CASE REPORT

Multiple glomuvenous malformations presenting in a child: follow-up over a period of 8 years

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SUMMARY

Multiple glomuvenous malformations (GVMs) are a rare condition which usually present in children with only a handful of cases reported in the literature. It is usually congenital and has an autosomal dominant inheritance pattern. They may be distributed throughout the body in either a localised, segmental or disseminated pattern. Pain, which is a characteristic feature of glomus tumours, is less often associated with GVMs. In addition, unlike glomus tumours which most commonly occur over acral skin surfaces, GVMs may occur throughout the body. A number of treatment options are available including surgical excision, laser treatments and sclerotherapy. We present the case of a 14-year-old boy with multiple GVMs which were treated with surgical excision and followed him up over a period of 8 years.

BACKGROUND

Glomus tumours were first described by Masson in 1924 and are broadly divided into two categories.¹ A solitary variant, occurring most commonly in young adults, which accounts for approximately 90% of cases and a rarer multiple variant occurring most commonly in children accounting for about 10% of cases. Blume-Peytavi *et al*² have provided criteria that distinguish the solitary variant from the multiple variant and this is provided in table 1. The multiple variant is further subdivided into a nodular form and a plaque-like form.

Glomus tumours are most commonly benign, and arise from modified smooth muscle cells located in the walls of the Sucquet-Hoyer canals which are specialised arteriovenous anastomoses (called glomus bodies) essential for thermoregulation.³ The glomus bodies are most frequently found in acral skin (palmar and plantar skin lacking hair follicles and having a thicker layer of stratum corneum), which explain the reason as to why the hands and feet are the two commonest locations where glomus tumours occur. However, glomus tumours do occur in regions of the body where glomus bodies are not thought to be present, hence suggesting that some may arise from differentiation of pluripotent perivascular or smooth muscle cells.

Histologically, a glomus tumour consists of varying proportions of glomus cells, smooth muscle and blood vessels. Three histological variants are recognised depending on the predominant component: angiomatoid (glomangioma), with predominant blood vessels; solid, consisting predominantly of glomus cells; and glomangiomyoma, which consists of predominantly smooth muscle.³

Recently there has been a drive to differentiate the angiomatoid (glomangioma) variant, which is considered to be avascular malformation caused by mutations in the glomulin gene, as a separate entity from glomus tumours, which is restricted to those solitary tumours consisting primarily of glomus cells.¹ Hence, the terms angiomatoid glomus tumours, glomangiomas and multiple glomuvenous malformations (GVMs) all correspond to the same condition. In this article we use the term GVMs to describe these lesions consisting of predominantly dilated irregular blood vessels with few glomus cells that occur in multiple locations in children in concordance with the most recent nomenclature.

Multiple GVMs are a rare phenomenon with an autosomal dominant inheritance pattern which is poorly covered in the literature. We report on the case of a 14-year-old boy with multiple glomus tumours with a disseminated pattern of distribution involving his face, chest, abdomen and thighs which was treated with surgical excision. As there is the possibility of recurrence, as well as the development of new lesions, we followed him up 8 years after excision of the primary lesions to determine his progress.

CASE PRESENTATION

A 14-year-old boy was referred to the dermatology clinic by his general practitioner (GP) due to the presence of three increasingly painful lesions on his body. They had been noticed when he was about 3-year-old; however, they had not caused any problems at that stage and hence his parents did not seek any medical attention. However, since the age of 10 years he began to experience occasional spontaneous paroxysms of pain over these sites with a gradual increase in size of the lesions. This happened over approximately 4 years triggering a presentation to the GP at the age of 14 years.

Family history revealed that both the mother and the father of the child had similar solitary lesions, the mother with a lesion over the left shoulder and the father with a lesion on the medial aspect of the right upper limb. As the parents of the child did not experience significant pain and they had not noticed any increase in size nor any other additional lesions, they were not keen to have these excised.

The patient's medical history revealed adenoidectomy and insertion of grommets for recurrent ear infection with poor hearing and persistent snoring at 5 years of age. Apart from that he was

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Table 1 Distinguishing features of the solitary 'glomus tumour' and the multiple variant referred to as 'glomovenous malformations'

Solitary variant	Multiple variant
Accounts for approximately 90% of cases	Accounts for approximately 10% of cases
May cause significant pain in most cases	Less painful and pain only affects 40–60% of cases
Localised to one anatomical site	Localised, segmental or disseminated distribution
Sporadic	Autosomal dominant inheritance pattern
Hard on palpation	Soft on palpation
Congenital or acquired	Usually congenital, can occasionally be acquired
Small endothelium-lined cavities	Large irregular vessels
Fibrous capsule	No clearly distinguishable capsule
High number of glomus cells	Few glomus cells

otherwise well and there was no history of gastrointestinal bleeding.

On examination there were three bluish lesions on his body, one on his cheek, another lesion on the inner surface of his right thigh (see figure 1A) and a third lesion at the right renal angle (see figure 1B). In addition to these three lesions he had two other lesions, one on his scalp and another on the medial side of his left foot. It was suspected that the three bluish lesions were most probably glomus tumours. The lesion on his scalp was thought to be a compound naevus while the one on

(a)

(b)

Figure 1 (A) Note the faint bluish tinge on the inner aspect of the patient's right thigh (B) The bluish colouration of glomovenous malformation is more visible in this lesion at the right renal angle.

his left foot was considered an intradermal naevus. He was referred to the in house plastic surgery team for excision of these lesions.

INVESTIGATIONS

A routine set of blood tests including full blood count, renal function, liver function and coagulation tests were performed. These were all normal. No imaging investigations were considered necessary as the child was otherwise well.

The excised tissue specimens were sent for histological examination. Macroscopic examination revealed six pieces of fibrofatty tissue, the largest of which was 6.7×3.0×2.0 cm and the smallest measuring 0.4×0.4×1 cm. Apart from the specimen on the head, which was a junctional naevus, the remaining five pieces of tissue showed dilated vascular spaces with some organising thrombus and a thin layer of glomus cells lining each space (see figure 2A–C). These views were consistent with GVMs.

DIFFERENTIAL DIAGNOSIS

GVMs usually occur in childhood and become more apparent as the child matures. They are usually asymptomatic with only around 40–60% of tumours causing paroxysms of pain and even then the pain experienced is not as severe as with solitary glomus tumours.¹ They do not have a predilection for subungual sites and may occur throughout the body in a localised, segmental or disseminated distribution. Furthermore, there may be a family history of similar lesions.⁴ Glomus tumours, (solitary variant) on the other hand, occur sporadically in young adults and are painful solitary lesions most commonly localised to the subungual region under the nailbed.⁴ Apart from this there are a number of other differential diagnoses which should be considered and include:

- ▶ Blue rubber bleb-naevus syndrome—a rare venous malformation which consists of multiple bluish lesions on the skin and in the small intestine and distal large bowel. The skin nodules are easily compressible and painless. The lesions occur in a sporadic distribution and may bleed easily. There is a high risk of bleeding from lesions in the gastrointestinal tract which is frequently responsible for significant morbidity and mortality in these patients.¹
- ▶ Maffucci syndrome—a sporadic condition consisting of multiple enchondromas together with multiple subcutaneous haemangio-endotheliomas localised to the finger and toes.¹
- ▶ Haemangioma—a benign vascular tumour characterised by a hyperplasia or proliferation of endothelial cells and increased mast cell activity. They usually appear during the first weeks of life and self-involute by the age of 8–10 years. Occasionally larger haemangiomas may cause damage to neighbouring tissues.
- ▶ Spiradenoma—also known as a spiroma or eccrine spiradenoma is a benign tumour of the sweat gland usually occurring on the ventral surface of the body. It is usually solitary and consists of a deep-seated dermal nodule approximately 1 cm in diameter.⁵
- ▶ Angiolipoma—a tumour comprised of varying amounts of adipose tissue, smooth muscle and blood vessels. They most commonly affect the kidneys as a solitary or multicentric mass. Cutaneous presentations are extremely rare.⁶
- ▶ Leiomyoma—a benign smooth muscle neoplasm which may occasionally show cutaneous involvement.
- ▶ Haemangiopericytoma—rare soft tissue sarcoma which usually have their origin in pericytes found within the wall of capillary vessels.⁷

Figure 2 Glomangioma: dilated cavernous type blood vessels lined by glomus cells: $\times 2.5$ magnification (A); $\times 5$ magnification (B) and $\times 20$ magnification (C).

TREATMENT

A number of treatment options exist for GVM. Observation maybe an option in non-symptomatic lesions while surgical excision is considered the gold standard for treatment of symptomatic lesions. However, there is still a possibility of recurrence even with complete surgical excision. The recurrence rate for these lesions following surgical excision is currently not documented within contemporary literature. In addition to surgical excision, a small number of isolated cases have been successfully treated with other techniques such as argon and carbon monoxide laser therapy and sclerotherapy with hypertonic saline or sodium tetradecyl sulfate.^{8–10} In this case we decided to surgically excise the lesions as this technique is the most effective according to the evidence base and also because it would enable histological confirmation.^{1–3}

OUTCOME AND FOLLOW-UP

The patient was reviewed in outpatient clinic at 1 month following excision of the lesions. Although he was offered to be reviewed 6 monthly in our plastic surgery clinic for any recurrences, he preferred to be discharged from our clinic and report to his GP 6 monthly. Eight years following excision of these lesions we telephoned the patient as he did not present to us again. He explained that he had a recurrence of the lesion on his thigh and had three new lesions developed, one on his left ear, another on his right hand and another on his lower back, all of them measuring approximately 1 cm in diameter. However, the recurrence on his thigh and the new lesions were not causing significant pain and were not affecting his function. We offered to see him in our clinic but he preferred to contact us if and when he needed.

DISCUSSION

Touraine was the first to describe GVMs in 1936.⁴ It is about 10 times more common in children compared with adults with about 60% of patients reporting a positive family history.⁴ There may be anywhere between 2 and 100 soft bluish lesions distributed either in a localised, segmental or disseminated manner throughout the body.⁴ The commonest areas to be affected are the trunk and upper extremities while the face, scalp and genitalia are the least common. In comparison with the solitary tumours where pain is invariably present in almost all patients, pain is less often associated with these lesions with only around 40–60% of patients with GVMs reporting of pain.¹¹ The lesions usually enlarge as the child grows and they may develop satellite lesions during the pubertal growth spurt.

GVMs may be congenital or acquired and it is thought that heterozygous germline mutations in the glomulin gene localised to chromosome 1p21–22 may be responsible.¹² The most consistent pattern of inheritance observed in most cases is that of an autosomal dominant pattern with incomplete penetrance and variable expressivity.⁴

In certain cases patients may have associated genetic malformations as well as involvement of internal organs, such as the gastrointestinal tract, liver, pancreas, bones and nerves.^{13 14} The history should include questions on loss of blood through the back passage, abdominal pain, poor appetite, unusual sensory phenomena and unexplainable severe limb pain. In our case the patient did not have any other sinister features in his history or on examination thus precluding the need for imaging studies. However, in situations where internal involvement is suspected appropriate imaging such as ultrasound scanning, endoscopy, CT and MRI should be organised. Furthermore, platelet sequestration is a possibility in GVMs and hence at least a full blood count and coagulation screen should be obtained.

Histologically, GVMs are less well circumscribed as they lack the fibrous rim of their solitary counterparts. Their appearance is more representative of a haemangioma and they contain several, irregular, dilated vascular spaces that are larger than those observed in the solitary variety.³ They also have fewer glomus cells than the solitary form with narrow, focal aggregates of glomus cells in the walls of the Sucquet-Hoyer channels.⁴

This case is the first to follow-up a patient following excision of these lesions after 8 years. It is clear that recurrence is a possibility at previous sites of surgical excision while there is also the potential to develop new lesions elsewhere. As is evident from the number of possible differential diagnoses, GVMs may prove to be a diagnostic challenge. However, awareness of this condition with an appreciation for its clinical presentation in the child, most often with a positive family, should make diagnosis less difficult.

Learning points

- ▶ Glomuvenous malformations may prove to be difficult to diagnose clinically. However, the presence of multiple painful lesions at a number of different sites on the body together with a positive family history should alert the physician to the possibility of it as a differential diagnosis.
- ▶ Histologically, glomuvenous malformations display fewer glomus cells, have larger irregular blood vessels and lack the well circumscribed fibrous rim of their solitary counterparts.
- ▶ Although surgery maybe curative, there is the possibility of recurrence at the same site.
- ▶ Children are more commonly affected by glomuvenous malformations and lesions may continue to develop throughout life at various different sites on the body.
- ▶ Close follow-up is essential, especially as internal organ involvement may lead catastrophic consequences including metastases and acute gastrointestinal haemorrhage.

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