *Indian J Pathol Microbiol*. 2005;48:375-376.

192. Tsugu H, Fukushima T, Ikeda K, Utsunomiya H, Tomonaga M. Hemangioblastoma mimicking tentorial meningioma: preoperative embolization of the meningeal arterial blood supply—case report. *Neurol Med Chir (Tokyo)*. 1999;39:45-48.

193. Uchino A, Ohno M. Cerebellar hemangioblastoma supplied by the artery of Davidoff and Schechter: a case report. *Nihon Igaku Hoshasen Gakkai Zasshi*. 1986;46:1194-1197.

194. Van Velthoven V, Reinacher PC, Klisch J, Neumann HP, Glasker S. Treatment of intramedullary hemangioblastomas, with special attention to von Hippel-Lindau disease. *Neurosurgery*. 2003;53:1306-1313 [discussion: 1313-1314].

195. Vatsal DK, Husain M, Husain N, Chawla S, Roy R, Gupta RK. Cerebellar hemangioblastoma simulating arachnoid cyst on imaging and surgery. *Neurosurg Rev*. 2002;25:107-109.

196. Vazquez-Anon V, Botella C, Beltran A, Solera M, Piquer J. Preoperative embolization of solid cervicomedullary junction hemangioblastomas: report of two cases. *Neuroradiology*. 1997;39:86-89.

197. Wang Y, Gao X. Intraoperative sonographically guided resection of hemangioblastoma in the cerebellum. *J Clin Ultrasound*. 2006;34:247-249.

198. Wang Z, Hu J, Xu L, Malaguit J, Chen S. Intratumoral hemorrhage in a patient with cerebellar hemangioblastoma: a case report and review. *Medicine*. 2015;94:e497.

199. Wierzba-Bobrowicz T, Schmidt-Sidor B, Szpak GM, Lechowicz W, Gorski R, Jagielski J, et al. Haemangioblastoma of the posterior cranial fossa: clinico-neuropathological study. *Folia Neuropathol*. 2003;41:245-249.

200. Wong CW, Wai YY, Lui TN, Chang CN. Bilateral glossopharyngeal neuralgia after excision of a solitary cervico-medullary haemangioblastoma: case report. *Acta Neurochir (Wien)*. 1992;114:64-67.

201. Wysocka B, Welnicka-Jaskiewicz M, Matuszewska K, Sloniewski P, Jassem J, Izycka-Swieszewska E, et al. The occurrence of cerebellar hemangioblastoma in numerous first degree relatives with von Hippel-Lindau disease. *Folia Neuropathol*. 1999;37:175-178.

202. Xiong J, Chu SG, Wang Y, Zhu JJ, Li C, Mao Y. Metastasis of renal cell carcinoma to a haemangioblastoma of the medulla oblongata in von Hippel-Lindau syndrome. *J Clin Neurosci*. 2010;17:1213-1215.

203. Yamada SM, Ikeda Y, Takahashi H, Teramoto A, Yamada S. Hemangioblastomas with blood supply from the dural arteries—two case reports. *Neurol Med Chir (Tokyo)*. 2000;40:69-73.

204. Yamamoto T, Wakui K, Kobayashi M. Hemangioblastoma in the cerebellar vermis: a case report. *Acta Cytol*. 1996;40:346-350.

205. Yang QX, Li Y, Tian XY, Liao B, Jiang XZ, Li Z. Bilateral cerebellar epithelioid hemangioblastoma with possible ependymal differentiation in a patient with von Hippel-Lindau disease. *Neuropathology*. 2012;32:662-667.

206. Yuceer N, Erdem A, Asir A, Bulay O. Multifocal hemangioblastoma associated with erythrocytosis. *Turkish Neurosurg*. 1995;5:16-20.

207. Zager EL, Shaver EG, Hurst RW, Flamm ES. Distal anterior inferior cerebellar artery aneurysms. Report of four cases. *J Neurosurg*. 2002;97:692-696.

208. Zhou F, Zhang R, Ji Y, Xu Q, Zhou L, Shi Y. Familial occurrence of hemangioblastoma of central nervous system. *Chin Med J*. 1997;110: 225-228.

209. Zilidis G, Cadoux-Hudson TA. Recurrent dural based cystic cerebellar haemangioblastoma in a patient with von Hippel-Lindau disease. *Acta Neurochir (Wien)*. 2007;149:433-436.

Conflict of interest statement: F.A.B. serves as a consultant for Medtronic. The other authors report no financial relationships or conflicts of interest.

Received 28 September 2017; accepted 30 November 2017

Citation: World Neurosurg. (2017). https://doi.org/10.1016/j.wneu.2017.11.173

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