

Haemangiopericytoma and solitary fibrous tumour of the parotid gland: a scoping review

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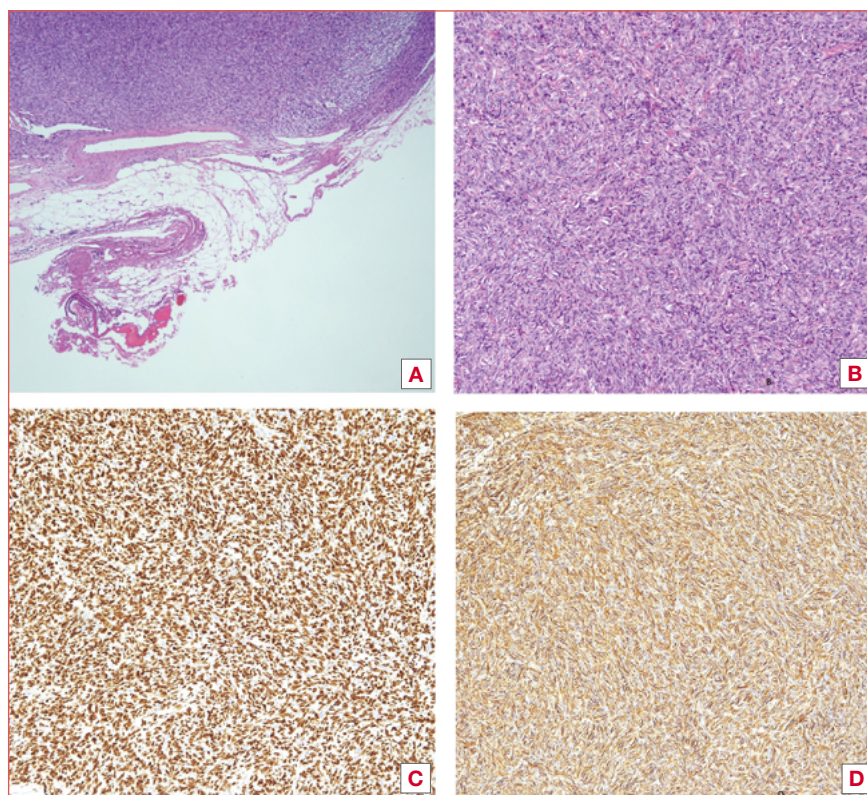
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Cover figure. Solitary fibrous tumour/haemangiopericytoma, well-circumscribed in relation to adjacent soft tissue (4×). Ovoid to fusiform spindle cells with indistinct borders, arranged haphazardly or in short, ill-defined fascicles (A,B). Staghorn-like, branching, hyalinised vasculature, hyalinised to collagenous stroma, occasionally with streaming of cells between collagen (10×). Nuclear STAT6 and cytoplasmic CD34 positivity observed (C,D).

Summary

Salivary gland tumours represent about 3-10% of head and neck tumours, with the parotid gland being the most affected. The World Health Organization classification of these tumours is continually evolving due to their diverse histology and biological behaviour. Haemangiopericytoma (HPC) and solitary fibrous tumour (SFT) have been reclassified as a single entity characterised by *NAB2-STAT6* gene rearrangement, typically presenting as slow-growing, painless masses in the parotid region, and immunohistochemistry is essential for diagnosis. This study aims to examine the clinical characteristics of these tumours to better understand their biological behaviour. Following PRISMA 2020 guidelines, we reviewed the literature using the search string (haemangiopericytoma), OR (solitary fibrous tumor) AND (parotid gland). Of the initially collected 201 papers, 49 were selected for detailed analysis, focusing on data from 53 patients, all of whom underwent surgery. Of these patients, 11.3% (n = 6) were diagnosed with malignancy, while 3 more were suspected to have malignancy. Our findings suggest that SFT morphology predominates among

lesions, but malignancy is more often associated with features of HPC. Further comprehensive study is needed to gather additional data on their biological behaviour.

Key words: haemangiopericytoma, solitary fibrous tumour, *NAB2-STAT6* gene rearrangement, parotid gland, recurrence

Introduction

Salivary gland tumours represent approximately 3-10 % of head and neck tumours, wherein the parotid gland is the most affected, and around 25% of such tumours are malignant¹. Because of their heterogeneous histology and biological behaviour, the World Health Organization (WHO) classification of these tumours continues to change. In this context, haemangiopericytoma (HPC) and solitary fibrous tumour (SFT) are rare entities. Despite historically being considered two different entities, the 4th Edition of the WHO classifies them as fibroblastic tumours characterised by haphazardly arranged spindled-to-ovoid cells, with prominent staghorn vasculature and *NAB2-STAT6* gene rearrangement².

HPC was described for the first time in 1942³; it originates from the pericytes of Zimmerman surrounding the capillaries and postcapillary venules⁴, and can be found in the head and neck region in 15-25% of cases⁵.

SFTs are composed of pleomorphic spindle cells, are distributed and patternless, and are situated within variably dense collagenous stroma. The most common sites for these tumours in the head and neck are the sino-nasal tract, orbit, oral cavity, and salivary glands⁶.

Tumours with high mitotic count, hypercellularity, necrosis, and atypia (round cell and anaplastic morphology, or nuclear pleomorphism) are considered malignant⁷. The *NAB2-STAT6* fusion gene is a unique molecular feature of the HPC/SFT family, present in up to 100% of cases⁸.

Immunohistochemistry is very important for correct diagnosis. The markers used include CD34, Bcl2, CD99, and vimentin expression in the absence of actin, desmin, S100 protein, and epithelial cells⁹. Immunostaining for *STAT6* rearrangement is also available in pathology laboratories^{10,11}.

These tumours typically present as slow-growing, painless masses in the parotid region. Due to their slow growth, symptoms are not always noticeable in the early stages. While they are generally considered benign, there have been instances of malignant behaviour, though there is currently limited knowledge about this type of tumour due to its rarity.

On CT scans, they are both often homogeneous in appearance, although cystic areas, calcifications, myxoid degeneration, or haemorrhage may be present, particularly in large tumours¹². They tend to displace rather than invade

surrounding tissues, and enhance after contrast administration. On MRI, HPC/SFT displays low T1 signal intensity and variable T2 signal¹³, and enhances intensely after intravenous gadolinium administration¹⁴ despite these characteristics are not pathognomonic for HPC/SFT. While HPC/SFT demonstrate benign behaviour, follow-up is essential to detect any sign of local recurrence early on. A tendency to both local and distant recurrence has been described¹⁵.

Treatment requires surgical removal, with approaches varying depending on location and extent of involvement¹⁶. This study endeavours to explore the clinical characteristics of these tumours to better understand their biologic potential and their transformation into a malignant entity through a review of the literature (Cover figure).

Materials and methods

This review was conducted with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) 2020 guidelines (Fig. 1)¹⁷. The research was carried out using the PubMed and Scopus database with the following research string: *[(haemangiopericytoma) OR (solitary fibrous tumor)] AND (parotid gland)*. Two reviewers (C.L. and E.S.) performed the literature search and the abstract and full text reading. All the articles found were included, without any period of restriction. The last research on the database was performed in April 2024.

The inclusion criteria for first abstract reading selection were:

- abstracts in English;
- articles about haemangiopericytoma or solitary fibrous tumour;
- studies on diseases of the parotid gland.

The exclusion criteria for this phase were:

- abstract in other languages;
- articles treating different topics;
- diseases of other salivary glands.

After the first abstract based selection, a full text reading was performed, using additional criteria.

The inclusion criteria for the second selection phase were:

- case report or case series as study design;
- full text available;
- full text in English;
- studies on diseases of the parotid gland.

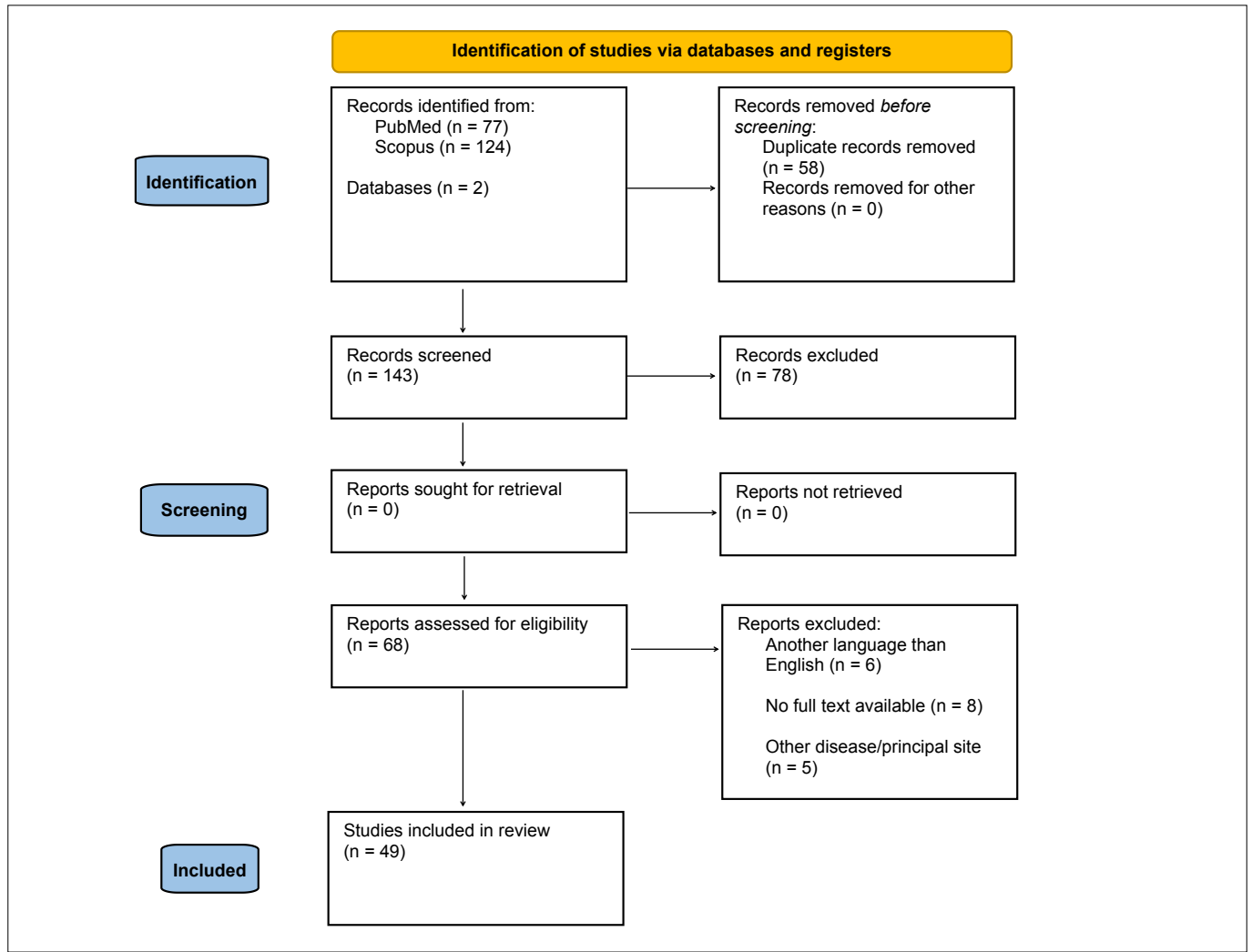


Figure 1. PRISMA 2020 flow diagram of the literature selection process.

The exclusion criteria were:

- review;
- the full text not being available;
- the full text being in another language;
- studies on disease of the other salivary glands.

Two-hundred and one papers were selected. In total, 58 duplicated articles were eliminated, resulting in 143 articles being eligible for further analysis. First, an abstract reading selection was made according to the inclusion criteria, in which 68 abstracts were selected. After this, a further exclusion following full-text reading and the pre-established criteria was made, with 49 articles being selected (Fig. 1).

The selected articles were then analysed in detail, extracting data on study design; publication year; age and gender of the patients; imaging and histologic reports of the first parotid disease and its metastasis; the type of treatment and outcomes; potential recurrence and related treatment and follow-up status.

Results

Ten of the 49 articles selected (20%) were published before the year 2000. A total of 53 patients (28 males and 25 females) were reported in the selected papers, and the mean age at diagnosis was 49.3 years (range, 11-82), while four (7.6%) cases were paediatric. In total, 22 pa-

tients developed the disease in the right parotid gland, while for 30 patients it developed in the left (for one patient, data were missing). Clinical data of the sample are reported in Table I. All the selected articles are listed in Table II.

Regarding clinical presentation, 48 patients showed swelling in the parotid area, 5 complained of loco-regional pain, and in 2 of 5 cases the mass was situated in the deep lobe^{21,25,55,56}. Only one patient showed facial nerve impairment at the first medical examination; this patient was a 72-year-old woman with a 5-year history of a slowly enlarging left parotid mass and a diagnosis of malignant solitary fibrous tumour⁵⁶. In the paediatric cases, 3 of 4 patients were females, and swelling in the parotid area was seen in each.

With regard to preoperative assessments, 39 (73.5%) patients in total were referred to imaging (25 underwent CT and 14 underwent MRI), while 17 (32%) underwent ultrasound only. From a cytopathology perspective, most of the cases did not report preoperative fine-needle aspiration cytology (FNAC) evaluation and cytologic description. In 5 studies an inconclusive result was indicated, even if repeated in one case.

Of all the subjects, the vast majority – 49 in total – underwent surgery. Specifically, 11 underwent enucleoresection, 14 underwent superficial parotidectomy, 20 had total parotidectomy, and 4 had subtotal parotidectomy. A transnasal/transoral surgical approach was taken in one patient⁴. However, treatment data were not disclosed for 3 cases of HPC^{25,56}.

Only one patient received primary chemotherapy (CHT) and subsequent surgery²¹. After failure of CHT, a stylohamular approach was taken and a suprahyoid neck dissection was performed.

The histological diagnosis was HPC (30.2%) for 16 patients, 4 of whom (25%) had malignancy, while SFT was diagnosed in 37 patients (69.8%), of which 2 (5%) had malignancy; overall, the total number of malignant cases was 6 (11.3%). In 2 cases, tumours with the histological characteristic of “aggressivity in nature”^{4,18} were described, and in one, undifferentiated spindle cells were reported²⁸. These 3 subjects each underwent RT and were diagnosed with HPC. Including these, the overall malignancy rate was 16.9%, and 43% (7/16) in HPC cases. All relevant histological markers are detailed in Table II.

Concerning malignant cases, one patient was disease-free for nearly 5 years after surgery. She subsequently developed pulmonary and hepatic metastases, which were surgically removed³⁶. The second patient with malignancy²¹ died due to distant metastases, with no specification regard-

Table I. Clinical and demographic characteristics of the sample (n = 53) sample.

Clinical presentation	Swelling in parotid region n = 48 (90.6%)
	Pain n = 5 (9.4%)
	Paraesthesia n = 1 (1.9%)
	Facial nerve impairment n = 1 (1.9%)
Mean age	49.3 y (11-82)
Gender	28 M (52.8%)
	25 F (47.2%)
Surgery	Enucleoresection n = 11 (20.7%)
	Superficial parotidectomy n = 14 (26.4%)
	Total parotidectomy n = 20 (37.7%)
	Subtotal parotidectomy n = 4 (7.5%)
	Transnasal-transoral approach n = 1 (1.9%)
	No data available n = 3 (5.6%)

ing the location or time of onset. In the third case, the tumour showed two different behaviours under microscopy: a histologically benign area of haemangiopericytoma was present and separated by a clear-cut border from a second area, in which the structure was that of a histologically malignant haemangiopericytoma. The patient developed fatal metastasis²⁰.

The fourth concerns a patient with a diagnosis of malignant HPC who died with recurrence of the disease after surgery¹⁹, although distant metastases were not mentioned. In the recent fifth case, a young adult with a malignant SFT underwent surgery and RT with no signs of recurrence or distant metastasis at 11 months⁶³. The final case⁵⁶ relates to a case of malignant SFT, in which distant metastases were not mentioned during follow-up. Four patients (7.5%) had postoperative RT^{18,63,28}, and one underwent both CHT and RT⁴.

Six patients (11.3%) had loco-regional recurrence of disease, while only one was malignant. In total, 4 of 53 patients (7.5%) developed distant metastasis, while 3 of 6 malignant cases (50%) and one uncertain case with peculiar characteristics presented metastasis at follow-up¹⁸. The most common site of metastasis was the lungs, although other sites included the pleura, pelvis, muscles, body of vertebrae, retroperitoneum, and liver, with details shown in Table III.

The mean follow-up of the patients was 24.1 months, although in 12 (22%) cases this information was not available.

Table II. Clinical data about the cases included in this review.

Authors	Year	Cases	Gender	Age	Treatment of parotid disease	Histology	Marker (+)	Marker (-)	Adjuvant treatment	Recurrence	Metastasis	Follow up time, months/status
Neal et al. ¹⁸	1973	1	M	21	TP	HPC malignant?	NA	NA	RT		yes	48/DOD
Katz ¹⁹	1975	1	F	69	ER	Malignant HPC	NA	NA		yes		168/DOD
Massarelli et al. ²⁰	1980	1	M	64	TP	Malignant HPC	NA	NA			yes	16/DOD
Katsantonis et al. ²¹	1989	1	M	22	CT	Malignant HPC	NA	NA			yes	18/DOD
Carrillo et al. ²²	1992	3	F	79	TP	HPC	NA	NA				18/AND
			F	38	SP	HPC						18/AND
			M	27	SP	HPC						5/AND
Lee et al. ²³	1992	1	M	14	SP	HPC	NA	NA				24/AND
Whittam et al. ²⁴	1993	1	F	82	ER	HPC	NA	S100, epithelial markers				12/AND
Hanau et al. ²⁵	1994	1	F	73	NA	SFT	VIM, CD34	CK, CD31				NA
Ferreiro et al. ²⁶	1996	2	M	46	SP	SFT	VIM, CD34	-				1/AND
			F	78	SP	SFT						12/AND
Sato et al. ²⁷	1998	1	M	52	TP	SFT	VIM, CD34	Desmin, S100, SMA				12/AND
Mortelé et al. ⁶⁵	2000	1	M	26	TP	HPC	NA	NA				NA
Sawh et al. ²⁸	2000	1	F	65	STP	Undifferentiated spindle-cell neoplasm HPC	VIM, CD34	SMA, desmin, S100, CK	RT			24/AND
Mohammed et al. ²⁹	2001	1	F	42	ER	SFT	VIM, CD34	CAM 5.2, AE1/AE3, EMA, S100, GFAP, SMA				3/AND
Kumagai et al. ³⁰	2002	1	F	47	TP	SFT	VIM, CD34, bcl-2	SMA, S100, CK, collagen type IV, CD117				14/AND
Sikes et al. ³¹	2003	1	M	62	TP	HPC	NA	NA				72/AND
Thompson et al. ³²	2004	1	F	11	TP	SFT	CD34, bcl-2	S100, desmin, EMA, SMA				24/AND
Gerhard et al. ³³	2004	1	F	34	SP	SFT	VIM, CD34	Actin, SMA, S100				24/AND
Wiriosuparto et al. ³⁴	2005	1	M	42	TP	SFT	CD34, bcl-2, CD99	AE1/AE3, CAM5.2, S100, calponin, p63	NA			NA
Sreetharan et al. ³⁵	2005	1	M	44	TP	SFT	NA	NA				NA
Balaji et al. ³⁶	2008	1	F	56	TP	Malignant HPC	VIM, actin, CD34	S100, GFAP			yes	60/AWD
Cho et al. ³⁷	2008	1	M	58	TP	SFT	CD34, bcl-2, CD99	S100, SMA, CK				67/AND
Manglik et al. ³⁸	2008	1	M	79	SP	SFT	CD34, bcl-2, VIM	SMA, S100 and EMA				3/AND
Bauer et al. ³⁹	2011	1	M	66	SP	SFT	CD34, bcl-2, VIM, CD99	CD68, S100, CK, EMA, CAM5.2, SMA, actin, desmin, MYOD1, myogenin, CD117, GFAP, CD31, p63, p53, CD56, NFP, ALK-1				9/AND
Nowlin et al. ⁴⁰	2011	1	F	28	SP	HPC	CD34, FLI-1, CD68	Desmin, SMA, S100, CK				18/AND
Iyengar et al. ⁴¹	2011	1	M	49	TP	SFT	VIM, CD34, CD99	Desmin, S100, CD117, CK	NA			NA
Cristofaro et al. ⁴²	2012	1	M	38	ER	SFT	CD34, CD99, bcl-2, and VIM	CK, S100, SMA				60/AND
Chen et al. ⁴³	2013	1	M	33	TP	HPC	CD34, CD99, bcl-2, VIM	CK, EMA, HMB45, S100, CD117, p63				12/AND
Sousa et al. ⁴⁴	2013	1	M	32	SP	SFT	CD34, CD99 and bcl-2	CAM5.2, SMA and S100				10/AND
Apuhan et al. ⁴⁵	2013	1	M	51	ER	SFT	CD34 and bcl-2, CD99	S100, Melan-A				NA
Liu et al. ⁴⁶	2014	1	M	55	ER	SFT	CD34, VIM, CD99, bcl-2	S100, CK, SMA				10/AND
Chis et al. ⁴⁷	2014	1	F	67	TP	SFT	VIM, CD34, bcl-2	S100, SMA, GFAP				NA/AND

Table II. *continues.*

Authors	Year	Cases	Gender	Age	Treatment of parotid disease	Histology	Marker (+)	Marker (-)	Adjuvant treatment	Recurrence	Metastasis	Follow-up time, months/status
Alonso-Rodriguez et al. ⁴⁸	2014	1	F	73	ER	SFT	CD34, CD99, bcl-2	AE/1, AE/2, EMA, S100		Yes		9/AND
Künzel et al. ⁴⁹	2015	1	F	46	STP	SFT	CD34, CD99, VIM, bcl-2	CK, S100		Yes		19/AND
Yu et al. ⁵⁰	2015	1	M	53	SP	SFT	CD34, CD99, and bcl-2	Pan-CK, EMA, SMA, desmin, S100, CD31, p63, ALK-1				24/AND
Gervasio et al. ⁵¹	2017	1	M	54	SP	SFT	CD34, CD99, bcl-2	NA				24/AND
Rais et al. ⁵²	2017	1	M	42	TP	SFT	CD34, STAT6	CK, SMA, S100, CD31				11/AND
Ralli et al. ⁵³	2018	1	F	14	ER	SFT	VIM, CD34, bcl-2, and CD99	S100, desmin, SMA, myogenin				NA/AND
Lim et al. ⁵⁴	2019	1	M	51	STP	SFT	CD34, bcl-2, CD99, STAT6	CK (AE1-3), CK14, SMA, CD21, CD35				3/AND
Chintale et al. ⁴	2020	1	F	14	Transnasal and transoral approach	HPC "Agressive in nature"	NA	NA	CHT-RT	Yes		NA/AND
Romano et al. ⁵⁵	2020	1	M	50	ER	SFT	CD34, bcl-2, STAT-6, CD99	Actin, desmin, CK CAM				NA
Velez Torres et al. ⁵⁶	2021	2	M	57	NA	SFT	CD34	Desmin, keratin, EMA, and p63				NA
			F	72	NA	Malignant SFT						NA
Vitale et al. ⁵⁷	2021	1	F	66	TP	SFT	CD34, VIM, EMA, bcl-2, CD99	CK, S100, HMB45, desmin, actin, CD117, CD31				NA
Li et al. ⁵⁸	2021	1	M	40	ER	SFT	VIM, CD34, STAT6	CD31, desmin, S100		Yes		NA
Abdulhaleem et al. ⁵⁹	2022	1	F	48	TP	SFT	CD34, CD99, bcl-2, STAT6	CK AE1/AE3, EMA, S100, CD21, CD23, SMA, CD31				12/AND
Goker et al. ⁶⁰	2022	1	F	80	ER	SFT	STAT6, CD34, CD99, bcl-2	SMA, desmin, CK AE1/AE3 and ALK1				7/AND
Boschetti et al. ⁶¹	2022	1	M	52	SP	SFT	STAT6, bcl-2, CD99	SMA, calponin, CD34, CD31, ERG, p63, GFAP, S100, CK AE1/AE3, CK7				6/AND
De Ravin et al. ⁶²	2022	1	F	81	TP	SFT	CD34, CD99, ALDH1, bcl-2, CD99	STAT6, S100, desmin				NA
Lee et al. ⁶³	2022	1	F	33	SP	Malignant SFT	CD34, STAT-6, FLI-1	Pan-CK, CAM5.2, p63, S100, CD31, SMA, calponin	RT			11/AND
Muñoz Guerra et al. ⁶⁴	2022	1	F	37	TP	SFT	CD34, bcl-2	S100, CK				12/AND

SFT: solitary fibrous tumour; HPC: haemangiopericytoma; TP: total parotidectomy; SP: superficial parotidectomy; ER: enucleoresection; STP: subtotal parotidectomy; NA: not available; DOD: dead of disease; AND: alive and without disease; AWD: alive with disease.

Table III. Details about recurrence and metastasis.

	Time (mean)	Sites	Histology
Metastasis (3/6 = 50%)	31.2 months	Lungs (3) muscles (1), liver (1), vertebrae (1), pelvis (1), retroperitoneal carcinomatosis (1)	Malignant HPC (3 + 1 uncertain case)
Recurrence (6/53 = 11.3%)	24.2 months	Local recurrence	SFT (4)
			Malignant HPC (1)
			HPC (1)

Discussion

To the best of our knowledge, this article presents the first systematic review of HPC/SFT within the parotid gland. The epidemiological characteristics confirmed by this review show a median age of incidence of 49.3 years, ranging from 11 to 82 years, and a male-to-female ratio of 28 to 25. However, the tumour incidence in the juvenile population and in females was not as low as expected. Indeed, it

has been reported that around 5% of salivary gland tumours occur in patients under 18 years⁶⁶ of age, although this review shows a higher percentage, namely 7.6% of paediatric cases.

Concerning clinical features, the vast majority of cases herein presented a slow-growing mass in the parotid region. Grossly, these tumours were mostly well circumscribed, with a fibrous pseudocapsule and a cut surface ranging from firm and white to tan and fleshy for cellular variants. His-

tological analysis usually revealed a patternless distribution of ovoid- and spindle-shaped cells within a variably dense collagenous stroma for SFT morphology, or a branching and dilated staghorn-like vascular network for HPC.

STAT6 and CD34 have proven to be very useful markers. Before the advent of immunohistochemistry, diagnosis relied solely on microscopic analyses without the use of molecular markers.

The precise definition of malignant HPC/SFT remains undetermined. However, certain characteristics such as a high mitotic index, substantial tumour size, increased cellularity, the presence of immature tumour cells, and the occurrence of haemorrhagic or necrotic areas are indicative of a malignant nature of the lesion⁵. While tumour characteristics included hyperchromatism and bone destruction, the set of histological data obtained from this review showed that the primary characteristic used for diagnosing malignant tumour was an increased number of mitoses.

The case series results collected herein suggest that SFT and HPC have different biological behaviour. In fact, SFT morphology represented the majority of lesions, but malignancy was mainly related to the HPC pattern, especially when taking into account the 3 cases of highly suspected malignancy. Moreover, one such case was paediatric. In other studies, it has been reported that childhood parotid neoplasms differ from those in adults, being primarily malignant but often presenting at lower grades^{67,68}.

As expected, surgical approaches tailored to each patient have been the treatment of choice, from superficial parotidectomy to extension to the parapharyngeal space²⁷. The extent of surgery should be determined by the size and location of the pathology and the structures it affects. Recurrence may occur due to incomplete resection, tumour seeding, within the near tissue, or distant haematogenous spread¹⁶.

We found the recurrence rate to be higher than expected; of 53 patients, recurrence was recorded in 11.3%, and treatment options included surgery, RT, or a combined approach. Local recurrence was observed in most cases in SFT, and the mean time of onset was 24.2 months.

Künzel et al.⁴⁹ reported a case of SFT located in the left parotid gland which was removed with no clear margins, carried out in consideration of the tumour's proximity to the carotid artery; the tumour relapsed after one year. Another case of recurrence was described by Chintale et al.⁴ in which a large parotid HPC invading the right maxillary and masticator space relapsed locally after excision and was treated using RT and CHT. The recurrence rate appears to be correlated with tumour dimension, and most importantly the feasibility of achieving clear surgical margins.

Distant metastases were described in 4 cases and were linked to a malignant HPC histology, with the most common site being the lungs. Metastases had a mean time of onset of 31.2 months and were approached with surgery in one case and CHT in another, while for the other patients the chosen treatment was not disclosed. Currently, there are no strict guidelines for adjuvant treatment such as RT. The decision for adjuvant treatment depends on individual patient factors, mainly histological results, and clinical behaviour. Follow-up is essential to detect any signs of malignancy or local recurrence early on, according to a multidisciplinary approach involving surgeons, oncologists, radiation oncologists, and pathologists. Due to the peculiar characteristics of HPC/SFT a tailored, multidisciplinary follow-up would be recommended in all cases and the role of pathologists appears important. Routine follow-up scans are generally not performed after surgery for benign tumours unless there are specific indications such as tumour rupture during surgery, spillage of cells into the parotid bed, or inability to achieve clear surgical margins. In these circumstances, MRI with gadolinium is preferred.

The scarcity of large case series and multicentric studies on these pathological entities has resulted in diverse treatment protocols and varying approaches in the management of patients with these tumours. The absence of comprehensive data impedes the development of standardised guidelines for their management, similar to other rare lesions in the head and neck region⁶⁹. Indeed, advances in immunohistochemistry and molecular discoveries have significantly improved our understanding of tumour classification and subtyping. The reclassification of HPC/SFT based on these new findings has likely led to more accurate diagnosis and identification of these tumours. However, due to the retrospective nature of some studies and a lack of comprehensive data, it is difficult to determine the number of misdiagnosed cases before the reclassification was made. The true incidence of HPC/SFT is underestimated due to the absence of immunohistochemistry and the inability to use molecular markers, especially in historical cases.

Conclusions

HPC/SFT is a mesenchymal tumour that rarely affects the head and neck region. This entity demonstrated different biological behaviour, as SFT represented the majority of lesions but malignancy was mainly related to HPC, especially considering the cases in which malignancy was strongly suspected. Surgery is the treatment of choice. When achieving optimal complete surgical excision, the risk of recurrence

for SFT/HPC is relatively low. Regular follow-up is recommended in all cases due to the unpredictable behaviour of these neoplasms, where benign and malignant areas can co-exist. When malignant behaviour is demonstrated, the risk of metastasis is high. Further comprehensive studies, particularly concerning histological and immunohistochemical characterisation, are essential to gather additional data and obtain more reliable and consistent results.

Conflict of interest statement

The authors declare no conflict of interest.

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Author contributions

DM, LS, AE: conceived and designed the analysis; ES, CL: collected the data; AV, SP, RN: contributed data or analysis tools; SP, AE VPF: performed the analysis; CL, VC, GA: wrote the paper; SP, AV, RN: revised the paper; LS, DM, AE, SP: completed the final revision and approval of the draft.

Ethical consideration

Not applicable.

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