Ponticulus Posticus is a Frequent Radiographic Finding on Lateral Cephalograms in Nevoid Basal Cell Carcinoma Syndrome (Gorlin–Goltz Syndrome)

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Abstract. *Nevoid basal cell carcinoma syndrome (NBCCS) is a predisposition to a rare tumor type with a variable phenotype. Besides tumors, skeletal alterations, such as bifid ribs or frontal bossing constitute the phenotype. Recently, a variant of the first cervical vertebra, the ponticulus posticus, was reported to occur in 50% of patients with NBCCS as revealed by analysis of lateral cephalograms. Materials and Methods: Lateral cephalograms of eight patients with NBCCS were studied for the presence of ponticulus posticus. Results: The ponticulus posticus was present in all patients. In one case, a series of cephalograms performed during a period of 20 years allowed the slow and continuous recording of a ponticulus posticus formation. Discussion: Besides the predisposition to developing neoplasms, NBCCS also affects bone development. Some diagnostic criteria for NBCCS rely on certain osseous transformations either in hard tissues, e.g. keratocystic odontogenic tumor in jaws, or in soft tissues, e.g. calcification of the falx cerebri. Furthermore, the physiognomy can be affected by skeletal alterations, e.g. frontal bossing or hypertelorism. Given this wide spectrum of osseous involvement in NBCCS, the high prevalence rate of ponticulus posticus should be added to the relevant diagnostic findings of the skull and vertebral column. However, the onset of ponticulus posticus formation in the life of such patients is unclear and thus the relevance of this finding in early diagnosis of NBCCS remains to be elucidated.*

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Key Words: Nevoid basal cell carcinoma syndrome, Gorlin–Goltz syndrome, *ponticulus posticus*, arcuate foramen, atlanto-occipital ligament, calcification, lateral cephalogram, phacomatosis.

Nevoid basal cell carcinoma syndrome (NBCCS), also known as Gorlin–Goltz syndrome (1-3), is a predisposition rare tumor syndrome (4-6). Disease prevalence is estimated at about one in 31,000 individuals (7) and birth incidence one in about 15,000 (7). Other researchers calculate the prevalence of NBCCS to be in the range of 1:57,000 to 1:256,000 (6). About every fourth patient with NBCCS is estimated to have a *de novo* mutation of PTCH gene on chromosome 9q (7). The entity is defined by a series of clinical findings, including skeletal abnormalities that can be visualized on radiographs (6, 8). In the skull, calcification of the *falx cerebri* and early onset of cystic jaw tumours are the most prominent radiographic findings (8-11). The phenotype is highly variable and findings diagnostic for confirming the suspicion of a syndrome are sometimes difficult to collect (6). Early diagnosis of NBCCS is of prognostic relevance and leads therapeutic decisions, *e.g.* screening for tumors known to be associated with the syndrome (6). Molecular genetics allow for identification of relevant mutations associated with NBCCS (4), but are yet far from routine application (12). On the other hand, clinical diagnosis is easier and often more rapidly performed and is also an economical alternative to molecular genetic analysis (13, 14).

Recently, the calcification of the atlanto-occipital ligament was proposed to be an additional radiological finding in NBCCS (15). The alternative term for this calcified structure is *posterior ponticulus* or *ponticulus posticus* (15). The *ponticulus posticus* was found to be present in nine out of 18 lateral cephalograms obtained of patients with NBCC (15). With respect to their study collective, these authors reported *ponticulus posticus* to be a more frequent than finding *falx cerebri* calcification (15), a major diagnostic criterion for NBCCS (Table I). Given the frequent requirement of having skull radiographs to assess radiological findings diagnostic of NBCCS and for planning surgery (6), *e.g.* for keratocystic odontogenic tumours (KOT) of the jaws, a further finding that is additionally visible on routinely performed skull radiographs would be of great value to substantiate the diagnosis.

Table I. *Diagnostic criteria in nevoid basal cell carcinoma syndrome (NBCCS) (6).*

Major criteria	Minor criteria
Multiple (>2) basal cell carcinomas or one prior to age 20 years	Macrocephaly determined after adjustment for height
Keratocystic odontogenic tumour of the jaws proven by histopathology	Congenital malformation: cleft lip or palate, frontal bossing, 'coarse face', moderate or severe hypertelorism
Palmar or plantar pits (3 or more)	Other skeletal abnormalities: sprengel deformity, marked *pectus* deformity, marked syndactyly of the digits
Bilamellar calcification of the *falx cerebri*	Radiological abnormalities: bridging of the *sella turcica*, vertebral anomalies such as hemivertebrae, fusion or elongation of the vertebral bodies, modeling defects of the hands and feet, or flame-shaped lucencies of the hands or feet
Bifid, fused or markedly splayed ribs	Ovarian fibroma
First degree relatives with NBCCS	Medulloblastoma

The detailed anatomical description of cervical vertebrae and their variants (16) is of particular importance in preparations for surgical procedures of this region, *e.g.* to gain access to vertebral artery diseases (17) and in vertebral trauma (18), but also in the diagnosis of skeletal dysplasias (19), and in the field of anthropology (20, 21). The *ponticulus posticus* is an anatomical variation of the dorsal part of the atlas vertebra and is closely associated with the course of the vertebral artery (22). The bony spicules cover the groove of the vertebral artery and may arise from either the superior articular facet or the posterior arch of the atlas, or from both sites. The spicules may approximate each other up to complete fusion. Ponticulus posticus is not rare: a large computed tomographic study on the cervical vertebral column revealed a prevalence of *ponticulus posticus* of 15.6% (23), but others found lower (16) and higher (17) prevalence rates. Hong *et al.* also described *ponticulus posticus* as a slightly more frequent phenomenon in males, but this finding was not confirmed by other studies (23). The classification of the *ponticulus posticus* is based on the origin and number of spicules and the eventual fusion of two processes into a complete bridging (23), forming the 'arcuate foramen' as a result of fusion, a term synonymously used for *ponticulus posticus* (15). Bilaterally converging spicules or complete bridging accounted for more than 75% of *posterior ponticuli* (23), but it is likely that both the prevalence of *ponticulus posticus* and the frequency of different ossification types relies on the research method applied in the particular study (24, 25).The classification of *ponticulus posticus* works on the basis of analyzing lateral views of the cervical vertebral column (23), one preferential projection in the fields of anthropometry and craniofacial diagnosis (26).

The aim of this study was to determine the frequency of *ponticulus posticus* on lateral radiographs in patients with NBCCS in order to reassess the recent report on the high prevelance of this finding.

Patients and Methods

The basis for this study were skull teleradiographs of patients with established diagnosis of NBCCS (10). All patients were investigated for associated lesions following pathologically-confirmed diagnosis of KOT or basal cell carcinoma of the skin. All patients or their relatives gave informed consent for radiographic investigation and analysis. The files of patients with NBCCS were searched for lateral cephalograms. Lateral cephalograms of eight such patients (female/male=4/4) were evaluable for analysis. In six patients, more than one lateral cephalogram was performed during the treatment period. Technical characteristics of lateral cephalometry are described elsewhere in detail (27). A *ponticulus posticus* was defined as a spicule arising from the superior articular facet or the posterior arch of the atlas, or from both sites. In cases of bilateral spicules, bridging could be complete or incomplete. In all eight cases, anterior-posterior cephalograms were also available for analysis.

Results

All eight patients exhibited *posterior ponticuli* and five also had a *sella* bridge. In one case, the development of the *ponticulus posticus* was demonstrated on consecutive radiographs (Figure 1A and B). In one further case, the ossification appeared to develop in the middle of the anticipated calcified arch (Figure 1C). Ponticulus posticus was complete in seven of eight cases (Figure 1D and E). Radiographic findings are summarized in Table II.

Discussion

The present study reveals a high prevalence of *ponticulus posticus* in patients with NBCCS and supports the conclusion of Leonardi *et al.* that this finding should be included in the radiological diagnostics for patients with suspected NBCCS (15). The frequency of *ponticulus posticus* is 100% in this collective and thereby much higher than in

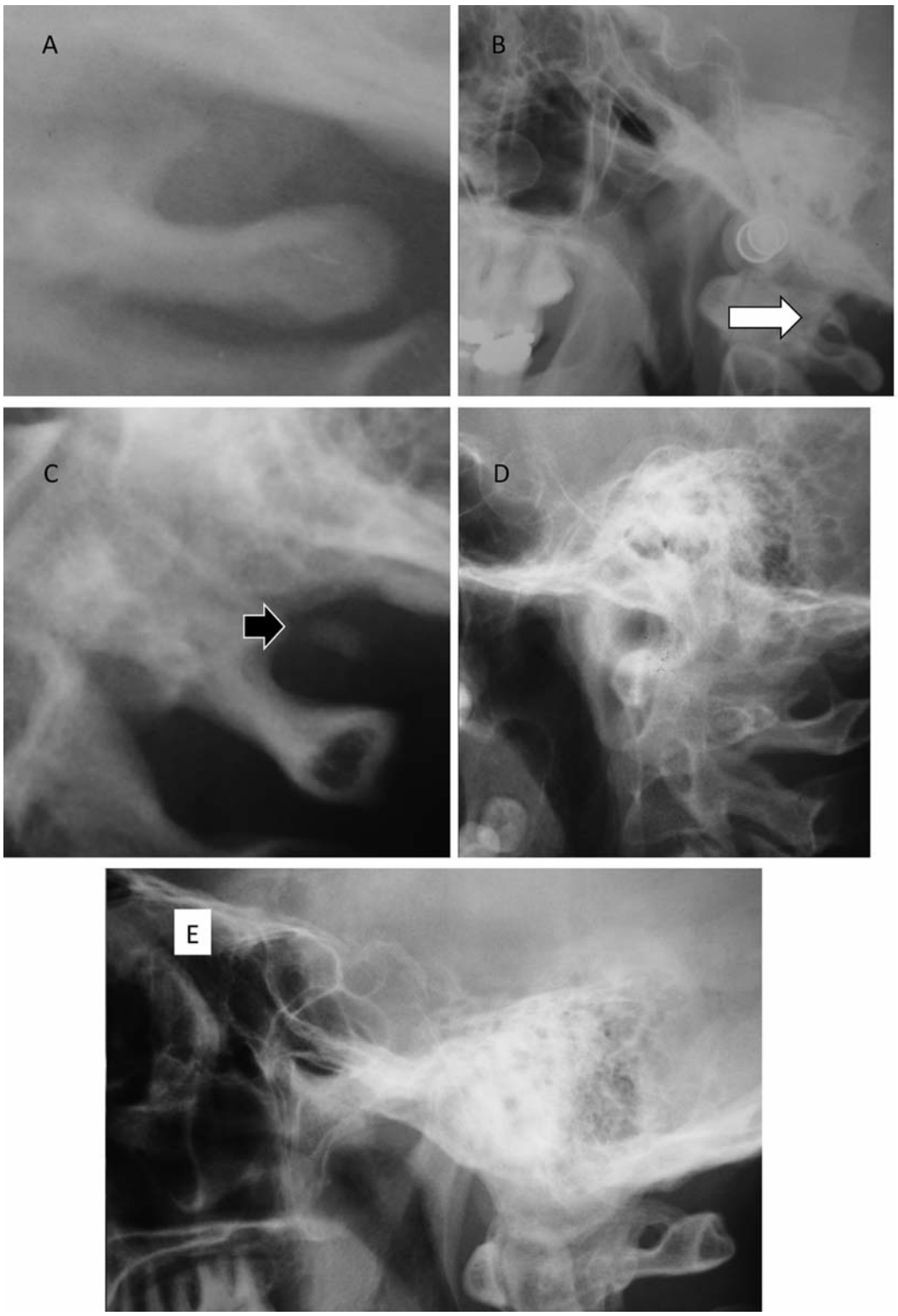

Figure 1. *Cropped images of lateral cephalograms of patients with nevoid basal cell carcinoma syndrome. A: Atlas region of a three-year old girl with initial superior spicule but no signs of bridging. B: The same patient at the age of 20 years with completely developed ponticulus posticus (arrow). Note associated pathology of the maxillary sinus. C: Image from a 12-year-old girl with radiopaque arch-like structure probably arising from the upper region of the atlas (arrow). D: Ponticulus posticus in a 12-year-old boy. Note osseous pathology of the mandible. E: Marked bridging in a 27-year-old male. Parts C-D are mirrored in order to align the facial aspect of all figures to the left side.*

Table II. *Ponticulus posticus, sella bridge and falx calcification on skull teleradiographs of patients with nevoid basal cell carcinoma syndrome (NBCCS). All patients had history of surgery for keratocystic odontogenivc tumors of the jaw. Age refers to the year of first radiograph.*

Patient no.	Age (years)	Gender	Ponticulus posticus	Sella bridge	Calcified falx cerebri	Keratocystic odontogenic tumour
1	29	F	×	×	O	×
2	12	M	×	O	×	×
3	45	M	×	O	×	×
4	12	F	×	×	×	×
5	25	M	×	×	×	×
6	63	M	×	×	×	×
7	3	F	×[1]	O	×	×
8	69	F	×	×	×	×

[1]*Ponticulus posticus* was visible on lateral cephalogram taken in adulthood.

the study of Leonardi *et al*. (15). However, the sample size of the present study is too small to draw far-reaching conclusions, such as inclusion of *ponticulus posticus* as a major diagnostic criterion. The first-time description of (skeletal) findings associated with a syndrome should include the discussion of coincidental discovery prior to their allocation to the diagnostic criteria to a given entity (28, 29).

Sella bridging was diagnosed in five out of eight patients and was less frequent than both calcification of the *falx cerebri* and *ponticulus posticus*. Sella bridging is a minor criteria for NBCCS diagnosis (Table II). This relationship between the frequencies of *sella* bridging and *ponticulus posticus* is in contrast to the initial report: *sella* bridging was slightly more frequent than *ponticulus posticus* formation in the first study (15). However, the numbers of investigated cases are currently too small to draw general conclusions.

Skeletal alterations are diagnostic in NBCCS. However, *ponticulus posticus* is a well-known variant of the first cervical vertebra (30-32). Furthermore, *ponticulus posticus* appears to be a more frequent finding than currently presumed (32). One recent study reported a 25% prevalence of *ponticulus posticus* of cone beam computed tomograms (CBCT) of the cervical vertebral column in a large collective (32). This large study group was based on CBCTs of children and adolescents undergoing orthodontic treatment (32). Even children of 10 years of age or younger had a 20% prevalence for *ponticulus posticus* formation (32). However, this relative frequency of an anatomical variant does not reach the value of *ponticulus posticus* identified in the present study and the first report on this item (15). It is likely that the prevalence rate of *ponticulus posticus* will be influenced by the applied imaging technique (24, 25, 32). Indeed, the prevalence of *ponticulus posticus* may be underestimated on plain radiographs (32). Nevertheless, as a result of these data, it has to be kept in mind that *ponticulus posticus* may be present in a high percentage of individuals with no apparent pathology. Furthermore, a cross-sectional study will most likely not gather all *ponticulus posticus* developing in humans. Interestingly, in one case of this series, lateral radiographs were taken over a period of 20 years, starting in early childhood up to the third decade of life. Here the *posticulus posticus* development could be tracked from discrete formation of the spicule until complete bridge formation (Figure 1). This finding recalls the well-known age-dependency of diagnostic findings in the case of NBCCS, *e.g.* the onset of KOT (10). Indeed, in a recent study, *falx* calcification was present in 37% of individuals with NBCCS younger than 20 years of age and 79% of those older than 20 years (14). *Falx* calcification in unaffected individuals is recognized but its frequency is low (33). In view of these age-dependent restrictions of expecting key radiological features of NBCCS on plain radiographs, the age composition of this study group has to be considered. In this study, the age ranged from 3 to 69 years at the time of first lateral cephalogram. This study cannot clarify the prevalence of *posticulus posticus* in the young patient possibly affected by NBCCS. Thus, the impact of this recently recognized skeletal finding on lateral skull radiographs in the early diagnosis of NBCCS remains to be elucidated, in contrast to early in life for development of KOT (10). Skull radiological diagnostics in patients suspected of being affected by NBCCS should consider the craniocervical junction.

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Received July 23, 2014
Revised September 8, 2014
Accepted September 15, 2014