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Striking Pathology Gold: A Singular Experience with Daily Reverberations: Sinonasal Hemangiopericytoma (Glomangiopericytoma) and Oncogenic Osteomalacia

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Abstract Sinonasal hemangiopericytoma-like tumors(SN HPC)(glomangiopericytomas)were originally conceived as histologically similar to, but biologically distinct from, their soft tissue counterparts. Re-evaluation of "hemangiopericytiomas" has determined that SNHPC (glomangiopericytomas) represent bona-fide pericyte-derived tumors, whereas most soft tissue neoplasms previously designated as hemangiopericytomas represent cellular variants of solitary fibrous tumors or other lesions with a hemangiopericytomalike growth pattern. We present an interesting case of a woman with SNHPC (glomangiopericytomas) causing oncogenic osteomalacia, and discuss the recent advances in our understanding of phosphaturic mesenchymal tumors. This particular case is an example of "Striking Pathology Gold"—a situation where the pathologist actively guides the diagnostic process, and witnesses its repercussions. "Striking Pathology Gold" may be a rare event in one's career. However it serves to remind us of our place in the world as physicians. Working behind the scenes, we quietly change the course of countless individual destinies for the better.

Keywords Oncogenic osteomalacia · Tumor induced rickets · Sinonasal hemagiopericytoma · Phosphaturic mesenchymal tumor

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Introduction

Sinonasal hemangiopericytoma-like tumors (SNHPC) (also referred to as glomangiopericytomas) were originally conceived as histologically similar to, but biologically distinct from, their soft tissue counterparts. Re-evaluation of "hemangiopericytomas" has determined that SNHPC represent bona-fide pericyte-derived tumors, whereas most soft tissue neoplasms previously designated as hemangiopericytomas represent cellular variants of solitary fibrous tumors or other lesions with a hemangiopericytoma-like growth pattern. We present an interesting case of a woman with SNHPC (glomangiopericytoma) causing oncogenic osteomalacia, and discuss the recent advances in our understanding of phosphaturic mesenchymal tumors (PMT). This particular case is an example of "Striking Pathology Gold"—a situation where the pathologist actively guides the diagnostic process, and witnesses its repercussions. "Striking Pathology Gold" may be a rare event in one's career. However, it serves to remind us of our place in the world as physicians. Working behind the scenes, we quietly change the course of countless individual destinies for the better.

Case Report

A 66-year-old woman presented with profound, immobilizing weakness and diffuse bone pain. Conventional radiography at a local hospital revealed multiple, bilateral osteolytic lesions; bone scan revealed multiple lytic lesions throughout the skeleton. A rib biopsy was non-diagnostic and evaluation for myeloma was negative. Urine and serum PTH were normal as was serum calcium. Alkaline phosphatase was minimally elevated (222 IU/l, normal range

25–140 IU/l). Serum phosphorus was low (1.8 mg/dl, normal range 2.5–4.5 mg/dl). The family was utterly distraught, as they had been told that their mother probably had a widespread metastatic malignancy from an unknown primary. After further questioning, the daughter confirmed that her mother had been suffering from nose bleeds, headaches, and nasal obstruction for many years. The patient was referred to an otolaryngologist for a head and neck examination that revealed a grey mass filling the right nasal cavity. A CT scan demonstrated a mass in the right nasal cavity, maxilla, and ethmoid sinuses extending to the cribriform plate. The tumor was resected and the patient's postoperative course was uneventful. She was placed on calcium and vitamin D supplements. Her bone pain and weakness dramatically regressed and at 25 months follow-up she was no longer wheelchair-bound and disease-free.

Pathology

This tumor was composed of short spindle cells which, for the most part, spared the immediate submucosal region of the Schneiderian mucosa (Fig. 1). A plethora of dilated venous spaces were seen along with erythrocyte extravasation (Fig. 2). Thick-walled hyalinized vessels were also present. The tumor cells had oval to short spindled bland nuclei with fine chromatin, scanty cytoplasm, and indistinct cell membranes. Mitotic figures were not seen. Tumor cells were uniformly spaced and formed fascicular structures. There was no mesenchymal matrix deposition, nor grungy calcifications, nor osteoclasts-like giant cells, to suggest a diagnosis of phosphaturic mesenchymal tumors—mixed connective tissue variant (PMTMCT). The diagnosis of SNHPC (glomangiopericytoma) was made.

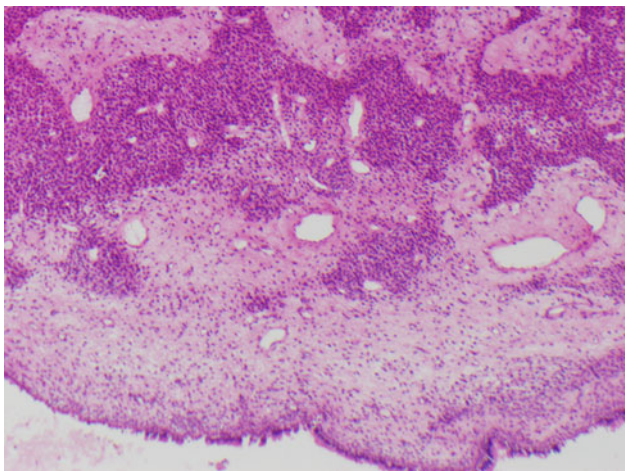

Fig. 1 Low-power view of SNHPC (glomangiopericytoma) sparing the immediate submucosal zone

Discussion

Sinonasal Hemaniopericytomas (Glomangiopericytoma): Evolving Nosology

Stout and Murray coined the term "hemangiopericytoma" to describe vascular tumors purportedly derived from "Zimmermann's pericyte" [1]—a perivascular smooth muscle cell which normally regulates capillary blood flow [2]. Compagno and Hyams first used the term "hemangiopericytoma-*like*" to describe a group of sinonasal vascular spindle cell tumors which differed from their soft tissue namesakes by the overall association with a better prognosis [3]. The diagnostic category of *soft tissue hemangiopericytoma* had long been derided as a "wastebasket" category; the current World Health Organization (WHO) classification of soft tissue neoplasia has now dropped the designation "hemangiopericytoma" for lack of evidence of pericytic differentiation [4]. It is now appreciated that most tumors formerly designated as soft tissue hemangiopericytomas are fibroblast-derived and represent the *cellular variant of solitary fibrous tumors*. As true hemangiopericytomas are related to glomus tumors, the designation "myopericytoma" or "glomangiopericytoma" is preferred by the WHO as the diagnostic category for these soft tissue tumors. From the onset, the group of sinonasal tumors designated as hemangiopericytoma-like (SNHPC) represented a homogenous group of bona fide "glomangiopericytomas"/hemangiopericytomas; these terms being diagnostically synonymous.

In an Armed Forces Institute of Pathology (AFIP) review of 104 SNHPC (glomangiopericytoma), there was a wide age range at presentation (5–86 years, mean 62 years) [5]. Most patients complained of nasal obstruction and bleeding. The majority of SNHPC (glomangiopericytomas) involved the nasal cavity, whereas sole involvement of the maxillary or ethmoid sinuses or the nasopharynx was relatively uncommon [5].

Microscopically, SNHPC (glomangiopericytomas) are submucosal polypoid tumors rimmed by a border of superficially spared stroma and respiratory epithelium. SNHPC (glomangiopericytomas) have pushing and/or locally infiltrative borders. SNHPC (glomangiopericytomas) are composed of short, bland spindle cells forming fascicular, storiform, or whorled patterns (Fig. 3). The degree of cellularity can vary within a tumor imparting a "Schwannoma"-like landscape (Fig. 4). Tumor nuclei are uniform and evenly spaced and tumor cells have a moderate amount of eosinophilic cytoplasm with *indistinct* cell membranes imparting a syncytial appearance. Tumor vessels are numerous, thin-walled and branching, (the so-called "staghorn" vessels) and form clefts and gaping spaces (Fig. 5). Perivascular hyalinization is a characteristic feature; tumor

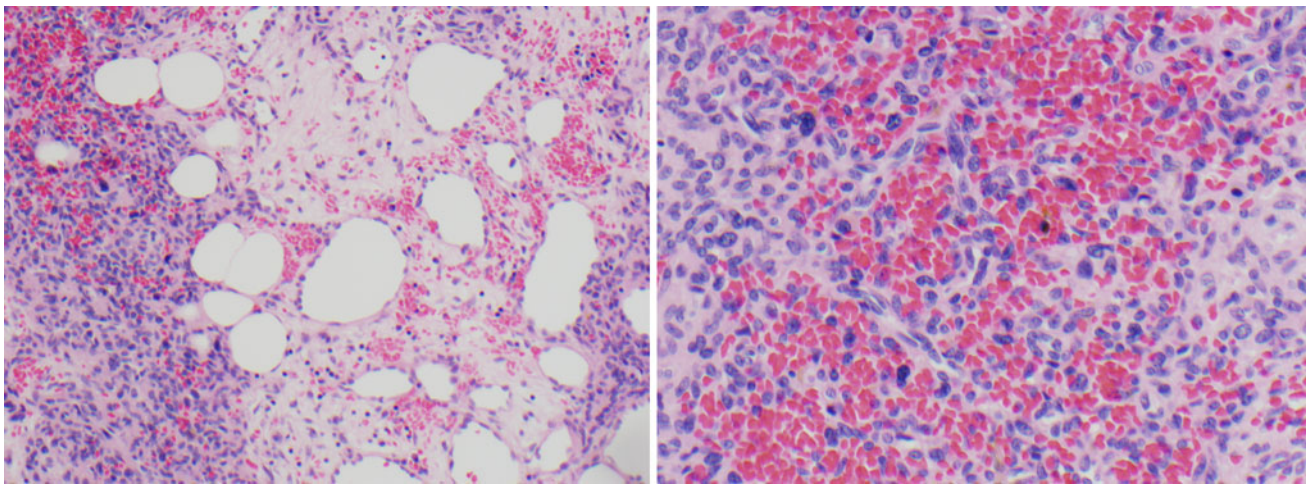

Fig. 2 SNHPC (glomangiopericytoma) (*Left*) Medium-power view of numerous dilated venous channels. (*Right*) High-power view of extravasated erythrocytes

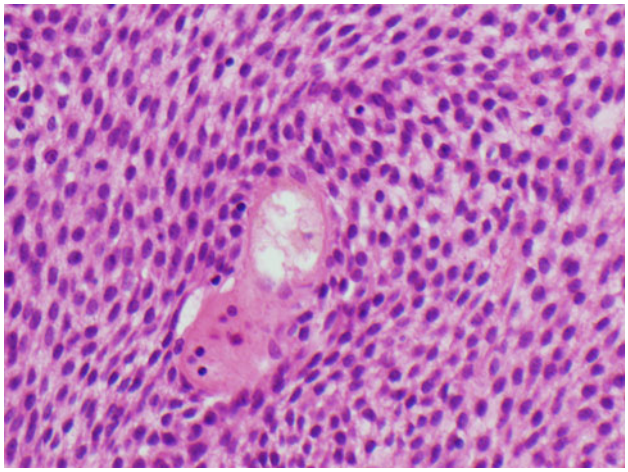

Fig. 3 SNHPC (glomangiopericytoma): high-power view of bland spindle cells forming short fascicles

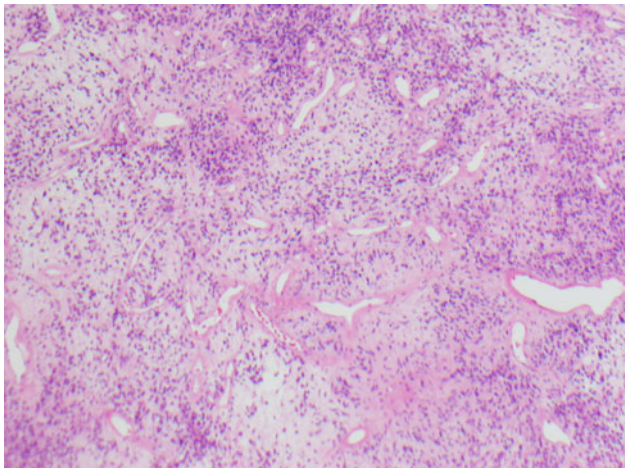

Fig. 4 SNHPC (glomangiopericytoma): low-power view of variable hypercellular and hypocellular regions imparting a "Schwannoma-like" landscape

cells may be seen oriented perpendicular to these hyalinized vessel walls. Generally, there is a low mitotic rate and nuclear pleomorphism is absent or minimal. Unusual reported features include keloid-like collagen deposition and lipomatous change [5].

SNHPC (glomangiopericytomas) characteristically express vimentin, smooth muscle actin (SMA), muscle specific actin (MSA), and factor XIIIa as assessed by immunohistochemistry [5–10]. Prior to the advent of antigen retrieval, most SNHPC (glomangiopericytomas) were reported as not expressing any smooth muscle antigens; current immunohistochemical techniques with antigen retrieval methods do confirm expression of smooth muscle antigens. Laminin expression has been demonstrated in 52% of SNHPC (glomangiopericytoma) [5]. There is usually no expression of desmin, CD34, bcl-2, factor VIII or S100 protein (Fig. 6). D2-40 stains vascular channels within all SNHPC (glomangiopericytomas) to a variable degree [11]. By comparison, conventional soft tissue HPC/solitary fibrous tumors reveal no intratumoral D2-40 vascular staining. Table 1 summarizes the IHC pattern of expression of SNHPC (glomangiopericytomas) and other tumors involved in the differential diagnosis.

Treatment for SNHPC (glomangiopericytomas) is local excision with negative margins. Most patients have an excellent outcome. The local recurrence rate is 17–18%, based on the AFIP series [5] and literature review [11]. Metastatic disease and disease-related mortality is extremely rare, on the order of 3% [11].

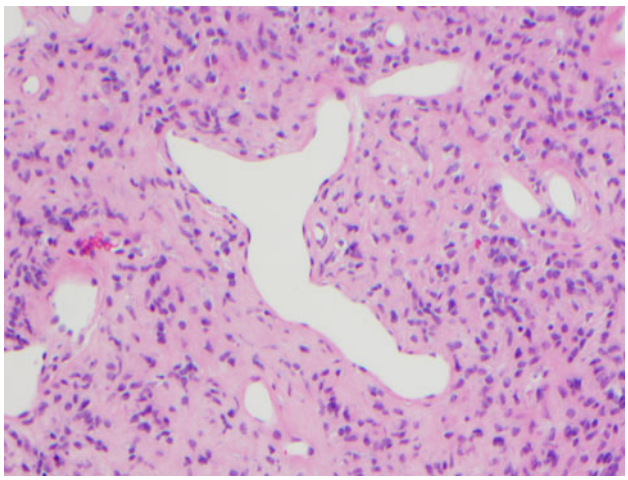

Fig. 5 SNHPC (glomangiopericytoma): Staghorn vessel (center). Note perivascular hyalinization of smaller vessels

Phosphaturic Mesenchymal Tumors (PMT) and Oncogenic Osteomalacia (OO)

Oncogenic osteomalacia (OO) (tumor-induced rickets, ossifying mesenchymal tumor associated with vitamin-D resistant rickets) is an extremely rare condition characterized by renal phosphate wasting, hypophosphatemia, normo- or hypocalcemia, and lytic bony lesions. As the diagnosis implies, this is a paraneoplastic condition; the phosphate wasting being reversible after tumor removal. The concept of OO was first codified by Weidner under the nosology of "Phosphaturic Mesenchymal Tumor" (PMT) [12–14]. A recent review estimates that *over 300 cases* of PMT have been reported in the English literature [15].

Patients with oncogenic osteomalacia (OO) usually have long-standing complaints of bone pain, loss of height, and profound muscle weakness; they present with lytic bony lesions, normal parathyroid hormone levels, normo- or hypocalcemia, hypophosphatemia, hyperphosphaturia, normal 25-hydroxyvitamin-D3 and low 1, 25-dihydroxyvitamin D3 levels. This biochemical profile is identical to that seen in autosomal dominant hypophosphatemic rickets, autosomal recessive hypophosphatemic rickets, and x-linked hypophosphatemia, the latter being the most common form of inherited rickets [16]. PMT may be small in volume, and in unusual locations (e.g. great toe), and therefore can be difficult to localize [15, 17]. The tumors can be radiographically localized by FDG PET/CT; scans should specifically include hands, feet, and the head. Targeted venous sampling for fibroblast growth factor-23 (FGF23, see below) may be necessary and helpful in localizing occult PMT. ^{111}Indium octreotide scintigraphy can also localize occult PMT, as ^{111}indium octreotide has a high affinity for somatostatin receptors, which are present in many PMT [15].

The Diverse Histologies of Phosphaturic Mesenchymal Tumors

The majority of reported PMT are benign; however, uncommon cases can be biologically malignant [18]. Weidner wrote of classifying PMT into four histological categories; the "mixed connective tissue variant" is by far the most commonly encountered type [13, 14, 18]. The three other types Weidner reported were: 1. PMT—ossifying fibroma-type, 2. PMT—non-ossifying fibroma-type, and 3. PMT—osteoblastoma type [13, 14]. These last three

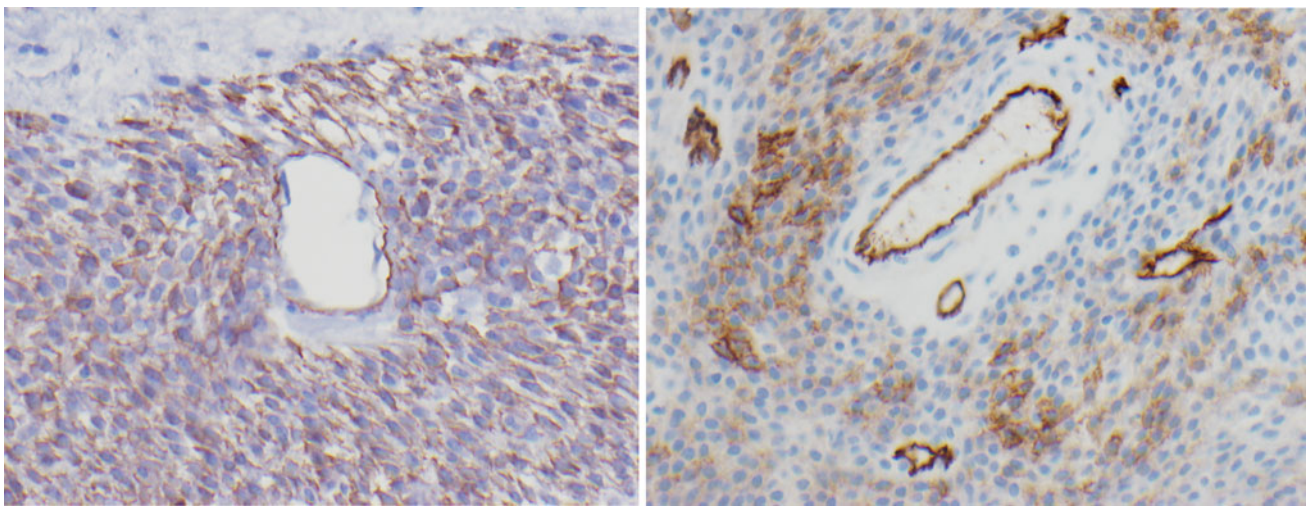

Fig. 6 SNHPC (glomangiopericytoma): Diffuse expression of smooth muscle actin (*left*). The antigen retrieval conditions were: sodium citrate buffer (cell conditioning 2, Ventana) for 60 min at 100°C. SNHPC (glomangiopericytoma) are usually negative for CD34, here we see focal tumor CD34 expression (*right*)

Table 1 Immunohistochemical profile of Sinonasal Hemangiopericytomas (Glomangiopericytoma) and Other Tumors

	Sinonasal hemangiopericytoma	Soft tissue glomangioma/ myopericytoma	Solitary fibrous tumor	Meningeal hemangiopericytoma
Vimentin	Pos	Pos	Pos	Pos
Smooth muscle actin	Pos	Pos	Rare	Neg
Muscle specific actin	Pos	Pos	Rare	Neg
Factor XIIIa	Pos	Pos	Pos	Pos
Desmin	Neg	Neg	Rare	Neg
CD34	Rare	Rare	B	Variable
Bcl-2	Rare	Rare	Pos	Pos
D2-40	A		Neg	Neg
S100 protein	Rare	Rare	Rare	Neg
EMA	Neg	Neg	Neg	Rare variable

A D2-40 stains vascular channels within all SNHPC to a variable degree. By comparison, soft tissue HPC/solitary fibrous tumors reveal no intratumoral D2-40 vascular staining.

B CD34 is positive in SFT-fibrous variant, but expression is less frequent in SFT-cellular variant

entities, though, are extremely rare. Therefore, it is logical to dichotomize PMT as either PMT-mixed connective tissue variant (PMTMCT) or PMT-Other. The histology of PMTMCT is discussed below. PMT-Other represents a heterogenous group of *bona-fide* examples of vascular tumors, sarcomas, and other bony tumors, which lack the histological features of PMTMCT.

Phosphaturic Mesenchymal Tumors: Mixed Connective Tissue Variant (PMTMCT)

PMTMCT can be conceptualized as a specific, albeit morphologically diverse, tumor entity. PMTMCT can occur either in the soft tissues or bone. Relevant to this discussion, a number of PMTMCT involving the craniofacial bones and sinonasal tract have been reported and illustrated [17–29]. Grossly, PMTMCT appear well-circumscribed, but microscopically, all tumors infiltrate the surrounding connective tissues.

PMTMCT are microscopically composed of small, primitive, *round to spindled mesenchymal cells*. The nuclei for most tumors are similarly small, spindled, and *bland*. Rarely, tumors reveal nuclear pleomorphism, warranting a malignant classification [18]. PMTMCT produce various *mesenchymal matrices*, typically myxoid or myxochondroid matrices with hyalinization, basophilic "smudginess", and net-like, flocculent, or "grungy" calcification (Fig. 7) [18]. Chondroid or osteoid-like matrix can be seen in either soft tissue or osseous PMTMCT. Importantly, the osteoid is produced by cytologically bland tumor cells. The chondroid areas can contain *dystrophic calcifications.* Chondroblast-like cells can be seen. Numerous clusters of osteoclastic giant cells admixed with plump spindle cells in a storiform or fasicular pattern are often seen, reminiscent of true giant cell tumor or giant cell reparative granuloma (Fig. 8). Cystic spaces filled with proteinaceous material are common. Aneurysmal bone cyst-like changes with

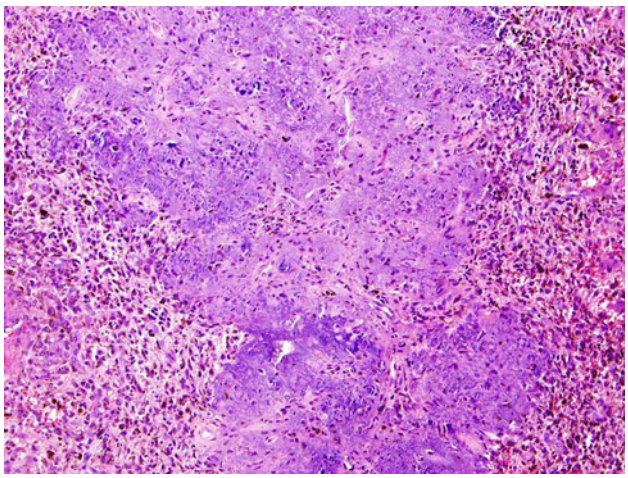

Fig. 7 Phosphaturic mesenchymal tumor: Chondromyxoid matrix with "grungy" calcifications. Courtesy of Dr. Michal Michal, Prague, Czech Republic

blood-lakes are well reported. Prominent, rich, intrinsic vascularity is common, and can mimic the hemangiopericytoma-like staghorn pattern. Hemorrhage may be prominent and comprise more than half the tumor [30]. Folpe et al. [18] noted that greater than half of soft tissue PMTMCT have a partial shell of woven bone. Adipose cell differentiation may be seen. By definition, hemangiopericytoma-like tumors associated with OO and containing intratumoral woven bone, osteoblasts, and grungy calcification are best classified as PMTMCT.

Phosphaturic Mesenchymal Tumors: Others

Other specific osseous entities can also be associated with OO including osteosarcoma, enchondroma, nonossifying fibroma, and hemangioma [18, 31–39]. The documentation in these reports has usually been sufficient to histologically rule out PMTMCT. PMT-Other *lack* the bland

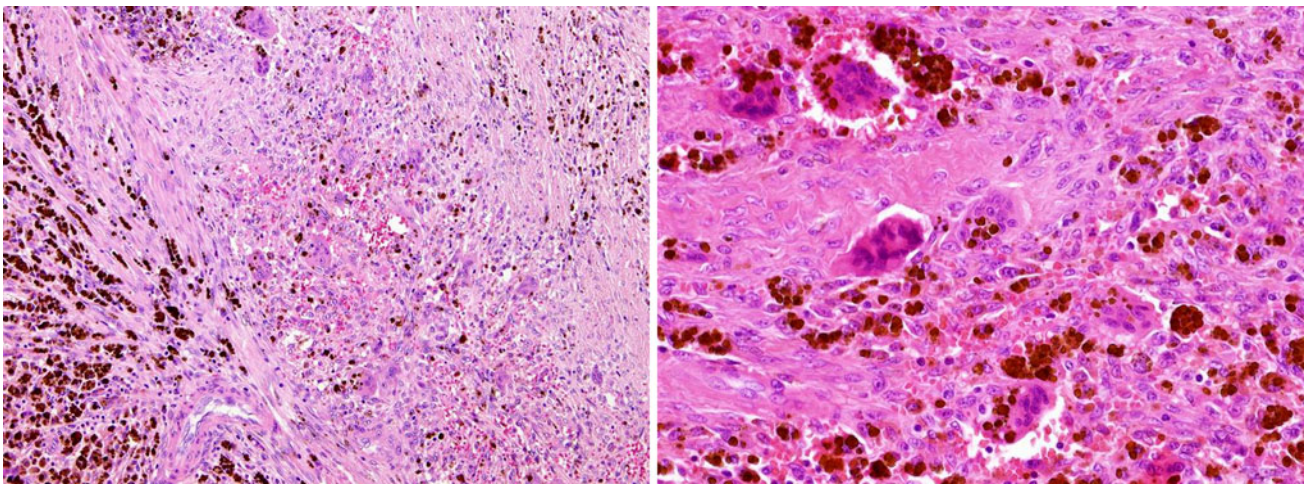

Fig. 8 Phosphaturic mesenchymal tumor: (*Left*) The bland spindle cell stroma reveals hemosiderin deposition and osteoclastic giant cells. (*Right*) High-power view of bland tumor spindle cells, osteoclastic giant cells, and hemosiderin. Courtesy of Dr. Michal Michal

mesenchymal cells, mesenchymal matrix, and grungy calcifications of PMTMCT. Soft tissue hemangiopericytomas causing OO can also be classified as PMT-Other. Approximately nine sinonasal and skull base hemangiopericytomas (glomangiopericytomas) associated with OO have been reported and illustrated in the English literature, albeit with variable pathological documentation [11]. One meningeal hemangiopericytoma causing OO has also been reported; [40] the distinction between sinonasal hemangiopericytoma (glomangiopericytoma) and meningeal hemangiopericytoma is discussed below.

The Discovery of Fibroblastic Growth Factor-23 (FGF23)

The existence of a phosphaturic substance ("phosphatonin") had long been hypothesized, and was identified, relatively recently, as fibroblastic growth factor-23 (FGF23) [41]. Normally, FGF23 is produced in bone by osteocytes, and their osteoprogenitor cells, including osteoblasts [42], and acts upon the kidneys and parathyroid glands. The functional FGF23-specific receptor is comprised of Klotho, a senescence-related molecule, and FGFR1(IIIc) [43]. Both PTH and FGF23 decrease phosphate reabsorption in the proximal renal tubule by downregulating expression of the sodium-dependent phosphate transport proteins (Npt2a and Npt2c) [44]. PTH appears to be necessary for fully developed hypophosphatemia, as patients with increased FGF23 but low or undetectable PTH do not develop hypophosphatemia [45]. Unlike PTH, FGF23 also downregulates expression of renal 25-hydroxyvitamin D3 1-ά-hydroxylase, which regulates the conversion of $25(OH)_2$ vitamin D to the active form $1,25(OH)_2$ vitamin D [45, 46]. FGF23 also directly impacts PTH production under experimental conditions [47] however; clinically, serum PTH is usually normal or suppressed in patients with OO.

Serum FGF23 is abnormally elevated in patients with OO, autosomal dominant hypophosphatemic rickets, autosomal recessive hypophosphatemic rickets, and x-linked hypophosphatemia [48, 49]. The tumors from patients with OO produce both an elevated FGF23 mRNA transcript and protein and serum FGF23 concentration decreases after tumor resection [50]. Mice injected with cells that stably overexpress FGF23 develop a metabolic profile identical to patients with OO [46]. Serum FGF23 is elevated in disease states either through impaired degradation secondary to a missense mutation in autosomal dominant hypophosphatemic rickets or inactivating mutations impairing its degradation; ENPP1 (ecto-nucleotide pyrophsphatase/phosphodiesterase-1) in Type 2 autosomal recessive hypophosphatemic rickets [51] PHEX (phosphate-regulating neutral endopeptidase) in x-linked hypophosphatemia, and DMP1 (dentin matrix-1) in Type 1 autosomal recessive hypophosphatemic rickets [52, 53].

Overexpression of mineralization-related genes, such as matrix extracellular phosphoglycoprotein (MEPE), frizzled-related protein, DMP, and FGF7 have also been demonstrated in PMT [41, 52, 54, 55]. It has been postulated that these proteins are responsible for the characteristic calcified matrix of PMTMCT, which subsequently recruits osteoblasts and provokes fibrohistiocytic and aneurysmal bone cyst-like reactions [18]. Conversely, there are rare tumors histologically identical to PMTMCT which have been documented as not being associated with osteomalacia [18]. These tumors might secrete inactive or insufficient FGF23, or patients with these neoplasma may have been able to compensate for elevated FGF23 [18].

Rarely, prostatic adenocarcinomas have caused OO [56]. Fibrous dysplasia [57] and schwannomas, in the setting of neurofibromatosis-1 [58, 59] have also been rarely associated with OO. Lastly, and of interest to surgical pathologists, familial tumoral calcinosis, a rare autosomal recessive condition characterized by progressively enlarging soft tissue calcium deposits, is associated with genetic mutations involving either FGF23, Klotho, or GALNT3, which encodes a glycosyltransferase responsible for FGF23 *O*-glycosylation [60].

Treatment of Phosphaturic Mesenchymal Tumors

Tumor resection is the treatment of choice, which, if successful, will be accompanied by a rapid decrease in serum FGF23. Serum phosphate returns to normal levels within days of definitive surgery. Oral replacement of phosphorus and high-dose 1, 25 (OH)2 vitamin D is usually indicated [16]. Long-term follow-up is recommended as bony lesions should resolve within months to 1 year. Most PMT are benign and therefore cured by resection. Rarely, if hypophosphatemia continues, then the PMT may be multifocal or incompletely removed [14, 26]. Development of metastases, usually pulmonary, is extremely rare, but may occur even with histologically benign PMTMCT [15].

Strategies are being developed to address intractably elevated FGF23, for patients with malignant PMT, or with unlocalizable or unresectable PMT. As previously mentioned, Gupta and colleagues noted that PTH appears to be necessary for fully developed hypophosphatemia, as patients with increased FGF23 but low or undetectable PTH do not develop hypophosphatemia [45]. This has served as the rationale for inducing hypoparathyroidism with Cinacalcet® a calcium-sensing receptor agonist which lowers PTH [15]. These patients also require thiazide diuretics to decrease urinary calcium and prevent nephrolithiasis. Use of the somatostatin analogue, octreotide, has been abandoned for lack of response. Future treatment strategies may also include the use of calcitonin, which awaits further investigation [15]. Dasatinib, a kinase inhibitor, has been used in a single patient with recurrent meningeal HPC with associated OO, based on the rationale that this inhibitor has activity against PDGFRβ, and the patient's neoplasm expressed PDGFR by immunohistochemistry [40].

Differential Diagnoses: Glomus Tumors

True glomus tumors are usually subcutaneous neoplasia of the hands, feet, or forearm, which are typically painful. Parenthetically, the term "glomus tumor" is also used for middle ear paragangliomas. Glomus tumors are derived from perivascular contractile cells (pericytes) and, therefore, are related to SNHPC (glomangiopericytomas). The light microscopic distinctions between glomus tumors and SNHPC (glomangiopericytomas) are relevant in the context of rare sinonasal glomus tumors [61]. Glomus tumors are composed of uniform, polyhedral, *epithelioid cells*, with more cytoplasm than SNHPC (glomangiopericytomas), and *distinct, prominent cell membranes* (Fig. 9). Soft tissue glomus tumors demonstrate the identical immunohistochemical staining pattern as SNHPC (glomangiopericytomas): they are positive for SMA and MSA, and negative for desmin and CD34.

Differential Diagnoses: Solitary Fibrous Tumor (SFT)

As noted, many soft tissue "hemangiopericytomas" are now reclassified as being a solitary fibrous tumor-cellular variant. Sinonasal SFT are less common than SNHPC (glomangiopericytomas) [62], and are usually the subject of case reports [62–67]. The unfortunate and uninformative descriptor of "patternless pattern" is usually applied to SFT. In practice, the SFT-fibrous variant lesions are predominantly fibrous, with regions of amorphous keloid-like collagen deposition, haphazardly arranged cells, and alternating hypercellular and hypocellular regions. Tumor cells can form fascicular and storiform patterns (Fig. 10). There is a morphological continuum between SFT-fibrous variant and SFT-cellular variant, with the latter containing numerous medium-sized ramifying vessels. CD34 expression is characteristic of SFT-fibrous variant, but is less frequent in SFT-cellular variant (Fig. 11). Most SFT appear cytologically benign; tumor nuclei are typically bland with an open, vesicular, chromatin pattern and occasional nuclear pseudoinclusions. However, some SFT can be classified as malignant based on nuclear atypia, increased cellularity, mitotic activity >4/10 HPF, hemorrhage, and necrosis. CD34 expression is also diminished in malignant SFT.

Differential Diagnoses: Meningeal Hemangiopericytoma

Meningeal hemangiopericytoma, formerly classified as angioblastic meningioma, [68] is now classified as a soft tissue-type hemangiopericytoma. Microscopically, it is composed of irregularly-shaped, randomly-oriented spindle cells which do not form any fascicles. There is a rich, branching vascularity (Fig. 12). The tumor cells have scant, ill-defined cytoplasm, tumor nuclei are crowded and overlapping. The immunohistochemical profile of meningeal hemangiopericytoma is similar to SFT-cellular type, as meningeal HPS are negative for SMA, MSA, and desmin; EMA and CD34 expression is variable [9, 69].

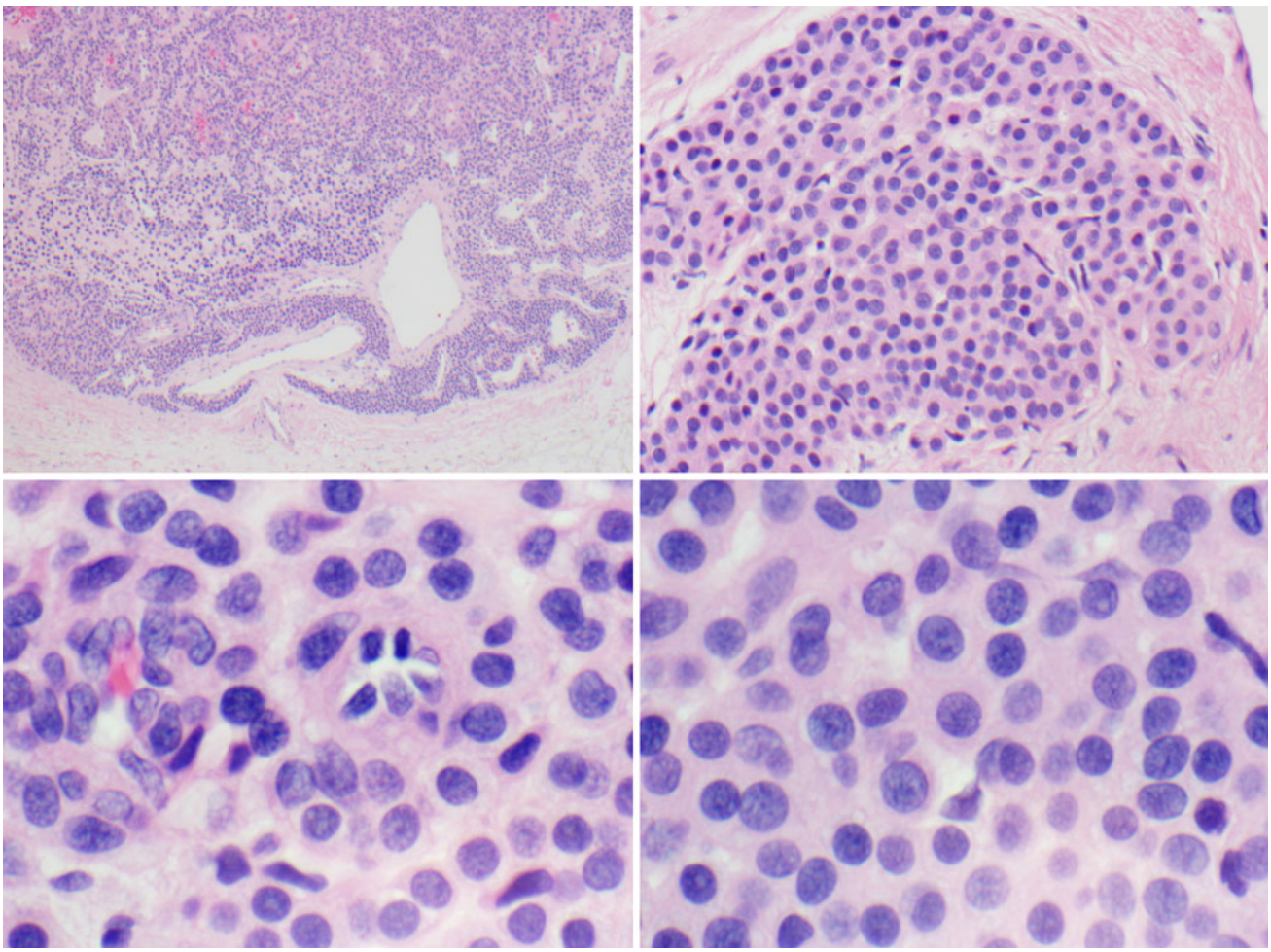

Fig. 9 Glomangioma: (*Upper left*) low-power view of circumscribed vascular tumor. (*Upper right*) Epithelioid cells forming a paraganglioma-like "zell-ballen" pattern. (*Lower left* and *right*) The spindled and epithelioid tumor cells have bland nuclei, abundant cytoplasm and discernable cell membranes

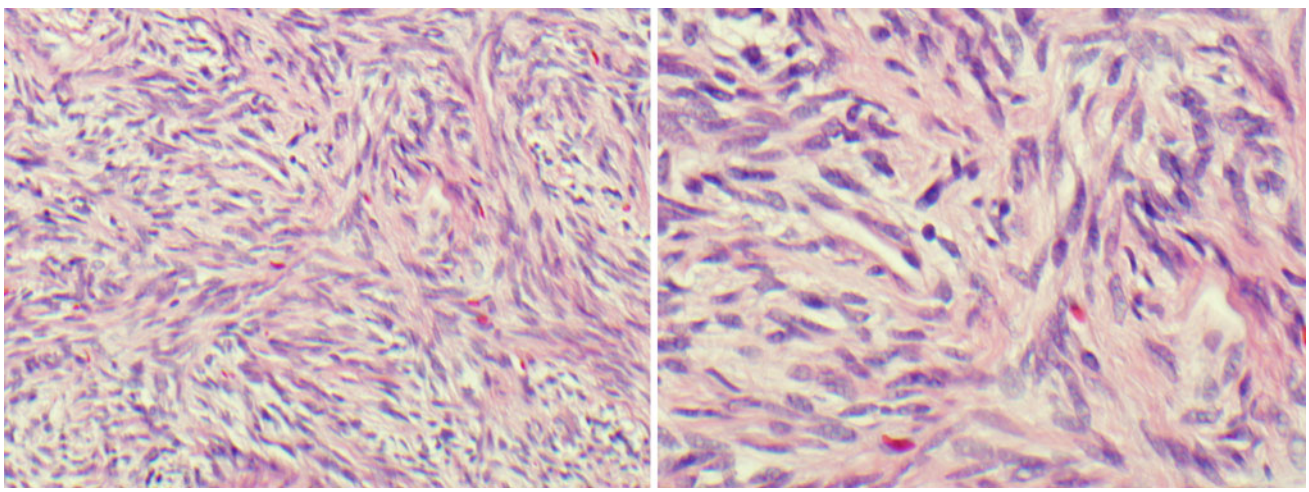

Fig. 10 Solitary fibrous tumor: low (*left*) and higher (*right*) power revealing fasicular arrangement of relatively bland spindle cells that are longer than those of the typical SNHPC (glomangiopericytoma)

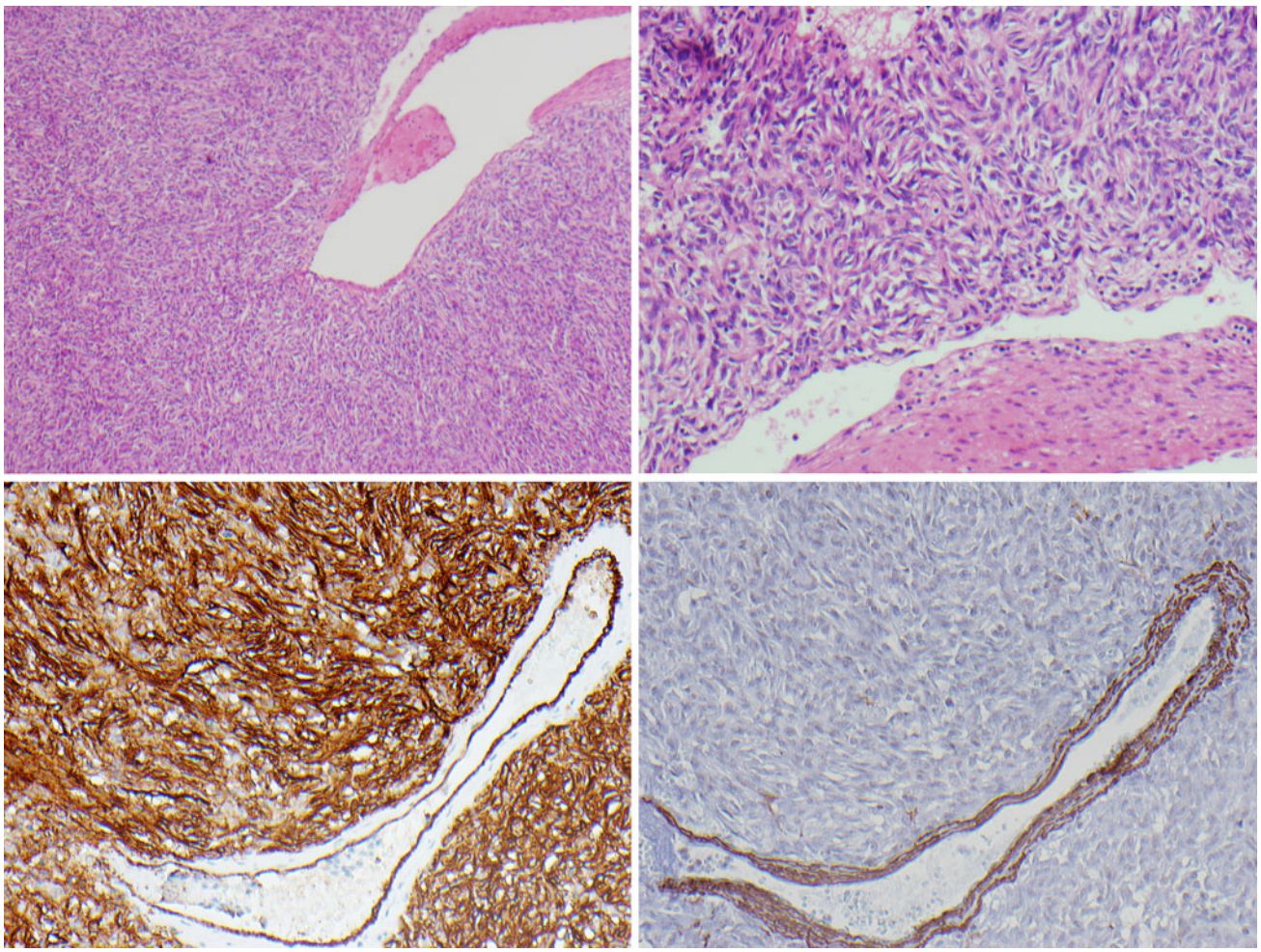

Fig. 11 Sinonasal solitary fibrous tumor, cellular variant: This vascular tumor was originally diagnosed as a sinonasal hemangiopericytoma. Low-power (*upper left*) reveals a cellular tumor. Note the absence of perivascular hyalinization. Medium-power (*upper right*) reveals relatively short spindle cells forming a "short herringbone" cascading pattern. There is strong diffuse CD34 expression (*bottom left*). Smooth muscle actin reveals a vascular staining pattern, the tumor cells are negative (*bottom right*)

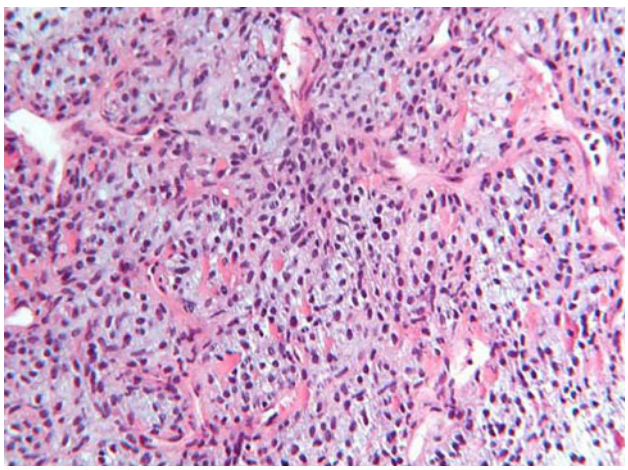

Fig. 12 Meningeal HPC: irregularly-shaped, randomly-oriented spindle cells embedded in a rich, branching vascularity

The Case That Taught the Most

This case was extremely interesting, but vanishingly rare. So why did it resonate so powerfully? The answer, in part, is due to its personal connection. The distraught woman in this story, which occurred decades ago, was the first author's daughter's piano teacher. She was the one who was told to "take her mother home to die". She brought us the medical records, was questioned further, was referred to a trusted otolaryngologist, which ultimately lead to the opportunity of diagnosing SNHPC (glomangiopericytoma) with OO. "Pathology Gold" had been struck! We were given the unique privilege of witnessing the diagnostic process from "the outside in": guiding the patient to the doctor, establishing the diagnosis, and then experiencing the reward of hearing how this woman's symptoms were "miraculously" reversed after tumor resection. As surgical

pathologists, we labor behind the scenes and almost never see the faces, nor hear the full stories, behind the diagnoses we render. We see neither the relief and joy, nor the despair and pain, on the faces of our patients. Regardless, surgical pathologists change the course of individual destinies every working day. Witnessing the "Striking Pathology Gold" is a rewarding, albeit singular experience. But more importantly, it reminds us of the quiet daily impact we make on peoples' lives as we change the course of countless individual destinies.

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