CASE REPORT

Osteogenesis imperfecta and congenital diaphragmatic hernia

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SUMMARY

Osteogenesis imperfecta and congenital diaphragmatic hernia are both conditions that can occur due to genetic mutation. We present the first case to be reported of a child with both osteogenesis imperfecta and congenital diaphragmatic hernias, showing that the incidence of this presentation may be more than chance.

BACKGROUND

Osteogenesis imperfecta (OI) is a group of heterogeneous conditions characterised by a varying degree of bone fragility. It is usually caused by a heterozygous mutation in either of the type I collagen genes and it is inherited in an autosomal-dominant manner. Mutations in the COL1A1, COL1A2, CRTAP and LEPRE1 genes are known to cause OI.^{1 2}

Type III is distinguished among the others as being the 'progressive deforming' type, wherein a neonate presents with mild symptoms at birth that progress throughout life.³

Congenital diaphragmatic hernias (CDH) are a common birth defect that is associated with considerable morbidity and mortality. The average prevalence of CDH was 1/4000 births whereas OI affects an estimated 7/100 000 people worldwide.⁴

Like OI, CDH can occur with additional malformations or as part of a single gene disorder or chromosome abnormality and although CDH has been reported in other connective tissues disorders there has not been any reported case of CDH presenting in a child with OI and may show a new genetic relationship between these conditions.^{4 5}

CASE PRESENTATION

A 6-week-old child was admitted via A&E with a progressive 6-day history of increased difficulty in breathing and reduced feeding. There were no signs of infection or trauma in the history.

Osteogenesis imperfecta type III had been diagnosed at birth as he was born with limb fractures. There were no new fractures prior to admission or a history of the disease within the family.

The patient had no symptoms suggestive of sepsis, no fever, no vomiting or abdominal pain. On examination, he was tachycardic at 188 bpm with respiratory distress, having signs of suprasternal and intercostal recession. The respiratory rate was 80 breaths per minute.

On auscultation, decreased air entry was noted on the right and normal air entry on the left. Cardiovascular and abdominal examinations were

normal; however, bowel sounds were heard in the chest.

INVESTIGATIONS

A venous blood gas taken in A&E showed a respiratory acidosis pH 7.26 pCO₂ 8.2 and lactate 2.3. Blood tests showed a raised white cell count 21.9×10^9 , neutrophils 6.1×10^9 and C reactive protein <2 units.

Chest x-ray (CXR) showed numerous bowel loops from the right base extending to the mid-zone consistent with a right diaphragmatic hernia. The left lung was a similar size to previous x-rays with only some patchy air space in the upper lobe. No new rib fractures were present. Initial assessment suggested that this presentation was likely to be due to a right diaphragmatic hernia with possible associated right pneumonia and followed with a CT scan.

The CT confirmed a right diaphragmatic hernia. The right lobe of the liver was herniated into the right hemithorax via a large posterior diaphragmatic defect. The majority of the right lung was collapsed.

The patient's parents declined formal genetic testing to assess the exact genetic relationship between these conditions as they felt it would not benefit their son directly.

DIFFERENTIAL DIAGNOSIS

- ▶ Congenital cystic adenomatoid malformation—based on x-ray findings
- ▶ In a child with OI, a second differential is whether the hernia was traumatic as a fractured rib may have punctured the diaphragm allowing the abdominal contents to herniate

TREATMENT

Initial fluid resuscitation, drip and suck regimen with nasogastric tube (NGT) placed on free drainage. Intravenous co-amoxiclav was started. Owing to his increased work of breathing, the patient was intubated and transferred to paediatric intensive care unit (PICU) for ventilation.

A laparotomy was performed the following day through a transverse right upper quadrant incision. A large diaphragmatic defect was seen with a good anterior but very small posterior rim which was directly attached to the liver. Viscera were reduced and a surgisis patch was used to close the defect.

OUTCOME AND FOLLOW-UP

Postoperative recovery on PICU was uneventful. The boy was extubated and the chest drain

To cite: Dholakia S, Cleeve S. *BMJ Case Reports* Published online: [please include Day Month Year] doi:10.1136/bcr-2012-007341

removed day 3 post surgery. Feeds were started day 1 post surgery via NGT with full NG feeds by discharge to the ward day 4. Repeat CXR showed re-expansion of the right lung. He was discharged on full oral feeds and normal saturations, 6 days post surgery. On follow-up 3 months postoperatively, he had no respiratory symptoms and was growing normally. He did not have any new fractures. He continues to receive pamidronate treatment every 2 months.

DISCUSSION

It is known that defective type I collagen with a reduced type I/III ratio predisposes to hernias.

Several cases with CDH have been reported in association with chromosome rearrangements producing disruption or deletion of chromosome band 1q41–q42.12, which lies close to the region where LEPRE1 is found (1p34.1). Genetic abnormalities on chromosome 22 including trisomy and translocations are also shown to cause CDH, t(11;22)(q23;q11).⁶

Mutations seen in COL1 include reciprocal translocations between chromosomes 17 and 22. Mutations are also seen in LEPRE1; which encodes an enzyme that is a member of the collagen prolyl hydroxylase family, and their activity is required for proper collagen synthesis and assembly.⁷

There has also been a case of CDH reported in a patient with Smith-Magenis syndrome, highlighting a new possible locus at chromosome 17p11.2.⁸

It is clear to see there are a number of overlapping areas where mutations for both disorders may clinically manifest together and so CDH should be considered in OI patients with respiratory distress.

Learning points

- Clinically, patients with osteogenesis imperfecta may present with abdominal or respiratory symptoms at any point during their lives.⁹
- It is clear that there are a number of overlapping areas where mutations for both disorders may occur together, affecting collagen and thus making hernia an important differential to be considered.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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