Familial predisposition of thoracic outlet syndrome: does a familial syndrome exist? Report of cases and review of literature

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ABSTRACT

Introduction: Neurogenic thoracic outlet syndrome (NTOS) is caused by compression of the brachial plexus. The clinical presentation of NTOS is characterized by symptoms of pain, paresthesia, numbness or muscle weakness in the neck, arm or hand. 

Methods: In this case report, five patients were diagnosed with NTOS. They all had a first degree relative with NTOS as well. 

Conclusions: These cases show familial predisposition in thoracic outlet syndrome. Could a form of familial TOS exist?

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1. Introduction

Three distinct types of thoracic outlet syndrome (TOS) exist: arterial thoracic outlet syndrome (ATOS), venous thoracic outlet syndrome (VTOS) and neurogenic thoracic outlet syndrome (NTOS) thoracic outlet syndrome, by compression of respectively artery, vein or plexus. Compression of the brachial plexus can be caused by fibromuscular ligaments, hypertrophic scalenus muscle, cervical ribs (CRs) or any other anatomic anomaly of the interscalene triangle, costoclavicular space or pectoralis minor space [1–4]. NTOS is the most prevalent type of TOS and accounts for 95% of all thoracic outlet syndrome patients [1,3–6].

The Catharina Hospital is a tertiary referral center for thoracic outlet syndrome in The Netherlands. Each year, up to 500 patients are referred to our TOS-Expert Center (TOS-EC). Diagnostic and therapeutic assessment is performed using the reporting standards published by Illig et al. [1]. If physiotherapy does not offer improvement in patients with a very likely diagnosis of NTOS, a trans-axillary thoracic outlet decompression (TOD) is offered to patients.

In 2017, five patients (1.6% of all patients) were referred to our TOS-EC by their physicians, because of symptoms similar to a family member diagnosed with NTOS. These patients were all diagnosed with NTOS – some of them received surgical treatment. In this paper, we try to look for possible explanations of a familial predisposition of TOS. Since anatomic variations are more prone to occur within the same family, the idea of TOS presenting in multiple family members is plausible. A review of literature is presented to assess possible etiological mechanisms of a familial predisposition in TOS. We also try to assess the possibility of the existence of a familial syndrome of TOS.

2. Cases

2.1. Case 1

A 21 year old female had complaints of pain in the neck radiating to the right arm and hand since 5 years (see Table 1). The complaints deteriorated 3 years ago with increased pain and muscle weakness. Breast reduction surgery did not improve complaints. Clinical examination with provocation tests pointed towards NTOS. Technical investigations showed no abnormalities. Physiotherapy was initiated without any improvement. A trans-axillary TOD was performed. Perioperative there was a squeeze of the T1 plexus branch caused by a
scarred middle scalene muscle which was taken down. At evaluation 12 months after surgery, her complaints had diminished. The complaints in her wrist and fingers were dissolved. Her mother had a 1st rib resection, allegedly for VTOS many years ago. We could not find any medical record about this procedure.

2.2. Case 2

A 41 year old male was referred to our department on advice of his sister. He had to seize his work as a bus driver due to pain in the left upper limb, 10 years before. However, recently, complaints worsened with numbness of the upper arm, paresthesia in the lower arm and muscle weakness leading to a more profound dysfunction of the hand. Work-up of complaints showed a clear diagnosis of NTOS. His complaints improved with intensified physiotherapy, and he started working again. His sister received a TOD for NTOS five years ago, in another hospital. Her complaints have improved, but are still present.

2.3. Case 3

A 33 year old female was diagnosed with recurrent NTOS on the right side. Four years earlier, a transaxillary TOD was performed with resection of a CR. Her complaints improved, however, chronic pain remained present. X-ray of the thoracic aperture showed quite a large remnant of the first rib (3 cm anteriorly and posteriorly).

A supraclavicular TOD was performed with resection of the whole remainder of the first rib, resection of the scalenus musculature and performing a thorough neurolysis from C5 to C8. Her complaints have completely disappeared. The patient’s mother and grand-mother both received TOD for NTOS with partial improvement of their complaints. There is no medical record of both family members.

2.4. Case 4

This 46 year old female has had complaints for more than 3 years and was sent to our center by her twin sister. She fell off an electrical bicycle in 2015. Since then, she has pain in her shoulders irradiating to the arm and digit 4 and 5. There is muscle weakness. Clinical examination with provocation tests pointed towards NTOS. X-ray of the thoracic outlet showed a prominent transverse part of C7. Three months of physiotherapy did not
diminish complaints. A trans-axillary TOD was performed. One year postoperative, complaints still persist. The complaints are identical to the preoperative scores. Case 5 is her twin sister.

2.5. Case 5
This 46 year old woman had complaints of pain, paresthesia and muscle weakness in the right shoulder and arm. Complaints started 6 years ago after falling from her bicycle onto the right shoulder. Clinical examination with provocation tests pointed towards NTOS. X-ray showed no abnormalities. Trans-axillary TOD was performed. We observed multiple scar strands overlaying C8-T1 which were resected. Initial results after surgery were hopeful; however, complaints have returned. Case 4 is her identical twin sister.

3. Discussion
These cases show a familial predisposition of thoracic outlet syndrome. A review of literature (Medline, EMBASE) could only identify two earlier case reports of familial predisposition of thoracic outlet syndrome [7,8]. One article reports on three patients in the same family (mother, daughter and aunt) diagnosed and treated for VTOS. They were all treated with a trans-axillary first rib resection with good results [8]. There is no description of possible anatomical variations of mechanism that caused three patients of the same family to end up with VTOS. Another case report describes the presence of CRs (described as apophysomegaly of the seventh cervical vertebra) in 13 family members of the same household (mother and 12 out of 13 children). All patients received physiotherapy and pain relief. Three children were additionally treated with TOD with resection of the CR [7].

The risk of anatomical anomalies causing pressure on the brachial plexus may possibly be more present in patients of the same family. If we look at our cases, we cannot clearly identify a familial anatomical anomaly causing stress to the brachial plexus. Case 1 shows a fibrosis of the MSM, probably caused by trauma, case 4 had a prominent C7 transverse process which is not seen in her identical twin sister. In literature, familial anatomical anomalies of the thoracic outlet have been researched, in particular the presence of CRs.

The presence of CRs and its influence on TOS has been researched thoroughly. There have been several case reports about CRs in multiple members of the same family. The skeletal system arises from the paraxial mesoderm [9]. The Hox genes are a family of transcription factors that regulate the embryogenesis of the body axis [10,11]. These genes regulate patterning of the axial skeleton in vertebrates and Hox gene mutants often display abnormalities of the vertebral column, including CRs [12]. The co-occurrence of rudimentary or even absent 12th ribs in 23.6% of cases with CR indicates that a homeotic shift occurred during embryogenesis [9].

Hox genes also play other roles. Furtado et al. reported a higher prevalence of CRs in stillborn fetuses (43.1%) compared to live-born ones (11.8%) who died in the first year [13]. This suggests that the presence of CR is markers of disadvantageous developmental events.

It is very difficult to estimate the actual risk of a CR in fetuses. There is limited information of the frequency of CR in fetuses and the natural developmental course in uterus. The chance of developing TOS, stillbirth, childhood cancer and genetic syndromes is far from clear [12].

The presence of CRs in the same families is therefore most likely based on differences in HOX genes. Fibromuscular bands are thought to be an anomaly of CR formation [14].

Developmental studies of the scalene triangle have shed light on some of the possible anatomical variations causing symptoms of TOS [14]. The scalene muscle mass is separated into anterior and middle scalene muscles by the traversing of the roots of the brachial plexus during embryogenesis. The presence of a scalenus minimus muscle represents one form of segmentation of the scalene muscle mass [14]. The location and width of the insertion of the scalene muscles onto the first rib have been described by Telford and Mottershead and shed light onto anatomical variations of the scalene musculature that may cause compression on the artery and plexus [15].

These cases show that a familial predisposition in thoracic outlet syndrome exists, even without the presence of obvious anatomical anomalies. We were not able to define the cause of familial predisposition by review of our clinical records. The lack of medical records of the family members is a flaw in this paper and we might have been able to identify similar anatomical anomalies of the thoracic outlet in family members if we had these reports at our disposal. Literature offers possible mechanisms of the origin of anatomical anomalies of the thoracic outlet, but no causal mechanism can be identified. Only anomalies in HOX genes...
have been identified to give rise to a great number of defects – including the interscalene triangle. In addition to these anatomical anomalies, no other etiology was identified. Should we be more aware that the posture of patients, the way muscles are used and other nurturing factors could also influence complaints of NTOS? Can we speak of ‘familial TOS’ or is this familial predisposition merely caused by chance?

We should consider the fact that we do not perform a consistent familial history investigation in our TOS patients. We were drawn to the familial connections because these families are all well known in our hospital.

Disclosure statement

There are no disclosures to report.

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