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CASES WITH A MESSAGE

Klippel–Feil syndrome misdiagnosed as spondyloarthropathy: case-based review

Stjepan Čota[1] · Iva Žagar[2,3] · Valentina Delimar[4] · Mislav Pap[3] · Doroteja Perić[2] · Porin Perić[2,3]

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Abstract

Spondyloarthropathy refers to any joint disease of the vertebral column, but the term is mainly used for a specific group of disorders called seronegative spondyloarthropathies (SpAs). The axial skeletal involvement, peripheral and extra-articular manifestations and an association with the major histocompatibility complex class I human leukocyte antigen-B27 (HLA B27) are commonly shared features of SpAs. Klippel–Feil syndrome (KFS) is a rare congenital disorder characterized by the fusion of one or more cervical vertebrae, accompanied by various skeletal and extra-skeletal anomalies. We report a case of an adult male patient with HLA B27 positivity presenting with chronic cervical spine pain accompanied by morning stiffness and periodic night pain, with radiologically confirmed ankylosis and fusion of several cervical segments. His medical history included urogenital abnormalities operated in childhood and mild mitral prolapse. Initially suspected diagnosis of an early axial form of SpA was rejected after thorough workup. Instead, the nature of vertebral defects along with the past medical history of urogenital and cardiac abnormalities pointed towards the diagnosis of KFS. HLA B27 presence can be a confounder in patients presenting with spinal pain and that is why the differential diagnosis of CSD-s and SpA can be challenging in some patients.

Keywords Klippel–Feil syndrome · Congenital spinal deformity · Spondyloarthropathy · HLA B27

Introduction

Spondyloarthropathies (SpAs) are a group of chronic inflammatory diseases, with a common clinical, genetic and pathophysiological characteristics [1]. Studies have shown that there is an unacceptably long period (5–10 years) between the onset of symptoms and the diagnosis [2]. The axial skeletal involvement, peripheral and extra-articular manifestations and an association with the major histocompatibility complex class I human leukocyte antigen-B27 (HLA B27) are commonly shared features [1, 3]. "Assessment of SpondyloArthritis International Society" (ASAS) has developed in 2009 new classification criteria for SpA [4, 5]. Two major groups were defined: axial SpA with dominant involvement of sacroiliac joints and/or spine and peripheral SpA with dominant peripheral manifestations, such as arthritis, enthesitis and dactylitis [1, 3–5]. The coexistence of SpA with congenital spinal deformities (CSD) is scarcely reported in the literature [6]. Klippel–Feil syndrome (KFS) is a congenital disorder characterized by the fusion of one or more cervical vertebrae [7, 8]. Patients with KFS also often have other skeletal anomalies and organ systems involved,

✉ Iva Žagar
iva.zagar@yahoo.com

Stjepan Čota
scota22@gmail.com

Valentina Delimar
valentina.delimar1@gmail.com

Mislav Pap
mislav.pap@gmail.com

Doroteja Perić
doroteja.peric@gmail.com

Porin Perić
porin.peric@gmail.com

1 Children's Hospital Zagreb, Klaićeva 16, 10000 Zagreb, Croatia

2 School of Medicine, University of Zagreb, Šalata 3, 10000 Zagreb, Croatia

3 Clinic for Rheumatic Diseases and Rehabilitation, University Hospital Centre Zagreb, Kišpatićeva 12, 10000 Zagreb, Croatia

4 Special Hospital for Medical Rehabilitation Krapinske Toplice, Gajeva 2, 49217 Krapinske Toplice, Croatia

such as auditory abnormalities, lung defects, congenital anomalies of the heart and the urinary tract [9–11].

Here we present a HLA B27-positive patient with KFS, to whom SpA was initially misdiagnosed.

Case report

A 44-year-old male patient, working as a computer technician, presented to our outpatient clinic with neck and bilateral shoulder pain that lasted for over a decade, accompanied by occasional left-arm paresthesia. He also complained of prolonged neck morning stiffness and periodic night pain. The pain was responsive to non-steroidal anti-inflammatory drugs (NSAIDs). His medical history included hypospadias and cryptorchidism documented in early childhood, with subsequent urethral reconstruction and orchiectomy. He developed mild mitral insufficiency as an adult. Family medical history was positive for chronic cervical spine pain, yet no member of his family was diagnosed with SpA. There was also no family history of CSD-s. Physical examination revealed cervical spine tenderness with a limited range of motion, especially lateroflexion and rotation movements. There was a loss of lumbar lordosis, with no tenderness over the lumbar spine or sacroiliac joints. Schober test was positive (4.5 cm) and chest expansion was normal (6.5 cm). The rest of the physical examination was within normal limits. HLA B27 testing was positive. Cervical spine radiograph showed alordosis, ankylosis with a fusion of the C2–C3, C4–C5, C5–C6 and calcifications of the anterior longitudinal ligament at the level of C5–C6. Cervical spine computed tomography (CT) confirmed the vertebral block of C2–C3, C4–C5 and C6–C7, with fusion anomaly of the posterior arch of C4, C5, C6 (Fig. 1). Considering suspected SpA, primarily an early axial form of AS, the patient was admitted for a more extensive hospital evaluation. Control radiograph of the cervical spine revealed no major changes (Fig. 2). Thoracic and lumbar spine radiographs were normal. Pelvis radiograph showed enthesopathy of the iliolumbar ligament and the pubic arches. Routine blood tests, inflammatory markers, rheumatoid factor, anti-cyclic citrullinated peptide, immunoelectrophoresis and bone densitometry were normal. Electrocardiogram revealed incomplete right bundle branch block, while echocardiography confirmed the aforementioned mild mitral insufficiency.

Considering the medical history of urogenital abnormalities, cardiac involvement with mitral prolapse and radiologically confirmed block fusion of the C2–C3, C4–C5 and C6–C7 vertebral body, while without certain elements that would support the definite diagnosis of an inflammatory rheumatic disease, the patient was diagnosed with KFS. He was consequently successfully treated with NSAIDs and intense physical therapy and remained symptom-free at 5-month follow-up. The timeline of interventions and outcomes regarding the presented case is shown in Fig. 3.

Search strategy

We searched MEDLINE/PubMed, Scopus and Web of Science databases for original articles, reviews, letters, comments and abstracts from scientific congresses published in English or at least with English abstract. There were no exclusion criteria regarding the date of publication to obtain the largest number of references, so we searched from database inception to January 2019. We used search terms including "Klippel–Feil syndrome", "congenital spinal deformity", "inflammatory joint disease", "spondyloarthropathy", "ankylosing spondylitis" and "HLA B27" and

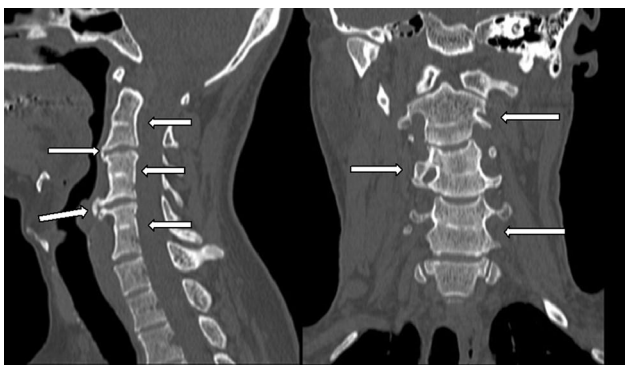

Fig. 1 Computed tomography showing a block of C2–C3, C4–C5 and C6–C7 vertebral body, with micro-discs and synostosis of the small joints of the vertebrae, fusion anomaly of the posterior arch of C4, C5, C6 and massive bridging osteophytes of the C3–C4 and C5–C6 segment, with the reduction of the retropharyngeal space

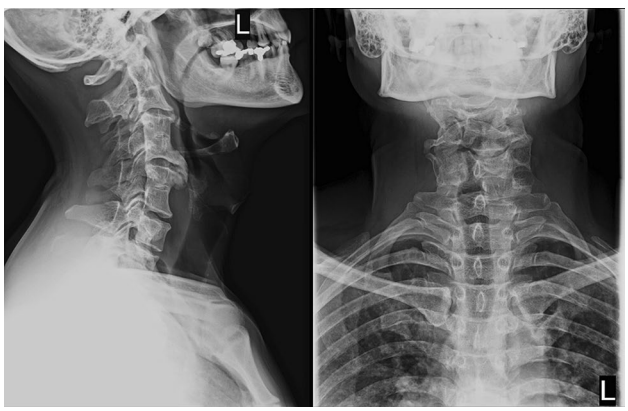

Fig. 2 Plain radiographs showing alordosis with congenital fusion of the C2–C3, C4–C5 and C6–C7 vertebral body. Massive bone appositions of the lower surface of C5 vertebrae as on the upper part of the C6 vertebrae with reduced length of the C2–C5 spinal processes with synostosis

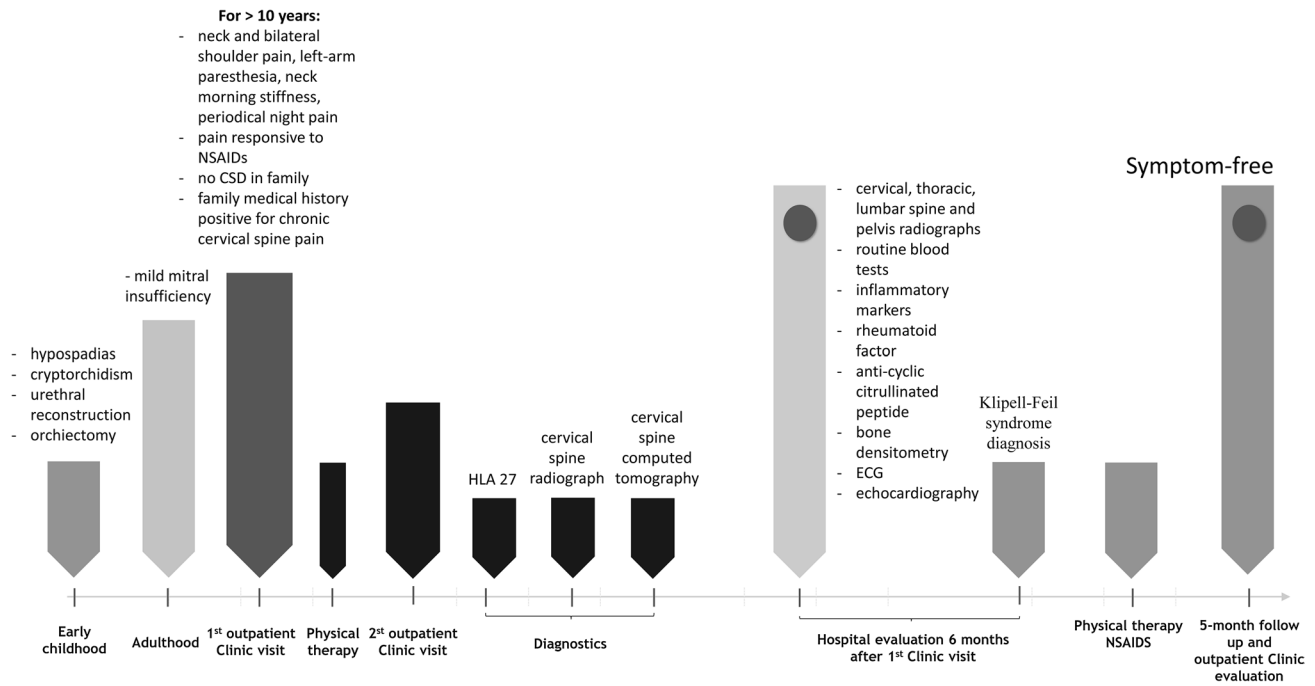

Fig. 3 The timeline of interventions and outcomes regarding the presented case

following Boolean operators "Klippel–Feil syndrome" OR "congenital spinal deformity" AND "spondyloarthropathy" OR "inflammatory joint disease" OR "ankylosing spondylitis". Titles, abstracts and full reports were screened by the first three authors (SČ, IŽ, VD) and the final search was verified by the last author (PP).

Discussion

The presented patient was HLA B27 positive with a history of chronic cervical spine pain accompanied by morning stiffness and good response to NSAIDs, with initial radiographs showing ankylosis and fusion block from C2 to C6, which laid suspicion for an early axial form of SpA. Today axial SpA term covers the entire spectrum of patients with radiographic sacroiliitis (radiographic axial SpA or ankylosing spondylitis, AS) and without radiographic sacroiliitis (non-radiographic axial SpA). There are still doubts as to whether radiographic and non-radiographic axial SpA should be considered as two distinct entities, or as a continuous disease spectrum. Currently, the prevailing view is that axial SpA includes one disease spectrum, in which the non-radiographic axial SpA may develop the radiographic changes over time [12]. HLA B27 positivity is considered as somewhat of a hallmark for the SpA spectrum, considering that its prevalence in the literature is similar between both forms: 86.4 vs 89.1%, 74.7 vs 82.2%, and 74.8 vs 81.5% for non-radiographic axial SpA and AS, respectively [3, 13–15]. However, the presence of HLA B27 can be misleading, especially in patients who experience symptoms as inflammatory pain, morning stiffness and good response to NSAIDs [1]. The differential diagnosis of CSD in these cases comes unlikely, especially when it comes to older patients. However, Qian et al. reported several cases of AS associated with CSD-s [6]. CSD-s and AS are different clinical entities with different underlying pathophysiological mechanisms. However, their clinical and radiological manifestations can sometimes overlap and lead to misdiagnosis [6]. To the best of our knowledge, there is only one case reporting a patient with KFS who was later also diagnosed with AS [16]. The fusion block of cervical vertebrae that our patient had can be present in both AS and KFS and distinguishing between them can be challenging, especially in sporadic cases of KFS in older patients [17]. Morning stiffness, itself not a typical feature of KFS, initially pointed us to the diagnosis of SpA. However, in the presented case, it can be understood as a symptom experienced due to the anatomical anomalies.

Over a century has passed since Maurice Klippel and Andre Feil described a patient with 'fused' cervical vertebrae. The presented patient was a 46-year-old tailor with a short neck, limited neck movement, and low posterior hairline, later typically known as the Klippel–Feil triad of symptoms [18, 19]. KFS results due to the failure of proper segmentation of vertebrae during embryonic development and is associated with derangements within the signaling pathways during paraxial mesoderm differentiation and somite development [9, 20]. Over the past few years, much

has been acknowledged about the inheritance of this disease and various dominant and recessive gene mutations were discovered [9]. Mutations in GDF6 (MIM#601147) and GDF3 (MIM#606522) have been associated with autosomal-dominant KFS [10, 21]. Mutation in the MEOX1 gene, located on chromosome 17q21.31 is associated with autosomal recessive KFS and according to Karaca et al., a homozygous frameshift mutation in RIPPLY2 is responsible for a new type of autosomal recessive KFS [22, 23]. The incidence of KFS is reported to be 1 in 40,000 newborns worldwide, with a slight female predominance of 3:2 [8, 24–26]. The latest cross-sectional study of Gruber et al. revealed a prevalence of KFS to be 0.0058% (1 in 172) [27].

This syndrome may be associated with many skeletal and extra-skeletal anomalies. The most common skeletal abnormality is cervical scoliosis, with a reported prevalence of 60–70% in different studies [25, 28]. The second most common skeletal abnormality is Sprengel deformity, a congenitally high scapula which was first described by Eulenberg in 1963, but the theory of its existence was proposed almost 30 years later by Otto Sprengel [29–31]. The Cavendish classification system based on the deformity was proposed in 1972 and consists of four grades [32]. Grade 1 describes a very mild deformity, unnoticeable when the patient is dressed, grade 2 describes a mild deformity visible as a lump in the web of the neck when the patient is dressed, grade 3 describes a moderate deformity visible with the shoulder joint elevated 2–5 cm and grade 4 describes a severe deformity with shoulder joint elevation of more than 5 cm, or evidence of the superior angle of the scapula near the occiput, with or without webbing. The first two grades are treated conservatively and higher grades require surgery [9, 32]. Other reported skeletal abnormalities include cervical ribs, spina bifida, limb anomalies, hemivertebrae and butterfly vertebrae [9, 22, 33] Out of the craniofacial anomalies that accompany KFS, the most common are facial asymmetry, cleft palate and bifid uvula, with an incidence of 13–15%, respectively [33, 34].

The extra-skeletal anomalies associated with KFS include genitourinary anomalies (renal agenesis, anomalies of the kidneys, urinary bladder and urethra, absence of uterus), cardiovascular anomalies (aortic and mitral insufficiency, mitral valve prolapse, atrial septal defect, coarctation of aorta), respiratory anomalies (supernumerary pulmonary lobes, sleep apnea), otological anomalies (external ear malformations, Eustachian tube dysfunction, sensorineural, conductive or mixed hearing loss, deafness), ophthalmological anomalies (strabismus, nystagmus, choroid retinal atrophy) and central nervous system anomalies (seizures, mirror movements, hydrocephaly, paresthesia, meningocele, syringomyelia, hemiplegia or tetraplegia, intracranial neoplasms and other) [17, 33–40]. There are reports that relate KFS to different other anomalies, such as variations in the course and origin of vertebral arteries, Arnold–Chiari malformation, autoimmune thyroiditis or spinal neurenteric cyst [7, 41, 42].

To date, multiple classification systems for KFS have been proposed. In 1919, Feil defined three morphological subtypes: Type I with multiple fused cervical and upper thoracic vertebrae, Type II with the fusion of only one or two intervertebral cervical spaces and Type III with both cervical and lower thoracic or lumbar fusion [19]. Clarke et al. have developed a new classification system in 1998 based on both fusion type and inheritance type: Type I with C1 fusion (O–C1 and/or C1–C2) and recessive inheritance, Type II with most anterior C2–C3 fusion and dominant inheritance, Type III with isolated cervical fusions and recessive inheritance or reduced penetrance and Type IV with cervical vertebrae fusion, possibly X-linked, which includes cases of Wildervank and Duane syndrome [43]. The latest, and currently most used classification, was proposed by Samartzis et al. in 2006 and is radiologically determined: Type I with a single, congenitally fused cervical segment, Type II with multiple, noncontiguous, congenitally fused segments and Type III with multiple, contiguous, congenitally fused segments [44].

The presented patient had a fusion from C2 to C6 and would, therefore, be classified according to Samartzis et al. as Type III KFS. Even though Type III KFS patients were reported to have an increased risk of neurological symptoms and complications that could require surgical intervention, that was not the case in our patient [44]. It is known that in milder forms of KFS spine-related neurological symptoms, such as paresthesia in our patient, can manifest in adulthood and warrant only careful follow-up in case of radiculopathy or myelopathy development [44, 45]. The presented patient had none of the most common described KFS-associated skeletal abnormalities. Out of the extra-skeletal abnormalities, he had urogenital and cardiac system involvement. Other than surgical treatment for specific skeletal and extra-skeletal abnormalities when needed, intense physical therapy was proven in KFS patients to give satisfactory results, decrease pain and maintain optimal functional status [44].

Literature shows that KFS has a highly variable phenotype expression, with actually less than 50% of patients having all three signs of the classic KFS triad [8]. As clinicians, although it is rare, we should bear in mind the possibility of KFS, as well as other CSD-s in the differential diagnosis when dealing with patients presenting with chronic spine pain, because early diagnosis and treatment are essential to prevent possible irreversible neurological damage in these patients. To the best of our knowledge, SpAs have not yet been connected with the spectrum of associated diseases when it comes to KFS. The coincidence of HLA B27 and KFS in the presented patient may only be just a coincidence, or it may possibly be a new piece to add to the pathophysiology of the KFS puzzle. The differential diagnosis of CSD-s and SpA can, therefore, be challenging in some patients.

Author contributions SČ: case design, first draft, search of the review of literature, timeline, and approval of the final version. IŽ: case design, first draft, search of the review of literature, and approval of the final version. VD: case design, first draft, search of the review of literature, timeline, and approval of the final version. MP: case design, first draft, and approval of the final version. DP: case design, first draft, and approval of the final version. PP: case design, first draft, and approval of the final version. All authors approve the final version of the manuscript and agree to be accountable for all aspects of the work.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Informed consent Informed consent was obtained from the participant included in the study.

References

1. Proft F, Poddubnyy D (2018) Ankylosing spondylitis and axial spondyloarthritis: recent insights and impact of new classification criteria. Ther Adv Musculoskelet Dis 10(56):129-139. https://doi.org/10.1177/59720X18773726
2. Feldtkeller E, Khan M, Van Der Heijde D, Van Der Linden S, Braun, J (2003) Age at disease onset and diagnosis delay in HLA-B27 negative vs. positive patients with ankylosing spondylitis. Rheumatol Int. 23(2):61–66. https://doi.org/10.1007/s00296-002-0237-4
3. Baraliakos X, Braun J (2015) Non-radiographic axial spondyloarthritis and ankylosing spondylitis: what are the similarities and differences? RMD Open 1(Suppl 1):e000053. https://doi.org/10.1136/rmdopen-2015-000053
4. Rudwaleit M, Landewé R, Van der Heijde D, Listing J, Brandt J, Braun JV et al (2009) The Development of Assessment of SpondyloArthritis International Society classification criteria for axial spondyloarthritis (part I): classification of paper patients by expert opinion including uncertainty appraisal. Ann Rheum Dis. 68(6):770–776. https://doi.org/10.1136/ard.2009.108217
5. Rudwaleit M, Van Der Heijde D, Landewé R, Listing J, Akkoc N, Brandt J et al (2009) The Development of Assessment of SpondyloArthritis International Society classification criteria for axial spondyloarthritis (part II): validation and final selection. Ann Rheum Dis 68(6):777–783. https://doi.org/10.1136/ard.2009.108233
6. Qian BP, Qiu Y, Wang B, Zhu ZZ, Wang WJ, Ma WW (2010) Unusual association of ankylosing spondylitis with congenital spinal deformity. Spine 35(25):E1512–E1515. https://doi.org/10.1097/BRS.0b013e3181f3cf63
7. Rizvi A, Iwanaga J, Oskouian RJ, Loukas M, Tubbs RS (2018) The course of the V2 segment of the vertebral arteries in Klippel–Feil syndrome: a case report. Cureus 10(7):e3038. https://doi.org/10.7759/cureus.3038
8. Tracy MR, Dormans JP, Kusumi K (2004) Klippel–Feil syndrome: clinical features and current understanding of etiology. Clin Orthop Relat Res. 424:183–190. https://doi.org/10.1097/01.blo.0000130267.49895.20
9. Stelzer JW, Flores MA, Mohammad W, Esplin N, Mayl JJ, Wasyliw C (2018) Klippel–Feil syndrome with sprengel deformity and extensive upper extremity deformity: a case report and literature review. Case Rep Orthop 2018:5. https://doi.org/10.1155/2018/5796730
10. Tassabehji M, Fang ZM, Hilton EN, McGaughran J, Zhao Z, de Bock CE, Manson FD et al (2008) Mutations in GDF6 are associated with vertebral segmentation defects in Klippel–Feil syndrome. Hum Mutat 29(8):1017–1027. https://doi.org/10.1002/humu.20741
11. Hensinger RN, Lang JE, Macewen GD (1974) Klippel–Feil syndrome: a constellation of associated anomalies. J Bone Jt Surg Am 56(6):1246–1253
12. Sieper J, van der Heijde D (2013) Nonradiographic axial spondyloarthritis: new definition of an old disease? Arthritis Rheum 65(3):543–551. https://doi.org/10.1002/art.37803
13. Weisman MH, Witter JP, Reveille JD (2012) The prevalence of inflammatory back pain: population-based estimates from the US National Health and Nutrition Examination Survey, 2009–10. Ann Rheum Dis Annrheumdis 72:369–373. https://doi.org/10.1136/annrheumdis-2012-201403
14. Reveille JD, Hirsch R, Dillon CF, Carroll MD (2009) Weisman MH (2012) The prevalence of HLA–B27 in the US: data from the US National Health and Nutrition Examination Survey. Arthritis Rheum 64(5):1407–1411. https://doi.org/10.1002/art.33503
15. Braun A, Saracbasi E, Grifka J, Schnitker J, Braun J (2011) Identifying patients with axial spondyloarthritis in primary care: how useful are items indicative of inflammatory back pain? Ann Rheum Dis 70(10):1782–1787. https://doi.org/10.1136/ard.2011.151167
16. Solis Cartas U, Prada Hernández DM, Gómez JAM, de Armas Hernandez A, Garcia DMA (2015) Espondilitis Anquilosante y Síndrome de Klippel–Feil Una asociación infrecuente. Revista Cubana de Reumatología 17(S1):206–210
17. Clarke RA, Singh S, McKenzie H, Kearsley JH, Yip MY (1995) Familial Klippel–Feil syndrome and paracentric inversion inv (8)(q22. 2q23. 3). Am J Hum Genet. 57(6), 1364. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1801422/pdf/ajhg00038-0111.pdf
18. Klippel M (1912) Un cas d'absence des vertebres cervicales. Avec cage thoracique remontant jusqu'a la base du crane (cage thoracique cervicale). Nouv Iconog Salpetriere 25:223–250
19. Feil A (1919) L'absence et la diminuation des vertebres cervicales (etude cliniqueet pathogenique); le syndrome dereduction numerique cervicales. Théses de paris.
20. Kaplan KM, Spivak JM, Bendo JA (2005) Embryology of the spine and associated congenital abnormalities. Spine J 5(5):564–576. https://doi.org/10.1016/j.spinee.2004.10.044
21. Ye M, Berry-Wynne KM, Asai-Coakwell M, Sundaresan P, Footz T, French CR, Drummond G et al (2009) Mutation of the bone morphogenetic protein GDF3 causes ocular and skeletal anomalies. Hum Mol Genet 19(2):287–298. https://doi.org/10.1093/hmg/ddp496
22. Karaca E, Yuregir OO, Bozdogan ST, Aslan H, Pehlivan D, Jhangiani SN, Erdin S et al (2015) Rare variants in the notch signaling pathway describe a novel type of autosomal recessive Klippel–Feil syndrome. Am J Med Genet A 167(11):2795–2799. https://doi.org/10.1002/ajmg.a.37263
23. Bayrakli F, Guclu B, Yakicier C, Balaban H, Kartal U, Erguner B et al (2013) Mutation in MEOX1 gene causes a recessive Klippel–Feil syndrome subtype. BMC Genet 14(1):95. https://doi.org/10.1186/1471-2156-14-95
24. Hensinger RN, MacEwen GD (1982) Congenital anomalies of the spine. The Spine. Philadelphia: WB Saunders 1982:188–315
25. Thomsen MN, Schneider U, Weber M, Johannisson R, Niethard FU (1997) Scoliosis and congenital anomalies associated with Klippel–Feil syndrome types I-III. Spine 22(4):396–401. https://journals.lww.com/spinejournal/Abstract/1997/02150/Scoliosis_and_Congenital_Anomalies__Associated.8.aspx. Accessed 10 Dec 2018

26. Warner WC (1998) Pediatric cervical spine. In: Canale ST (ed) Campbell's operative orthopaedics, 9th edn. Mosby, St Louis, pp 2815–2847
27. Gruber J, Saleh A, Bakhsh W, Rubery PT, Mesfin A (2018) The Prevalence of Klippel–Feil syndrome: a computed tomography–based analysis of 2917 patients. Spine Deformity 6(4):448–453. https://doi.org/10.1016/j.jspd.2017.12.002
28. Pizzutillo PD, Woods M, Nicholson L, MacEwen GD (1994) Risk factors in Klippel–Feil syndrome. Spine 19(18):2110–2116
29. Eulenberg M (1863) Casuistische mittelheilungen aus dem gembeite der orthopadie. Arch Klin Chir 4:301–311
30. Kolliker T (1891) Mittheilungen aus der chirurgischen casuistic und kleinere mittheilungen. Bemerkungen zum aufsatze von Dr Sprengel Die angeborene verschiebung des schulterblattes nach oben. Arch Klin Chir 42:925
31. Sprengel O (1891) Die angeborene Verschiebung des Schulterblattes nach oben. Arch Klin Chir 42:545
32. Cavendish ME (1972) Congenital elevation of the scapula. J Bone Jt Surg Br 54(3):395–408
33. Naikmasur VG, Sattur AP, Kirty RN, Thakur AR (2011) Type III Klippel–Feil syndrome: case report and review of associated craniofacial anomalies. Odontology 99(2):197
34. Stupar NV, Pavlov-Dolijanovic S, Hatib N, Banko B, Djukic M, Jakoba NN (2016) Multiple major and minor anomalies associated with Klippel–Feil syndrome: a case report. Arch Rheumatol. 31(1):82. https://doi.org/10.5606/ArchRheumatol.2016.5714
35. Yildirim N, Arslanoğlu A, Mahiroğullari M, Şahan M, Özkan H (2008) Klippel–Feil syndrome and associated ear anomalies. Am J Otolaryngol 29(5):319–325. https://doi.org/10.1016/j.amjoto.2007.09.009
36. Zhang YK, Geng SM, Liu PN, Lv G (2016) Association of craniovertebral junction anomalies, Klippel–Feil syndrome, ruptured dermoid cyst and mirror movement in one patient: a unique case and literature review. Turk Neurosurg 26(1):153–165. https://doi.org/10.5137/1019-5149.JTN.12145-14.2
37. Sharma D, Sharma CM (2014) A sporadic case of Klippel–Feil syndrome type II. J Clin Neonatol. 3(1):57–58. https://doi.org/10.4103/2249-4847.128748
38. Moore WB, Matthews TJ, Rabinowitz R (1975) Genitourinary anomalies associated with Klippel–Feil syndrome. J Bone Jt Surg Am 57(3):355–357
39. Brokinkel B, Wiebe K, Hesselmann V, Filler TJ, Ewelt C, Müller-Hofstede C et al (2013) Surgical treatment in a patient with Klippel–Feil syndrome and anterior cervical meningomyelocele: a case report and review of literature. Eur Spine J 22(3):517–520. https://doi.org/10.1007/s00586-013-2769-6
40. Adorno A, Alafaci C, Sanfilippo F, Cafarella D, Scordino M, Granata F et al (2015) Malignant teratoma in Klippel–Feil syndrome: a case report and review of the literature. J Med Case Rep 9(1):229. https://doi.org/10.1186/s13256-015-0700-y
41. Guidoni E, Lotti F, Geronzi U, Sorrentino LA, Grosso S, Municchi G (2018) Autoimmune thyroiditis in Klippel–Feil syndrome with Arnold Chiari and syringomyelia. Thyroid 381, P2. https://abstracts.eurospe.org/hrp/0089/eposters/hrp0089P2-P381_eposter.pdf. Accessed 15 Dec 2018
42. Can A, Rubio EJDS, Jasperse B, Verdijk RM, Harhangi BS (2015) Spinal neurenteric cyst in association with Klippel–Feil syndrome: case report and literature review. World Neurosurg. 84(2):592–e9. https://doi.org/10.1016/j.wneu.2015.03.015
43. Clarke RA, Catalan G, Diwan AD, Kearsley JH (1998) Heterogeneity in Klippel–Feil syndrome: a new classification. Pediatr Radiol 28(12):967–974
44. Samartzis D, Herman J, Lubicky JP, Shen FH (2006) Classification of congenitally fused cervical patterns in Klippel–Feil patients: epidemiology and role in the development of cervical spine-related symptoms. Spine 31(21):E798–E804. https://doi.org/10.1097/01.brs.0000239222.36505.46
45. Guille JT, Miller A, Bowen JR, Forlin E, Caro PA (1995) The natural history of Klippel–Feil syndrome: clinical, roentgenographic, and magnetic resonance imaging findings at adulthood. J Pediatr Orthop 15(5):617–626