CASE REPORT

Propranolol as an effective therapy for infantile haemangioma of the urinary bladder

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SUMMARY

Infantile haemangiomas are one of the most common tumours in infancy, but typically present as cutaneous lesions; haemangiomas of the urinary bladder are incredibly rare. Although benign, these can sometimes ulcerate and bleed, causing haematuria in the case of bladder lesions. Propranolol is a well-documented medical therapy for cutaneous lesions, but surgical treatment dominates the literature on bladder haemangiomas. We present the case of a child with infantile haemangiomas of the urinary bladder, as well as internal and cutaneous lesions, treated with propranolol. At 6-week follow-up cystoscopy and MRI, there was a significant improvement in both bladder and internal lesions, respectively. Follow-up with dermatology 9 months after initiation of propranolol demonstrated excellent regression of the cutaneous lesions with a marked decrease in both size and prominence. This case demonstrates the potential role of propranolol in the treatment of bladder haemangiomas in lieu of more invasive surgical techniques.

BACKGROUND

Infantile haemangiomas are a common tumour in infancy, affecting 4%–5% of infants.¹ Haemangiomas of the bladder, however, are extremely rare. These are documented primarily through a few case reports and comprise only 0.6% of bladder tumours.² Although benign, these vascular tumours can sometimes cause large volume haematuria and, in rare cases, even haemorrhagic shock.^{3,4} Medical therapy with propranolol is well documented as an effective treatment for infantile haemangioma, as well as the recent literature suggesting its effectiveness in cavernous haemangiomas.^{5–7} Despite this, surgical treatment, either endoscopically or with partial cystectomy, appears to dominate the literature for haemangiomas of the bladder.^{8–10} We present the case of a child with infantile haemangioma of the urinary bladder, as well as cutaneous manifestations, with significant improvement after initiation of propranolol.

CASE PRESENTATION

A patient initially presented to the Paediatric Urology Clinic as a 10-day-old term girl, a product of a spontaneous vaginal delivery with no pregnancy complications, for evaluation of bilateral prenatal hydronephrosis. She is otherwise healthy and has no known relevant medical family history. She is an only child and lives with both parents. On

initial presentation in the clinic, she was found to have right grade 1 and left grade 3 hydronephrosis without any hydroureter or bladder abnormalities on ultrasound. Further workup involved voiding cystourethrogram showing no evidence of vesicoureteral reflux or urethral abnormality. Repeat renal ultrasound showed resolution of the right hydronephrosis and worsening of the left hydronephrosis to grade 4.

At 6 weeks of age, she underwent a nuclear renal scan which demonstrated preserved function in both kidneys, but high-grade obstruction of the left kidney consistent with the left ureteropelvic junction obstruction.

Shortly after this, she underwent cystoscopy with left ureteral stent placement and open left dismembered pyeloplasty. During the cystoscopic portion of the procedure, she was found to have multiple polypoid, erythematous lesions along the floor and posterior wall of the entire left bladder (figure 1A).

INVESTIGATIONS

MRI of the abdomen and pelvis was performed at 2 months of age and demonstrated a 1.4×0.5 cm enhancing soft tissue mass of the posterior bladder wall and 4×2.5 cm enhancing soft tissue mass of the left inferior pelvic floor adjacent to the posterior bladder (figure 2A).

Cystoscopy with bladder biopsies was performed on the same day as MRI with pathology showing numerous vascular spaces lined by plump endothelial cells that had small and inconspicuous lumens (figure 3A). Immunostaining of the cells was positive for Glut-1 (figure 3B). These findings were consistent with the diagnosis of infantile haemangioma.

She was also found to have cutaneous lesions so the case was discussed extensively with our vascular

Figure 1 (A) Cystoscopic image of bladder haemangioma prior to treatment. (B) Cystoscopic image of bladder haemangioma 6 weeks after initiation of propranolol therapy.

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Figure 2 (A) Internal haemangioma as seen on MRI prior to treatment. (B) Internal haemangioma as seen on MRI 6 weeks after initiation of propranolol therapy.

anomalies clinic, which is a multidisciplinary team consisting of Paediatric Dermatology, Paediatric Surgery, Paediatric Orthopaedics, Paediatric Plastics and Interventional Radiology. She was subsequently referred to Dermatology and examination revealed large, well-demarcated, red to pink coalescing plaques of the buttocks, perineum, vulva and lower back (figure 4A) consistent with segmental infantile haemangiomas.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for the bladder and retroperitoneal masses included rhabdomyosarcoma, atypical haemangioma, Burkitt lymphoma and neurogenic tumours such as neuroblastoma.

TREATMENT

Shortly after dermatological evaluation, and after biopsy results confirmed the diagnosis of infantile haemangioma, she was started on propranolol therapy. Propranolol was administered

Figure 3 (A) Histopathological slide from the bladder lesion, showing numerous vascular spaces lined by plump endothelial cells that had small and inconspicuous lumens. (B) Immunostaining positive for Glut-1, consistent with infantile haemangioma.

Figure 4 (A) Perineal/gluteal lesion prior to treatment. (B) Perineal/gluteal lesion after 3 months of propranolol therapy.

orally and initiated at a dose of 1 mg/kg two times per day. The dose was adjusted for weight.

OUTCOME AND FOLLOW-UP

Repeat cystoscopy was performed for removal of ureteral stent 6 weeks after initiation of propranolol. Cystoscopy showed significant improvement in both size and thickness of the haemangiomas (figure 1B).

MRI performed on the same day as cystoscopy showed a minimal residual lesion on the posterior bladder wall and a marked decrease in the size of the left inferior pelvic lesion to 1.4×1.6 cm from 4×2.5 cm previously (figure 2B).

Most recent dermatology follow-up 9 months after initiation of propranolol notes a decrease in size and prominence of cutaneous lesions. Images from a 3-month follow-up are shown in figure 4B.

She tolerated the propranolol well, with the exception of one instance of sleep pattern disturbance. This was self-limited and resolved without any interruption in therapy or dosage decrease. She continues on propranolol currently for her persistent cutaneous lesions. Due to the location of the lesions in the perineal region, she is at higher risk of ulceration, thus dosing has remained consistently adjusted for weight. The current plan is to continue therapy until approximately 1 year of age based on the progression of her skin lesions.

DISCUSSION

Infantile haemangiomas are the most common childhood tumours, present in 4%–5% of all infants.¹ These lesions can be present on the skin, internal organs or both. Haemangiomas of the urinary tract are very rare but present most often in the kidneys and bladder.¹¹

There is a known association of segmental haemangiomas of the lumbosacral/perineal region with lipomas/lipomyelomeningoceles, vesicorenal abnormalities, spinal bony abnormalities/spinal dysraphism, anorectal anomalies, tethered cord, intraspinal haemangiomas and sinus tract. The acronyms LUMBAR¹² and PELVIS¹³ have been used to describe this constellation of associated findings. We feel that abnormal bladder findings in conjunction with the external and internal haemangiomas found in this case represent an example of these syndromes.

Medical therapy with propranolol is well established as first-line therapy for cutaneous infantile haemangiomas.⁷ Despite its known effectiveness for cutaneous lesions, it is not typically employed for the treatment of haemangiomas in other locations. Recent literature has also emerged that demonstrates the effectiveness of propranolol in the treatment of internal haemangiomas.^{5 6}

Haemangiomas of the urinary bladder are less well studied and documented mostly in isolated case reports. A review of

the literature demonstrates surgical treatment as the preferred approach for the treatment of bladder haemangiomas. Surgical options that have been described include transurethral resection, fulguration, YAG laser therapy, and partial or simple cystectomy.^{3 4 8–10 14}

Our review of the literature did not identify any cases of bladder haemangiomas treated primarily with medical therapy. Itesako *et al* recently published a case report of a 3-year-old boy with urethral haemangioma successfully treated with propranolol; this is the only known prior case of a urinary tract haemangioma treated with medical therapy.¹⁵ This case presents a child

with cutaneous, internal and urinary tract haemangiomas treated effectively with propranolol alone.

Learning points

- Infantile haemangiomas are common tumours of infancy that can be multifocal with cutaneous and/or visceral involvement.
- Haemangiomas of the bladder are incredibly rare and account for only 0.6% of tumour.
- In patients with infantile haemangiomas, extracutaneous involvement should be considered.
- Propranolol may be an effective non-surgical treatment for internal haemangiomas, including those of the urinary bladder.

Patient's perspective

From around 20 weeks during pregnancy we knew our daughter had an enlarged kidney. We saw a specialist who watched it and released us back to our regular doctor. As first-time parents we did not think it was a big deal. However, when she made her arrival we were referred to a urologist and found out this kidney stuff was hydronephrosis. Still not largely concerned due to great explanations by our care team, it was watched with several ultrasounds and tests. At 6 weeks, they decided to do surgery because her left kidney was not draining and was getting worse. Having to watch our tiny baby go under anaesthesia made all of these medical terms I had not heard before so much more real. During that surgery, they removed a blockage in her ureter and reattached it to her kidney. During this, they discovered a tumour inside her bladder. That word 'tumour' just hung in the air. We had no idea what it was but your mind immediately goes to the worst. They scheduled an MRI and decided to take a sample to be tested. During the MRI, they discovered a second tumour behind her bladder and then we had to wait. Thankfully, the results came back as haemangiomas. But, we still did not know about the tumour behind her bladder. Was that also haemangioma like they are suggesting? Can we assume that without a biopsy of that lesion behind the bladder? What if the internal tumours behind the bladder are something else more aggressive? Our minds wandered. We saw dermatology who put her on propranolol to shrink the tumours. Will the propranolol shrink the bladder tumour and the 'unknown' internal tumours behind the bladder as well? Well, miraculously, the repeat look inside the bladder and the MRI of the lesions behind the bladder showed dramatic improvement after a few weeks of our daughter being on propranolol. So, yes, the skin and bladder lesions improved and so did the 'unknown' internal lesions behind the bladder noted on the MRI. What a relief! They continue to monitor her in both urology and dermatology. Although we are ready to put this all behind us, we are so thankful for the fantastic care and patience of our great doctors who have gently explained what is going on with our baby girl in terms we can understand.

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