CASE REPORT

Congenital scoliosis: an anomalous association with endosulfan

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SUMMARY

Endosulfan is an organochlorine pesticide that is used extensively across the world to kill insects. Incidence of acute and chronic toxicity with endosulfan poisoning has been reported, and nearly 80 countries have banned its use. However, it is still being used in many low-income/middle-income countries. One of the most severe tragedies because of endosulfan poisoning has taken place in the Indian state of Kerala due to persistent aerial spraying of endosulfan. Even though there are reports of skeletal and other congenital abnormalities in humans and experimental animals following exposure to endosulfan, very few have been documented. We report two cases of congenital scoliosis in siblings living in a community affected by high levels of endosulfan in the environment. High index of suspicion is essential during the screening of school children exposed to endosulfan. Congenital scoliosis is a progressive deformity that leads to severe disability, unless detected and corrected at an early stage.

CASE PRESENTATION

Case 1

A 15-year-old girl with a deformity of the spine was brought to us by her parents. She had a large thoracic hump on the back for which no prior treatment was given. She hailed from the endosulfan-affected area in the Kasaragod district of Kerala. Her parents have been residing in one of the affected villages for many decades. Standing anteroposterior (AP) and lateral X-rays of the spine revealed the presence of a right congenital thoracic kyphoscoliosis. There were multiple wedge vertebrae with contralateral bar (figure 1A). The Cobb's angle measured from the AP radiograph was >100°, indicating the severe nature of the curve. Supine stretch film did not show a significant correction (figure 1B). Hence, it was decided to treat the patient non-operatively as the curve was very rigid, and the patient could not benefit from a surgical procedure. Moreover, surgical correction of such a severe rigid curve carries a high risk of neurological damage. Hence, she was treated with a modified Boston brace to maintain the alignment and prevent further progression.

Case 2

The parents noticed a deformity of the back in the 9-year-old, younger sister of the first patient. She was brought to the hospital, and during screening X-rays of the spine revealed the presence of a left congenital thoracic scoliosis with a hemivertebra at D6 (figure 2A). In the standing AP view, the Cobb's angle was 36°, whereas the supine stretch film demonstrated good correction of the curvature, indicating it to be a relatively flexible spinal curve (figure 2B). Hence, it was decided to treat her aggressively, and surgical correction of the deformity with posterior instrumentation and fusion was performed. Correction of the deformity was satisfactory. Postoperative period was uneventful. She was fitted with a custom-made polypropylene modified Boston brace. The patient is on regular follow-up, and at 1-year follow-up the correction was well-maintained with excellent spinal alignment (figure 3). She is studying in sixth standard and is good in academics. The child also had a bicuspid aortic valve with trivial aortic regurgitation detected during preoperative evaluation. Even though the child was asymptomatic for cardiac anomalies, evaluation in the form of echocardiogram (echo) was done during the 1-year follow-up. No active intervention was recommended for the same by the cardiologist.

Investigations

Radiographs

AP and lateral X-rays of the whole spine in standing position and an AP stretch film of the spine in supine position were done for both patients to detect and assess the deformity. The severity of the curves was measured by Cobb's angle.

MRI

MRI was done to rule out any cord anomalies, such as syrinx, tethered cord, split cord and others. Both of the children did not have any spinal cord abnormalities.

Echocardiogram

This investigation is done to rule out cardiac anomalies that can be associated with congenital scoliosis. Echo scan was normal for the elder sibling; however, the younger girl had a bicuspid aortic valve with trivial aortic regurgitation.

Ultrasound scan

Ultrasound scan of the abdomen and pelvis was found to be normal in both of the children. It was done to rule out genitourinary anomalies.

Pulmonary function test

Preoperatively, this test was done as a routine investigation to determine the tidal volume and lung reserve, as a progressive scoliosis deformity can lead

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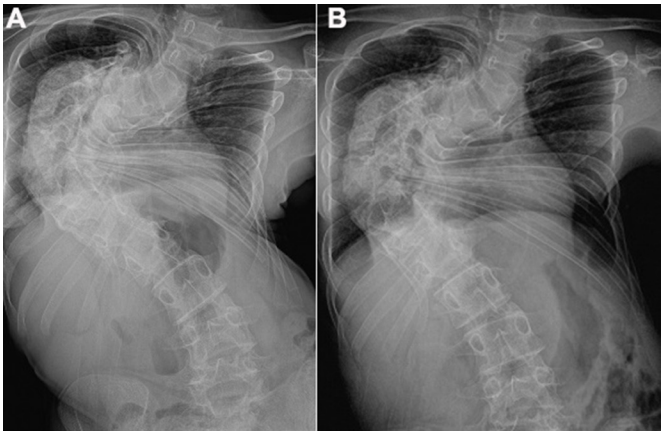

Figure 1 (A) Standing anteroposterior radiograph of the spine showing a severe right thoracic scoliosis. (B) A supine stretch film of the same patient without significant correction, indicating the rigidity of the curve.

to restrictive lung disease. Both girls had a restrictive pattern on pulmonary function test.

History of exposure to endosulfan and family history

Both of the children hailed from one of the 11 villages detected by the state government, national and international study agencies as areas affected by endosulfan poisoning, where heavy spraying of endosulfan has been practised for over three decades. These 11 villages were considered as affected by endosulfan poisoning based on examination of patients in health camps organised by the government, and by measuring endosulfan level in water, soil, vegetation and blood samples from school children. The parents and their ancestors have lived their entire life in the endosulfan-affected village. The father was 46 years old and the mother was 40 years old when they first came to our hospital with their children. Hence, the parents have been exposed to 25–30 years of aerial spraying of endosulfan before their first child was born. The elder sister was born in 2000. In 1998–2002, heavy spraying of endosulfan was done in their village, which involved three to four times of aerial spraying in a year. The mother is a housewife and had one spontaneous abortion (reason unknown) before the elder child was born. Their father did not have any medical ailment apart from dry skin. The possible development of vertebral defects and congenital scoliosis in our patients may be a result of exposure of their parents to the harmful chemical or fetal exposure to endosulfan during pregnancy. This is so in the absence of other explanatory factors beyond chance that could explain the health hazards in the area.

No other family member had any spinal deformity. Their maternal uncle had asthma, which has aggravated after aerial spraying of the chemical was started.

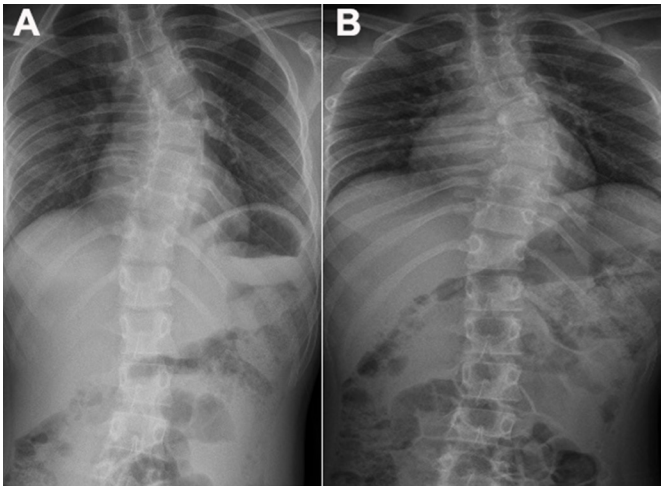

Figure 2 (A) Standing anteroposterior radiograph of the spine showing left thoracic scoliosis. (B) A supine stretch film of the same patient showing some amount of decrease in the curve on stretching the spine, indicating that the curve is flexible.

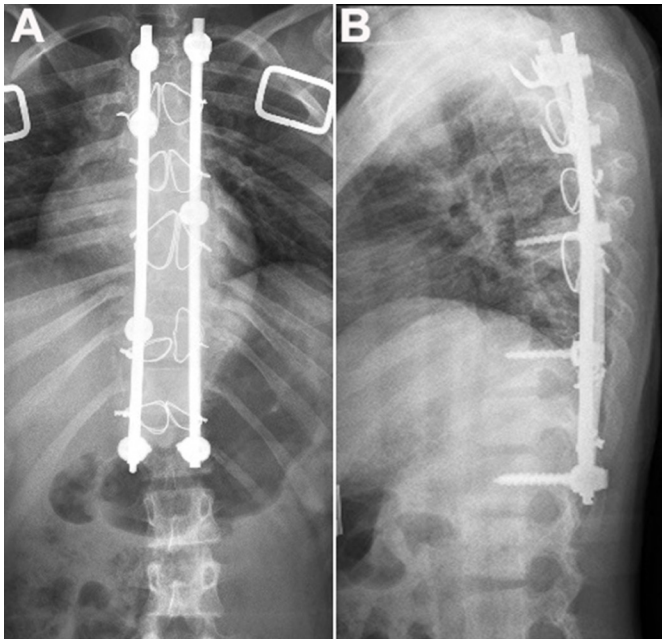

Figure 3 (A,B) Anteroposterior and lateral radiographs of the spine at 1 year after deformity correction, instrumentation and fusion. The correction is well-maintained.

GLOBAL HEALTH PROBLEM LIST

1. Protracted use of endosulfan by several countries across the globe despite evidence on the deleterious effects of this chemical on humans, animals, plants and the ecosystem.
2. A persistent organic pollutant, with crippling toxic effects, spanning multiple generations.
3. Lack of knowledge among the public about the toxic effects of pesticides such as endosulfan and their safe handling.
4. Lack of awareness concerning potential anomalies associated with endosulfan and other environmental pollutants in children living in exposed areas.
5. Delay in the detection of congenital scoliosis, which results in a severely rigid spinal deformity, thereby leading to a poorer treatment outcome.

GLOBAL HEALTH PROBLEM ANALYSIS

Endosulfan: the silent killer

Endosulfan is an organochlorine group of pesticides with the chemical formula 6,7,8,9,10,10-hexachloro-1,5,5a,6,9,9a-hexahydro–, 6,9-methano-2,4,3-benzodioxathiopine-3-oxide. It was first used in the 1950s, and since then has emerged as a popular pesticide against a broad spectrum of pests in the

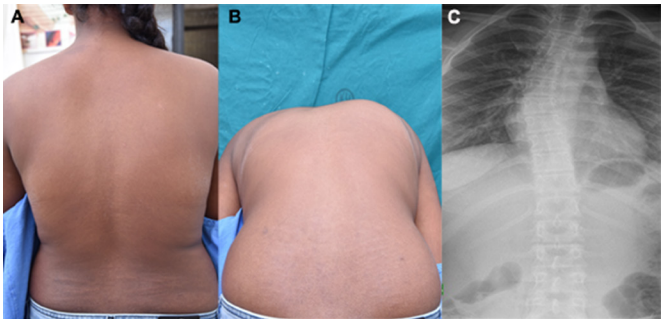

Figure 4 The Adam's Forward Bend Test, which is used as a screening test for scoliosis. (A) The patient to be screened for scoliosis is made to stand with both feet together and the knees straight. The spine should be fully visible and the back of the patient facing the examiner. (B) The patient is asked to fully bend forward with the arms hanging down freely. The curve in case of structural scoliosis gets more apparent and the rib hump becomes more prominent. (C) The anteroposterior radiograph of the same patient showing scoliosis of the spine.

agricultural field, especially cotton, cashew, tea, coffee, paddy and timber.

Numerous cases of poisoning of animals, insects, and aquatic flora and fauna, and many cases of human poisoning including deaths, with endosulfan have been reported from across the globe. Some of the countries from which endosulfan poisoning has been reported are Sudan, Sri Lanka, Indonesia, Columbia, Northern India, Philippines, Turkey, Guatemala, Costa Rica and South Africa.[1–8] Hence, the US Environmental Protection Agency (US EPA) and the European Union have classified endosulfan as a highly hazardous chemical, whereas the WHO has classified it as a moderately hazardous (category II) chemical.[9] As part of the global ban, many countries have already banned this chemical due to its toxicity, and many others are in different stages of phase-out. However, it is still being used as a pesticide in many low-income/middle-income countries including India.

The biggest tragedies of endosulfan poisoning have been reported in Benin, Cuba and India. In Benin, in 1999–2000, there were 37 deaths and another 36 got seriously ill due to endosulfan poisoning from cotton plantations and from consumption of corn.[10] According to the official records, due to consumption of food contaminated with endosulfan in Cuba in 1999, more than 60 people became sick, which included 15 deaths.[9]

Endosulfan tragedy in Kasaragod, India

Kasaragod is the northernmost district of the state of Kerala in India. In many parts of this district, the terrain is hilly, where cashew plantations have been established for many decades. The Plantation Corporation of Kerala initiated aerial spraying of endosulfan using small aeroplanes and helicopters in the cashew plantations spread over 12 000 ha to counter the attack of tea mosquitoes destroying the crop. This process of aerial spraying violated the rules laid down by the US EPA on endosulfan application.[11]

Between 1976 and 2000, more than 50 000 villagers of Kasaragod district have been exposed to endosulfan, a persistent organochlorine pesticide. This led to an increased incidence of health disorders in cattle and humans, which caught the attention of the local physicians, activists and the local government. Later, studies revealed an alarming increase in the number of congenital anomalies, hydrocephalus, neurological disorders, delayed puberty, skin malignancies and psychiatric disorders in the villages exposed to endosulfan.[12–15] The concentration of endosulfan in the groundwater of Padre Village in Kasaragod was found to be 7–51 times more than the maximum residual limit.[16] The honourable High Court of Kerala banned the use of endosulfan in the state in 2003, which was followed by the state government. After massive public outcry and long legal battles, finally in May 2011 the honourable Supreme Court of India banned the production, storage, sale and use of endosulfan in the country. The Indian Government has requested the Supreme Court in 2012 to allow the use of endosulfan in all other states except Kerala and Karnataka. It has agreed to phase out all endosulfan use by 2017.[17]

Routes of endosulfan poisoning

The air, water and soil in areas where endosulfan is used get contaminated. People can get exposed to endosulfan through contaminated drinking water, breathing air, and direct ingestion by eating contaminated vegetables, fruits and animal products. Exposure can also occur through local contact with contaminated soil and smoking tobacco contaminated with endosulfan. It can affect the fetus through the mother via placenta or by breast feeding.[9 12 18–20]

Endosulfan poisoning in humans

According to the WHO and the United Nations Environment Programme, approximately three million agricultural workers in low-income/middle-income countries suffer from severe poisoning with pesticides, which includes 18 000 deaths.[20] Endosulfan can cause both acute and chronic poisoning in humans. However, the toxicity and harmful effects of aerial spraying of endosulfan are much higher. In the villages of Kasaragod district, where aerial spraying of endosulfan was carried out, a geographical association was observed in the occurrence of the health problems from the period of aerial spraying.

Endosulfan is known to be highly toxic to small animals, birds, fish, bees and many other insects. A committee was appointed by the Government of Kerala to study the toxic effects of aerial spraying of endosulfan in Kasaragod. It detected high levels of endosulfan in all samples, including water, soil, plants, milk as well as human blood.[20] Many national and international bodies conducted health and toxicological studies and arrived at the conclusion that the abnormal health problems at Kasaragod were due to endosulfan spraying.[12–14]

An epidemiological study was done by Embrandiri *et al* to analyse the ill effects of endosulfan in the affected areas. Out of the 270 children under the age group of 14 years, 46% boys and 42.5% girls were born with some form of handicap or birth defect.[15] These percentages for congenital anomalies are exceedingly high compared with a study done 10 years earlier by the National Institute of Occupational Health, which had stated a prevalence of 0.83% and 1.94% for men and women, respectively. Embrandiri *et al* believed that the marked difference in the prevalence data was due to the lack of manifestation of anomalies during the previous study period. However, in the study by Embrandiri *et al*, people of all groups were affected either directly or indirectly through exposure to the chemical or by genetic route.

Acute poisoning

A large number of acute poisoning cases due to endosulfan in humans have been reported. It can be fatal if inhaled, swallowed or absorbed through the skin.[9] Endosulfan can affect the central nervous system, causing dizziness, tremors, loss of memory, lack of coordination, recurrent epileptic seizures, loss of consciousness and death.[21–25] It can cause irritation to the skin and eyes,

causing blurred vision, bluish discolouration of skin, itching and cyanosis. Inhalation of air with high amount of endosulfan can cause dyspnoea, apnoea and exacerbation of asthma. It can also cause diarrhoea, headache, nausea, vomiting, dry mouth, haematuria and albuminuria.[24 25] Ingestion of endosulfan can cause damage to the liver, lung and brain.[26 27]

Chronic poisoning

Chromosomal aberrations and embryo toxicity

Animal studies have found that endosulfan can cause chromosomal aberrations and dominant mutations in hamsters and mice and sex-linked recessive mutations in *Drosophila*.[28 29] In vitro and in vivo studies in humans also showed that endosulfan caused chromosomal damage.[30 31] Embryo toxicity in animals has been noted with endosulfan.[32] This effect can probably explain the higher rates of abortions, congenital anomalies and stillbirths observed among the cattle and humans residing in the affected villages of Kasaragod district in Kerala.

Central nervous system

Both studies on animals and reports on human poisoning with endosulfan involving the central nervous system have been reported. The conditions include mental disorders, neurobehavioural disorders, hydrocephalus, cognitive disorders, epilepsy, cortical blindness and parkinsonism.[33–35]

Reproductive system

There are numerous reports on animals that suggest that endosulfan poisoning can lead to degeneration of seminiferous tubules, leading to decreased sperm count, altered spermatogenesis, aspermatogenesis and testicular necrosis.[33 36]

Endocrine system

Endosulfan is considered to be an endocrine disruptor. Studies have shown dose-dependent decrease in testosterone, follicle-stimulating hormone and luteinising hormone due to endosulfan.[3] Endosulfan can also lead to precocious puberty, recurrent miscarriages, endometriosis, cervical cancer and other oestrogen-mediated abnormalities.[33 37]

Immune system

Endosulfan has been found to affect the immune system in rats, leading to decrease in immunity.[38] In humans, it promotes allergic responses in affected individuals. It can cause inhibition of leucocytes, decrease serum IgG levels and enhance mast cell degranulation.[33 39 40]

Carcinogenic/mutagenic effects

Endosulfan has not yet been classified as a human carcinogen by any international governing bodies. However, there is evidence indicating the carcinogenic and mutagenic potential of endosulfan. It was found to be mutagenic in various assay systems, including the Ames test, micronucleus test and the yeast conversion test.[41–43] Animal studies have shown that endosulfan can cause lymphosarcoma, and it is considered to be a potential liver tumour promoter.[44 45] It has shown genotoxic and mutagenic effects in mammalian germ cells and lymphocytes.[43 46]

Skeletal abnormalities

Defective ossification of skull bones, rib anomalies, caudal regression syndrome and vertebrae agenesis have been reported with endosulfan in Wistar rats.[47 48] However, the exact skeletal deformities have not been described in any of the studies done to date. Incidence of limb hypoplasias, ectrodactyly (cleft hand or split hands) and contractures has been reported among endosulfan victims in Kasaragod.[13 49]

Congenital scoliosis

Vertebral anomalies in congenital scoliosis are present at birth. However, they manifest as a visible deformity only much later. Many a time, socioeconomic and macrosocial factors contribute to the delay in detection. Vertebral anomalies can be due to either a failure of formation or a failure of segmentation of the vertebra. Hemivertebra is the most common vertebral anomaly associated with congenital scoliosis. Vertebral anomalies cause an imbalance in the longitudinal growth of the spine. As a congenital anomaly, children can have intraspinal anomalies such as diastematomyelia (15%), cardiac anomalies or genitourinary malformations.[50] Congenital scoliosis differs from idiopathic scoliosis in the following ways:

1. Vertebral anomalies are present.
2. The deformity progresses rapidly and becomes rigid.
3. Congenital scoliosis can be associated with genitourinary, cardiovascular and general anomalies.[50]

Patient's perspective

"Both my daughters have been diagnosed to have scoliosis. Many people including children in our village had diseases and deformities due to the endosulfan poisoning. Now the use of endosulfan is stopped and the area is gradually recovering from the ill effects. Hopefully the future generations will be free from the harmful effects. My younger daughter's spine deformity was corrected due to early detection. I am sad that my elder daughter was not so fortunate since we were not aware about the proper treatment. We have got some financial aid from the government for the elder daughter but we have not received any financial help for the younger daughter who had undergone surgery. Financial and emotional burden on the family has been tremendous due to the spine anomalies. My second child also has a heart problem for which doctors have given reassurance and has not undergone any surgery. Many more people in our district are suffering from endosulfan related diseases and require help for rehabilitation."

Learning points

- Health professionals should maintain a level of suspicion to detect rare conditions such as congenital scoliosis and other congenital anomalies in communities/areas exposed to endosulfan poisoning.
- Health check-ups and screening by health professionals for scoliosis among healthy children in affected areas can help in early detection and treatment of congenital scoliosis.
- Awareness should be created among the authorities, decision makers and the public, especially farmers, on the toxic effects of pesticides and their safe handling.
- Irrational and non-scientific use of these chemicals should be prohibited.
- Newer alternatives to harmful pesticides such as endosulfan should be encouraged, preferably bioherbicides and biopesticides.
- A global ban on endosulfan should be enforced.

4. Congenital scoliosis is more likely to have kyphoscoliotic deformity. The kyphoscoliotic curve has to be surgically corrected earlier to achieve gratifying results, whereas in idiopathic scoliosis deformity correction is preferred after the growth spurt.

Hence, to detect congenital scoliosis and associated anomalies, a high degree of suspicion should be maintained, and screening among healthy children in areas exposed to endosulfan by health professionals/practitioners is recommended. Scoliosis screening can be done using the Adam's Forward Bend Test (figure 4). In doubtful cases, it is important to investigate further with radiographs.

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