CASE REPORT

Not so mass effect? Finding of a remarkable 'incidentaloma' in a teenager with neurofibromatosis

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SUMMARY

A 13-year-old boy with neurofibromatosis type 1 presented to the emergency department twice in a fortnight with moderate intermittent abdominal pain, radiating to the back and associated with nausea and vomiting. He examined as a well child with a soft abdomen and minimal tenderness. A history of constipation was identified but he failed to respond to a trial of laxatives. Subsequent ultrasound abdomen demonstrated a large mass surrounding the porta hepatis. MRI further characterised a focal, non-aggressive lesion extending from his liver, encapsulating his pancreas, portal vessels and laterally displacing his spleen and left kidney. Biopsy performed at a specialist cancer treatment hospital of our reference later confirmed this to be a benign neurofibroma of a size not previously reported in the literature. He will be managed conservatively with surveillance imaging and the potential for chemotherapy should the lesion continue to grow.

BACKGROUND

Neurofibromatosis type 1 (NF1) is a relatively common inherited disorder with an incidence of 1 in 3500.¹ Cellular manifestations of the condition are attributed to a number of pathological sequelae with a neurofibroma of this scale being exceptionally remarkable compared with tumours reported in the literature. Despite this, the mass remained exceptionally difficult to palpate among several clinicians from the paediatric and surgical teams. The lesson to be learnt is that a patient with NF1, particularly if they are known to have neurofibromas identified on imaging, should be treated with a low incidence of suspicion for new growth of tumours. Lesions can develop in anatomically disparate loci and cause seemingly unrelated symptoms.

CASE PRESENTATION

A 13-year-old boy with a background diagnosis of NF1 presented for the second time to the emergency department with a 10-day history of intermittent pain in the left upper quadrant, described as sharp and squeezing in nature. His pain fluctuated in severity but had been waking him from sleep and was particularly bad in the morning. This had initially been associated with vomiting and loose stools but had subsequently developed into constipation. He was known to have multiple café-au-lait patches over his abdomen, two cerebral neurofibromas and he suffered from generalised

tonic-clonic seizures, which were well controlled on sodium valproate. Examination revealed a soft abdomen with mild tenderness on deep palpation of his left upper quadrant, flank and iliac fossa. He was afebrile and haemodynamically stable. He was suspected to have palpable abdominal faecoliths.

INVESTIGATIONS

Owing to this being his second presentation within 2 weeks and an ongoing requirement of simple analgesia, an ultrasound was organised. Blood work had demonstrated mild iron deficiency anaemia, normal inflammatory markers, renal and liver function tests. His urinalysis was normal. His ultrasound scan, shown in [figure 1](#), demonstrated a focal mass measuring 7.6×7.4 cm overlying the right lobe of his liver and some distended loops of bowel.

Urgent MRI abdomen further characterised this lesion as a single mass extending from the midline ([figure 2](#)). This non-enhancing mass encapsulates his pancreas, coeliac axis, portal and superior mesenteric veins and extends inferiorly to the point of bifurcation of the abdominal aorta. In the coronal plane, the mass gently effaces the porta hepatis and stretches laterally to displace his spleen and left kidney. The lesion demonstrated high T2 and low T1 intensity and, despite its significant size, gave the appearance of being non-invasive, maintaining patency of the pancreatic duct and portal veins.

OUTCOME AND FOLLOW-UP

Following the result of his MRI, he was referred for tertiary opinion at a specialist centre for the treatment of cancer in children. Reassuringly for the patient and his family, the histology from a biopsy identified the mass as a benign neurofibroma in keeping with his existing diagnosis of NF1. Given the complexity and size of the lesion, it was felt not to be amenable for surgical resection as there would be a substantial risk of incomplete removal and tumour regrowth. It was initially suspected that his pain was secondary to the presence of such a large lesion with his abdomen, through compression of the abdominal organs. However, to the patient's relief, the abdominal pain had subsequently subsided without intervention and as such may have simply heralded this significant incidental finding. The patient and his family were counselled about the necessity and risks of medical or surgical treatment at this stage and a plan was agreed to undergo careful surveillance over the next few years in order to assess if the mass is indolent or in a proliferative

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Figure 1 Abdominal ultrasound demonstrating a non-invasive mass with coarse echotexture and minimal vascularity.

phase. Should it be demonstrated that the lesion is increasing in size, or causing new symptoms, consideration of mitochondrial apoptosis-induced channel inhibitor therapy would be an option, with the overall aim of shrinking the mass and preventing symptoms caused by significant mass effect.

DISCUSSION

NF1 is an autosomal dominant neurocutaneous syndrome with an incidence of 1 in 3500 and typically presenting in childhood.¹ There are three recognised subtypes; of which, our patient carries a diagnosis of NF1. 17q11.2 mutation in NF1 has a strong penetration within the genome but is a novel mutation in approximately one-third of patients and as such a strong family history may be absent.¹ The NF1 gene encodes for the tumour suppressor protein neurofibromin; an imported regulator of Ras mitogen-activated protein kinase (MAPK)-mediated mitosis for multiple cell lines but in particular the nerve associated with oligodendrocytes and Schwann cells.² Its dysregulation leads to uncontrolled proliferation resulting in the characteristic features of NF1; optic gliomas, Lisch nodules, café au lait spots, axillary freckling and the formation of multiple nerve sheath nodules (neurofibromas).² Onset of fibromas is suspected to herald the loss of the wild-type NF1 by somatic mutation and

also contributes to an increased risk of malignant peripheral nerve sheath tumour, myeloid leukaemia and glial tumours.³

The development of extensive plexiform neurofibromas (PN) is an unusual presentation of the condition with abdominal involvement, such as this case, being much less common. Unlike cutaneous neurofibromas, they are suspected to be congenital lesions arising from spinal nerve roots and grow insidiously.³ From the literature, we have identified 12 similar cases of intra-abdominal, large plexiform neurofibroma worldwide in children with NF1. Most also involved the pancreas, coeliac axis or portal vessels; however, none of these described have been quite as extensive in volume as that described in our patient.⁴⁻¹⁰ In the cases identified, the intra-abdominal lesions have been identified incidentally or as in our case following investigation of insidious non-specific symptoms, such as lower back pain. Indeed, three of the identified cases presented in a similar manner to our patient, with non-specific abdominal pain in a well child.⁸⁻¹⁰ In each case, on identifying the mass, the cause of pain was attributed to the compression or disruption of surrounding abdominal organs. For a 14-year-old girl with a neurofibroma within the porta hepatis, the mass effect led to a mild obstructive jaundice, likely due to distortion of the extra-hepatic biliary ducts.⁸ Interestingly, her pain also became more manageable without intervention and she is currently being monitored in the same way as our patient.

In the majority of cases, the patients have an existing diagnosis of NF1; however, Scheurkogel *et al* describe a 9-year-old boy whereupon the identification of a PN was the sole diagnostic feature of NF1.⁵ A 5-year-old boy presented for investigation of a left-sided mass in his neck but was subsequently noted to have a distended and firm abdomen, which parents reported had been present for many years. Subsequent imaging identified an extensive, infiltrative lesion abutting the porta hepatis and extending along vasculature to the left renal hilum, very much resembling an invasive tumour.⁷

All 12 cases shared characteristic MRI findings for PNs with our case. PNs demonstrate hypoattenuation on T1 weight images, hyperattenuated T2 signals and a central target sign on water-sensitive sequences.⁴ The fascicular structure is represented by a septated, ring-like lesion and the low central signal of the target sign are on occasion caused by haemorrhage or necrosis of central tissue mass.¹¹ The configuration is that of a gentle and non-destructive space-occupying lesion that follows the contours of major vessels and the surface of major organs, often encasing them in tissue but not compromising integrity.⁵ As such, this differentiates them from malignant differential diagnoses.

It is important that these children are carefully managed by a multidisciplinary team including a paediatrician, neuro-oncologist, neurosurgeon, geneticist, histopathologist and ophthalmologist.⁶ Patients referred will undergo biopsy of the mass, which will often demonstrate a chaotic array of Schwann cells and extracellular matrix.⁷ PNs are naturally benign, extensively ill-defined lesions that integrate readily with surrounding structures and as such complete surgical resection is almost impossible, with a high risk of regrowth. As such intervention is only advocated in patients whose tumours generate unbearable symptoms or significant physiological compromise.⁶ Enhanced surveillance is the preferred management option as the prospect for progressive enlargement is significant and there is an associated 10% risk of transformation to a malignant peripheral nerve sheath tumour.^{3,5}

Alternative medical therapy to halt tumour growth is an active field of investigation with promising new developments

Figure 2 MRI abdomen; axial images characterising a prominent abdominal mass. (A) T2-weighted image; (B) T1-weighted image; (C) post-gadolinium and (D) fat-saturated images.

in the pipeline. As previously discussed, tumour growth associated with a dysregulated MAPK signalling, key component of which are the enzymes mitogen-activated protein kinase 1 and 2 (MEK1 and 2). Dombi *et al* have recently described a phase 1 trial in 24 affected children of selumetinib, a selective MEK1 and 2 inhibitor and report that 71% of patients exhibited a $\geq 20\%$ reduction in tumour volume.¹² Further fields of research include the use of agents such as 13-cis-retinoic acid, thalidomide and interferon α -2a.⁶ For our patient and such like him, these are promising trials demonstrating hopeful non-surgical therapy if the surveillance imaging demonstrates malignant change or intolerable extension of the mass.

Learning points

- ▶ Neurofibromatosis type 1 (NF1) is a neurocutaneous syndrome caused by autosomal dominant mutation of neurofibromin with an incidence of 1 in 3500.
- ▶ Presentation of a plexiform neurofibroma is often insidious manifesting with non-specific symptoms and may be the first indication for a diagnosis of NF1.
- ▶ Characteristic MRI findings reveal a gentle non-destructive space occupying lesion with low signal on T1 images and hyperattenuation T2 signalling.
- ▶ Radiological surveillance is the mainstay of management with intervention reserved for patients with physiological compromise.

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