

## Giant cell angioblastoma in an adult: a unique presentation

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### Abstract

Giant cell angioblastoma is a very rare, locally destructive vascular tumor of intermediate malignancy without metastatic potential. There are only a few cases reported in the literature exclusively in the soft tissue of children. For the first time, we report on an adult patient with a giant cell angioblastoma in the popliteal fossa. The therapy included tumor resection with favorable clinical, oncological and functional outcome. Due to its locally destructive nature, surgery remains the mainstay of treatment. Histologically, giant cell angioblastoma is comprised of nodular aggregates of histiocytoid cells arranged around bland angiomatous spaces. Because of insufficient available data in regard to the definition of the entity, diagnostic criteria and its biological potential, it is not included in the new World Health Organization classification of tumors of soft tissue and bone. The differential diagnosis includes plexiform fibrohistiocytic tumor, myofibroma and giant cell fibroblastoma.

### Case Report

A 41-year old patient presented with pain in the dorsal aspect of his right knee for 4 months. Physical examination revealed pain at deep flexion and a knee-joint effusion. Magnetic resonance imaging (MRI) of the knee showed a solid mass of 1.2×2.4×2.1 cm extent adjacent to the dorsal joint capsule and the posterior cruciate ligament (PCL) (Figure 1, T1-weighted image after administration of gadolinium). Puncture of the knee joint didn't reveal any malignant cells, CT-guided core biopsy contained retrospectively no lesional tissue and included small fragment of the joint

cartilage leading to the suspicion of a synovial chondromatosis. The patient ultimately decided in favor of resection of the painful mass. Intraoperatively, the tumor mass represented as a palpable, well-demarcated mass between the dorsal joint capsule and the PCL. The mass was R0-resected with preservation of both PCL and popliteal vessel and a favorable functional outcome.

Histologically, the lesion was poorly demarcated and vaguely zoned. The first and most striking feature was the presence of numerous thick-walled blood vessels (Figures 2A and 3A) with marked concentric proliferation of bland spindle cells with smooth muscle actin (SMA) (1A4 clone, Sigma; 1:20 000) (Inset Figure 2A) and desmin (not shown) expression. Between these vessels, there was a diffuse spindle cell proliferation with a loosely myxoid or collagenous matrix and there were focally several small nodule and linear and plexiform aggregates of histiocytoid cells (Figures 2B and 3B) containing some multinucleated, CD68 positive giant cells of osteoclastic type (inset Figure 2B; clone PG-M1, DAKO; 1:50). Furthermore there were similar smaller nodules of cells, some of which appeared to be centered around a vascular lumen, almost giving the impression that these aggregates are vasculocentric. Interestingly, the histiocytoid cells expressed partially microphtalmia-associated transcription factor (MITF) (inset Figure 2B; clone C5+D5; Abcam Limited; 1:50), were weakly positive for S100 and negative for CD68, CD34, SMA, desmin. The histopathological differential diagnosis included plexiform fibrohistiocytic tumor. However, the typical angiomatous character of the lesion (as shown in Figure 2A and Figure 3A, respectively) didn't

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fit to a plexiform fibrohistiocytic tumor, and there was not seen the more orderly fascicular spindle cell component of the plexiform fibrohistiocytic tumor. So the diagnosis of a giant cell angioblastoma was revealed. A CT scan of

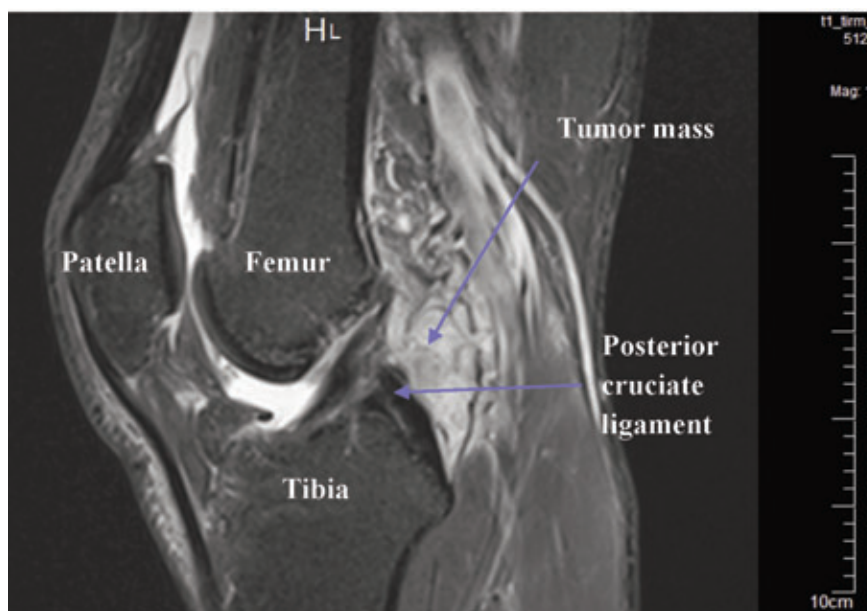


Figure 1. T1-weighted magnetic resonance imaging of the right knee after administration of gadolinium.

chest and abdomen for staging was completed, without any signs of metastases or pathological lymph nodes. 16 months following the resection of the lesion there are no clinical and radiological signs of a local relapse or metastases, and the patient is free of complaints and is back to his activity level as before surgery.

## Discussion

Giant cell angioblastoma belongs to vascular tumors of intermediate malignancy, even though as yet it is not certain that this is primarily an endothelial tumor. It is a very rare and a locally aggressive disease with no or only very low metastatic potential.<sup>1</sup> It was first described as a congenital soft-tissue tumor by Gonzalez-Crussi in 1991.<sup>2</sup> Until now, it was not included in the WHO classification because the available data are insufficient in regard to the definition of entity, its diagnostic criteria and its true biological potential.<sup>3</sup>

The typical histological findings in giant cell angioblastoma are thick-walled vascular channels with an outer proliferation of fibroblastic spindle cells, nodular aggregates of histiocytoid cells and giant cells and a loose mesenchymal stroma. Features typically associated with malignancy, such as mitoses, cytological atypia or necrosis are absent in giant cell angioblastoma.<sup>1</sup> Immunostains show focal positivity for SMA (smooth muscle actin) in the spindle cells, suggesting a vascular smooth muscle origin, whereas CD 68 stains the multinucleated giant cells.

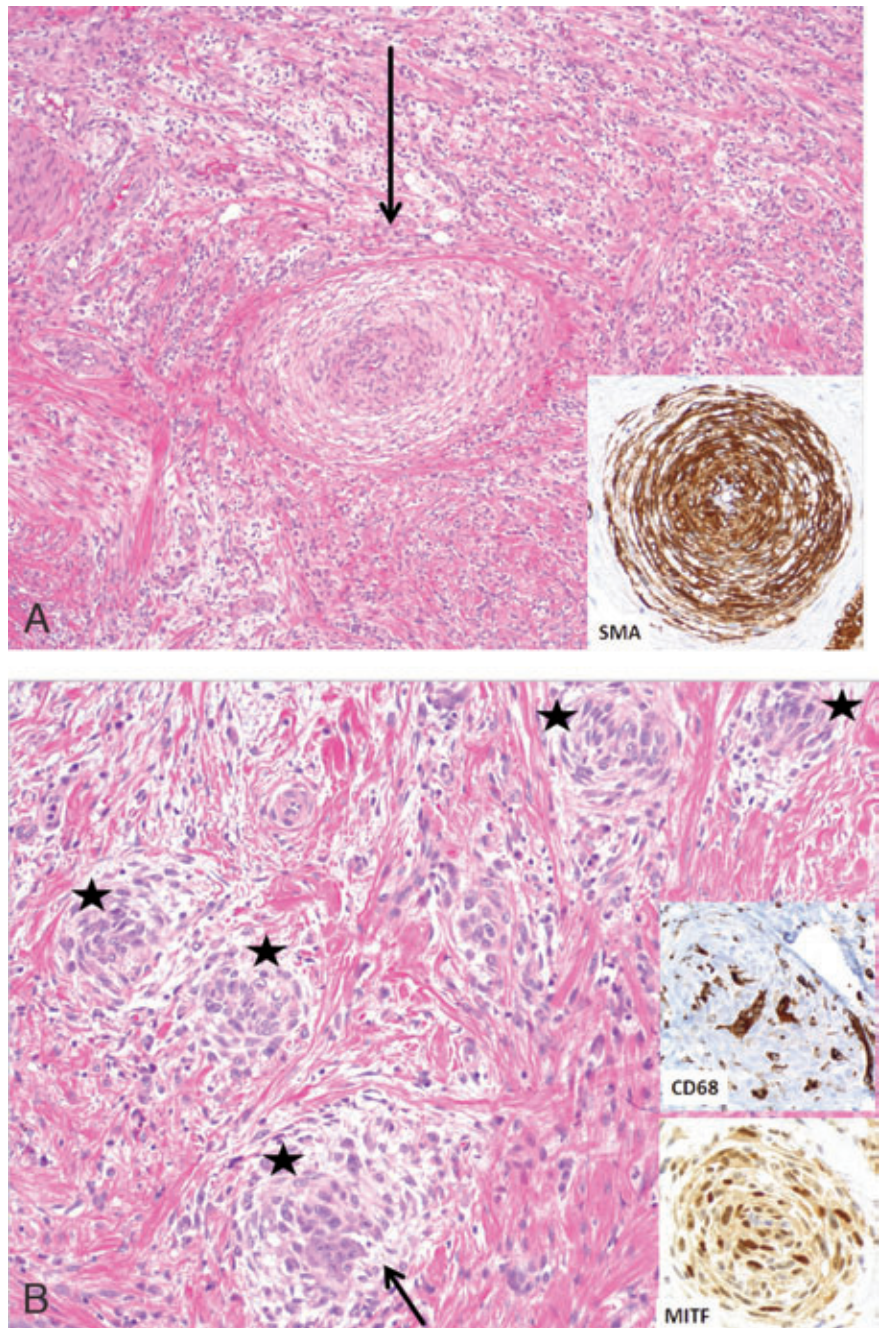
These histological features led to the diagnosis of a giant cell angioblastoma in our patient, despite the exceptional patient age and the atypical location of the lesion in the popliteal fossa. There has never been described a giant cell angioblastoma in an adult and in the popliteal fossa in the literature before. In the previously reported cases in the literature the tumor was located in the hand, forearm, scalp and palate of infants.<sup>2,4</sup> Because of the typical angiomatous character of the lesion and the lack of the more orderly fascicular spindle cell component of a plexiform fibrohistiocytic tumor, it was believed that the histology fits best with a giant cell angioblastoma and not with a plexiform fibrohistiocytic tumor, a differential diagnosis in this setting. Other differential diagnoses include other congenital or vascular neoplasms containing giant cells, such as myofibroma or giant cell fibroblastoma.

Plexiform fibrohistiocytic tumor is a neoplasm of children and young adults. The tumor is characterized by the plexiform and nodular growth of rounded histiocytoid cells with interspersed osteoclast-like giant cells, but lacks the angiomatous character or an onion skin-

ning arrangement of giant cell angioblastoma.<sup>2</sup>

Myofibroma tends to be well demarcated and usually shows immature round cells in a hemangiopericytoma-like arrangement with bundles of mature myofibroblasts with focal hyalinization. It lacks the plexiform vascular pattern and multinucleated giant cells.<sup>3</sup> Giant

cell fibroblastoma is another pediatric tumor of multinucleated cells lining pseudovascular spaces. This tumor expresses CD34, a characteristic that lacks in giant cell angioblastoma. Another differential diagnosis of giant cell angioblastoma includes an infectious etiology because of areas similar to granulation tissue



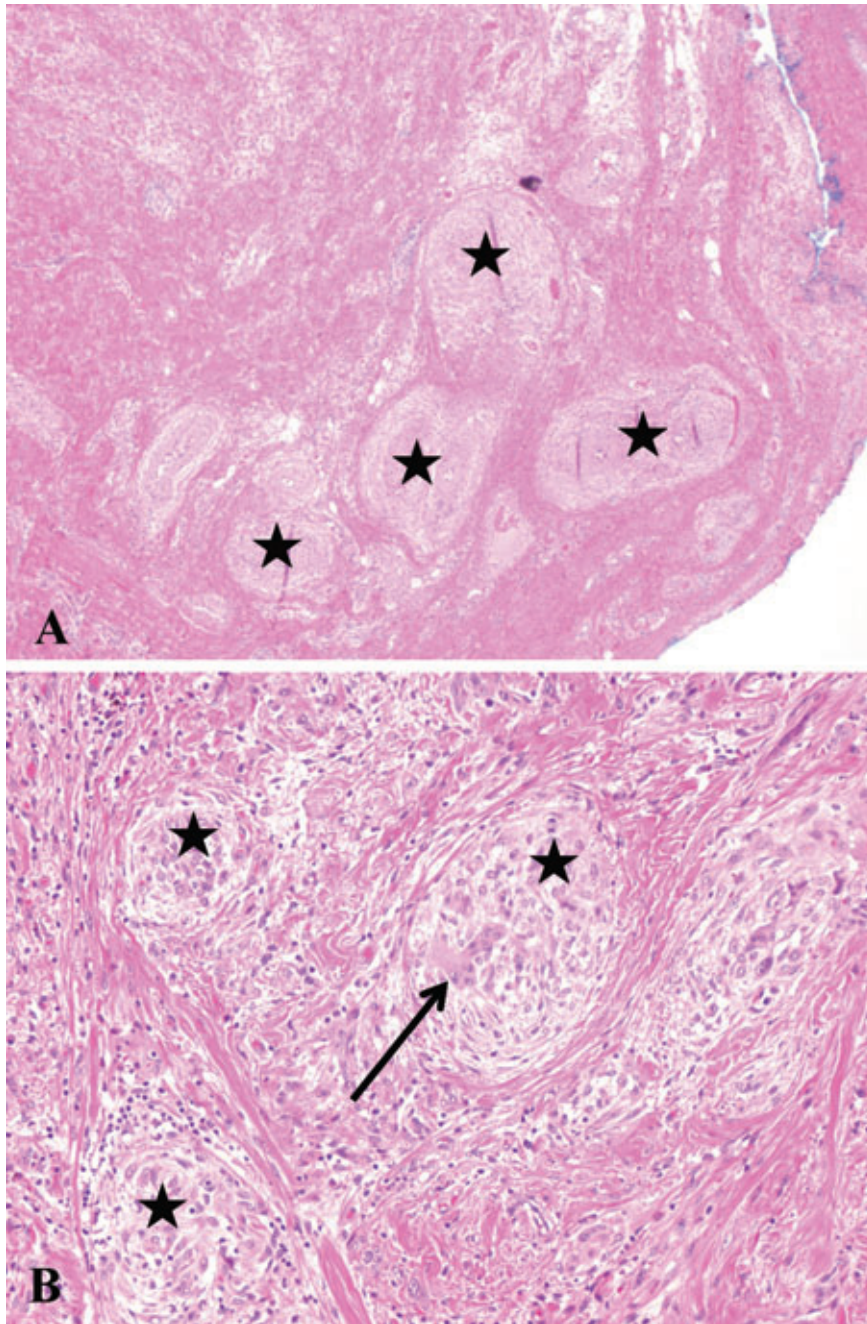
**Figure 2.** A) Small and middle sized arteries (arrow) with concentric proliferation of SMA positive spindle cells (inset; original magnification 200x) in the outer layers are seen accompanied by myxoid and collagenous connective tissue in the background (hematoxylin and eosin staining; original magnification 50x). B) Several small, whorly nodules (asterisks) consisting of histiocytoid bland cells and containing (arrow) some multinucleated giant cells of osteoclastic type (CD68 positive as seen in the upper inset; original magnification 200x) are seen in the center of the lesion (hematoxylin and eosin staining; original magnification 100x). These cells show partial nuclear expression of MITF (lower inset; original magnification 200x)

and granulomas.

The optimal therapy of giant cell angioblastoma is not known. Because of the locally infiltrative character of the lesion, surgery remains the mainstay of therapy. In the first reported case of a giant cell angioblastoma by Gonzalez-Crussi, the upper extremity tumor required an amputation of the arm.<sup>2</sup> Three additional

occurrences of this tumor were also treated by surgery, but in a different way.<sup>4</sup> The palatal giant cell angioblastoma in a 10-month-old male could not be completely resected; given the deforming nature of further excision, no additional surgery was performed and the patient was treated with interferon alfa 2b (IFN $\alpha$ 2b) for 4 years. After nearly 5 years no

progression is shown. In a male neonate with a giant cell angioblastoma involving the right hypothenar eminence, a surgical cure would have required amputation of the hand. So, a therapy with IFN $\alpha$ 2b was started, and the tumor diminished in size over 11 months. Then, the tumor was subtotally excised and did not progress after 27 months. Based on these 2 cases, it seems that the antiangiogenic regimen of interferon alfa 2b is successful in suppression of the unregulated growth of blood vessels,<sup>5</sup> and that the giant cell angioblastoma may represent an unusual form of neoplastic angiogenesis. Another child with a giant cell angioblastoma on the scalp got also a tumor resection, follow-up data are unavailable. In our case of a giant cell angioblastoma in popliteal fossa, a limb-sparing resection of the tumor was performed. Imaging controls 12 months later show neither residual tumor nor local recurrence. Even though it can be difficult to control the tumor surgically, data about adjuvant chemotherapy or radiotherapy do not exist.



**Figure 3.** A) There are numerous thick-walled blood vessels (asterisks) with an outer concentric proliferation of bland spindle cells. Between these vessels, there is a diffuse spindle cell proliferation with a loosely myxoid or collagenous matrix (hematoxylin and eosin staining; original magnification 25x). B) Focally there are striking nodular aggregates (asterisks) of pale eosinophilic histiocytoid cells admixed with occasional osteoclastic giant cells (arrow) (hematoxylin and eosin staining; original magnification 100x).

## Conclusions

In summary clinical features, histological findings and follow-up data suggest that giant cell angioblastoma is a non-malignant tumor with no or only very low metastatic potential, but the potential of local complications by its infiltrative character. It isn't only a rare tumor during infancy, but can also occur in adults, as we describe here for the first time.

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