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內文：

Introduction

- Nevoid basal cell carcinoma syndrome (Gorlin-Goltz syndrome)
- infrequent multisystemic disease
  - Developmental anomalies
  - predisposition to a range of neoplasms
- ancient Egyptian skeletons
- The first reported literature in 1894, highlighting the presence of multiple basocellular carcinomas (BCCs).
- Gorlin and Goltz in 1960 first established a classical triad of characteristics of NBCCS
  - multiple BCCs
  - multiple keratocysts of jaws
  - bifid ribs
- The odontogenic keratocysts associated with NBCCS are usually multiple and of the parakeratinized variety
- 2005 odontogenic keratocyst (OKC)
  - Parakeratinized (Keratocystic odontogenic tumor)(KCOT)
  - Orthokeratinized (orthokeratinized odontogenic cyst)
- Other clinical manifestations
  - hyperkeratosis of the palms and toes,
  - Skeletal abnormalities,
  - intracranial ectopic calcifications,
  - facial dysmorphism
  - Neurological, ophthalmic, sexual,cardiac, and auditory system anomalies have also been reported
- Prevalence 1 ： 57,000~ 1 ~256,000,
- Male-to-female ratio of 1:1
- The diagnostic criteria of NBCCSIs at least 2 major or 1 major and 2minor criteria are present

Table I. Diagnostic criteria in NBCCS[15]

Major criteria	Multiple (>2) BCCs or 1 younger than 20 years
	Odontogenic keratocysts of the jaws proven by histopathology
	Three or more palmar or plantar pits
	Bilamellar calcification of the falx cerebri
	Bifid, fused or markedly splayed ribs
	First-degree relatives with NBCCs
Minor criteria	Macrocephaly after adjustment for height
	Congenital malformation: cleft lip or palate, frontal bossing, "coarse face," moderate or severe hypertelorism
	Other skeletal abnormalities: Sprengel deformity, marked pectus deformity, marked syndactyly of the digits
	Radiological abnormalities: bridging of sella turcica, vertebral anomalies, such as hemivertebrae, fusion or elongation of the vertebral bodies, modeling defecta of the hands and feet, or flame-shaped lucencies of the hands or feet
	Ovarian fibroma
	Medulloblastoma

NBCCS, nevoid basal cell carcinoma syndrome.

- **NBCCS is inherited as autosomal dominant**
- **The mutations in tumor suppressor gene called Patched (PTCH 1),**
- **located in the 9q22.3–q31 chromosome,**
- **2-hit hypothesis**
- **Cancer require 2 mutagenit hits**
- **Various physical abnormalities need only one hit**
- **6 case in this article**
- **17 cases reported in Indian**
- **purpose is to present characteristic clinical or radiological finding that is typically seen in Indian**
- **and to find out if these are different from those reported from others**

Material and method

- **Six cases undergoing treatment from 2009 to 2011 in the study.**
- **5 male 1 femal**
- **Age 11~38**
- **Case 2 are father of case 1**
- **Family history of cysts/tumors.**

- **Extraoral and intraoral clinical examination orthopantomogram (OPG)**
- **Radiological evaluation of skull bones, chest, hands, feet, long bones, pelvis, and spine.**
- **Examination for palmar/planter pits**
- **Other departments for a multisystem evaluation.**
- **Cystic lesions in the jaw bones were biopsied and histopathological evaluation.**

Result

Table II. Clinical and radiological findings in present case series of Indian patients with NBCCS

Case no.	*Age/Sex*	*Major criteria*	*Minor criteria*	*Others*
1	11/M	Multiple KCOT (5) Calcification of falx cerebri Bifid 4th and 5th rib on R Father affected (Case 2)	Macrocephaly Coarse facies Hypertelorism Scoliosis Polydactyly (Accessory toe L feet) Bridging of sella turcica	Congenital hydrocephalus Frontal bossing Fused eyebrows Malocclusion Unerupted supernumerary teeth* (2 in max incisor, 2 in mandibular incisor region) Impacted teeth (2,15,16,17,18,27,31,32,58,59,74,75)
2	38/M	Multiple KCOT (5) Calcification of falx cerebri Bifid 3rd rib on R Son affected (Case 1)	Macrocephaly Coarse facies Hypertelorism Scoliosis Bridging of sella turcica	Congenital hydrocephalus Frontal bossing Fused eyebrows Impacted teeth (16,17,32)
3	12/F	Multiple KCOT (6) Calcification of falx cerebri Bifid 5th rib on L, prominent anterior end 3rd and 4th rib on R	Coarse facies Hypertelorism Polydactyly (accessory finger R and L hands)	Frontal bossing Fused eyebrows Depressed nasal bridge
4	11/M	Multiple KCOT (4) Calcification of falx cerebri Bifid 5th rib on R	Bridging of sella turcica Macrocephaly Coarse facies Accessory toe with syndactyly L foot Bridging of sella turcica	Impacted teeth (6,15,16,17,23,27,28) Frontal bossing Fused eyebrows Posteriorly angulated ears Depressed nasal bridge Malocclusion Talons cusp* (in 10) Hypospadias Impacted teeth (6,11,16,29)
5	18/M	Multiple KCOT (3) Calcification of falx cerebri Bifid 4th rib on L	Hypertelorism Bridging of sella turcica	Frontal bossing Fused eyebrows Impacted teeth (6,17,32)
6	12/M	Multiple KCOT (4) Fused 1st and 2nd ribs on L and bifid 5th rib on R	Hypertelorism Elongated 5th cervical vertebra	Frontal bossing Fused eyebrows Impacted teeth (1,6,17,18)

NBCCS, nevoid basal cell carcinoma syndrome; *KCOT*, keratocystic odontogenic tumor; *R*, right; *L*, left; *()*, total number of KCOT in each case.
*Findings not previously reported in NBCCS.

- **Major creteria**
  - **Multiple KCOT (3~5)**
  - **Calcidication of falx cerebri**
  - **Bifid rib (4^{th} and 5^{th})**
- **Minor creteria**
  - **Macrocephaly**
  - **Coarse face**
  - **Hypertelorism**
  - **Bridging of sella turcica**
  - **Syndactyly /polydactyly**

Table III. Clinical features associated with KCOT in present series of Indian patients with NBCCS

Case no. (age/sex)	Extraoral swelling	Intraoral swelling	Duration	Pain	Paresthesia/ anesthesia	Discharge	Aspiration	Incidental finding	Recurrent lesion	Follow-up*
1 (11/M)	Absent	L Max tuberosity	4 mo	Absent	Absent	Absent	Cheesy material	No	No	No recurrence in healed lesions/no new lesions (20 months)
2 (38/M)	Absent	Absent	—	Absent	Absent	Absent	Cheesy material	Yes	No	No recurrence in healed lesions/no new lesions (20 months)
3 (12/F)	R canine fossa	R Max alveolus buccolabial	6 mo	Present	Absent	Present	Cheesy purulent material	No	No	No recurrence in healed lesions/no new lesions (16 months)
4 (11/M)	R canine fossa	R Max alveolus, buccopalatal	5 mo	Absent	Absent	Absent	Cheesy material	No	No	No recurrence in healed lesions/no new lesions (15 months)
5 (18/M)	R Mand angle	R Mand alveolus, retromolar	12 mo	Present	Absent	Present	Cheesy, purulent material	No	No	No recurrence in healed lesions/no new lesions (11 months)
6 (12/M)	L Mand angle, R malar	L.Mand alveolus, retromolar R.max tuberosity	6 mo	Absent	Absent	Absent	Cheesy material	No	No	No recurrence in healed lesions/no new lesions (11 months)

Table IV. Radiological features of KCOT in present series of Indian patients with NBCCS

Case no.	Site as seen in OPG*	Internal structure	Periphery	Shape of margin	Cortication	Buccolingual expansion	Displacement/ erosion of lower border of mandible	Antral involvement/ displacement of IDN canal	Follicle/tooth displacement	Root resorption/ dilaceration	Associated impacted/ Unerrupted tooth	Additional findings in CT scan	Total no. of KCOT
1	L Max tuberosity	Completely radiolucent Unilocular	Well defined	Smooth	Partial	Absent	—	Antral involvement	Yes, 15, 16	Root resorption 14	15, 16	Perforation of medial cortex in R mand ramus region,	5
	L Mand molar retromolar	Completely radiolucent Unilocular	Well defined	Smooth	Partial	Absent	Absent	Absent	Yes, 18, 17	Absent	17, 18	Calcification of falx cerebri	
	R Mand molar retromolar	Completely radiolucent Unilocular	Well defined	Smooth	Present	Present	Absent	Absent	Yes, 31, 32	Absent	31, 32		
	R Max tuberosity	Completely radiolucent Unilocular	Well defined	Smooth	Present	Absent	—	Antral involvement	Yes 2	Absent	2		
	R Mand canine	Completely radiolucent Unilocular	Ill-defined	Smooth	Absent	Absent	Absent	Absent	Yes, 27, 75	Absent	27, 75		
2	L Max tuberosity	Completely radiolucent Multilocular	Well defined	Smooth	Present	Absent	—	Antral involvement	Yes, 16	Absent	16	Not done	5
	L Mand canine	Completely radiolucent Unilocular	Well defined	Scalloped	Present	Absent	Absent	Absent	Yes, root displacement 23, 22	Root resorption, 23, 24, 25	—		
	L mand retromolar ramus	Completely radiolucent Unilocular	Well defined	Smooth	Present	Absent	Absent	Absent	Absent	Absent	17		
	R Max tuberosity	Completely radiolucent Unilocular	Ill defined	Smooth	Absent	Absent	—	Antral involvement	Yes 32	Root resorption 31	32		
	R Mand retromolar	Completely radiolucent	Ill defined	Smooth	Partial	Absent	Absent	Absent	Absent	Absent	—		

Result

- **All 25 KCOT**
- **Sites**
  - **Max. tuberosity: 7**
  - **Max. canine premolar: 5**
  - **Mand. Retromolar : 8**
  - **Mand. Caine:5**
- **Internal structure**
  - **All radiolucent: 17 uniloculor 8 multiloculo**
- **Periphery**
  - **15 well-defined, 10 ill-defined**
- **Shape of margin**
- **Cortication**
- **BL expansion**
- **Shape of margin**
  - **16 smooth, 9 scalloped**
- **Cortication**

- 21 present, 4 absent
- BL expansion
  18 absent, 7 present

- Displacement of lower border of mand.
  - None
- Max. 12/12 antral involvement
- Mand. 5/13 displacement of IDN canal
- Tooth/follicle displacement
  - 3 absent；others yes
- Root resorption/dilaceration
  - 8 resorption；1 dilaceration；16 absent
- Associated with impacted tooth
  - 23 present
- Most common symptom was swelling with pain, foul-smelling discharge.
- Paresthesia/anesthesia was not associated
- Multiple cystic lesions in the jaws number ranged from 3 to 6 per patient,
- Site being the mandibular retromolar ， maxillary tuberosity ，maxillary canine-premolar ，mandibular canine-premolar region.
- Radiographic findings radiolucent, unilocular, well defined, and corticated、smooth borders
- Associated with impacted teeth and tooth follicle/tooth displacement
- Antral involvement was common
- Not previously reported
  - Supernumerary teeth in case 1
  - Talons cusp in case 4
- Small KCOTs enucleation aggressive Curettage Carnoy solution. (larger marsupialized)
- no recurrence in healed lesions and no new lesions in a follow-up ranging from 11 to 20 months.

Table V. Frequency of major and minor diagnostic criteria for NBCCS reported in Indian patients (1977-2010)[20-34]

	Major criteria						*Minor criteria*						
Author	*Mul KCOT**	*Mul BCC*	*Mul P/P pits*	*CFC*	*RA*	*FH*	*MC*	*FB*	*HT*	*SD*	*S/P*	*BST*	*VA*
Kamath A (1977)	+	+	+	–	–	–	–	–	–	–	–	–	–
Yesudian D (1995)	+	+	+	–	–	–	–	–	–	–	–	–	–
Chavan R (1998)	+	+	+	–+	+	–	–	+	+	–	–	–	+
(3 cases)	–+	+	+	+	–+	–	–	–+	+	–	–	–	–
		+	+			–	–		+	–	–	–	–
Gupta A (2000)	+	+	–	–	–	–	–	–	–	–	–	–	–
Gandage SG (2003)	+	–	–	+	–	–	–	–	–	–	–	+	+
Patil K (2005)	+	–	+	+	–	–	+	–	–	–	–	–	–
Karthiga KS (2006)	+	–	–	–	+	–	+	+	+	–	–	–	+
Rao S (2006)	+	+	+	–	+	–	–	–	–	–	–	–	+
Rai S (2007)	+	–	–	+	+	–	–		+	–	+	–	+
Jawa DS (2009)	+	–	–	+	+	–	–	–	+	–	+	–	–
Kohli M (2010)	+	–	–	–	+	–	–	–	–	+	–	–	+
Guruprasad and Prabhu (2010)	+	–	+	+	+	–	–	–	–	+	–	+	+
Rahman F (2010)	+	+	–	–	+	–	–	–	–	–	–	–	–
Shivaswamy et al. (2010)	+	+	+	+	+	–	–	–	+	–	–	–	+
Baliga and Rao (2010)	+	+	+	–	+	–	–	+	+	–	–	–	–
Total[17]	16	10	10	8	11	0	2	4	7	2	2	2	8

NBCCS, nevoid basal cell carcinoma syndrome; *Mul*, multiple; *KCOT*, keratocystic odontogenic tumor; *BCC*, basal cell carcinoma; *P/P*, palmar/plantar; *CFC*, calcification falx cerebri; *RA*, rib abnormalities; *FH*, family history; *MC*, macrocephaly; *FB*, frontal bossing; *HT*, hypertelorism; *SD*, Sprengal deformity; *S/P*, syndactyly/polydactyly; *BST*, bridging of sella turcica; VA vertebral abnormalities; +, present; –, absent.
*Reports before 2005 have described the lesions as odontogenic cysts/odontogenic keratocyst.

Table VI. Comparison of major and minor diagnostic criteria in NBCCS among studies from various countries[14-19]

	Evans et al. UK 1993	*Shanley et al. Australia 1994*	*NIH study USA 1997*	*Muzio et al. Italy 1998*	*Ahn et al. Korea 2004*	*Provost et al. France 2006*	*Habibi A Islamic Republic of Iran 2010*	*Present study India† 2011*
Major criteria								
No. of cases	84	118	105	37	33	22	19	23
Mean age, y	NA	35	34.5	31.4	21.2	44.9	35.4	22.9
Sex ratio M:F	1:1.3	1:1.3	1:1.2	1:1.3	1:1.1	1:1.75	1:1.1	1:0.7
Multiple BCC‡	47	75	80 (38)*	30	15	100	43	43
Multiple KCOT‡	66	75	74	92	91	62	100	95
Palmer/planter pits‡	71	80	87	35	67	45	74	43
Calcification of falx cerebri‡	NA	92	65	70	21	66	89	56
Bifid/fused/splayed ribs‡	NA	45	43	32	36	16	58	74
No. of families with NBCCS‡	29	64	26	7	4	5	1	1
Minor criteria								
Macrocephaly‡	NA	80	50	NA	NA	27	5	21
Cleft lip/palate‡	5	4	3	3	9	0	5	0
Frontal bossing‡	NA	66	27	70	42	18	47	43
Coarse facies‡	NA	NA	54	NA	NA	NA	5.2	17
Hypertelorism‡	NA	6	42	78	49	18	53	52
Sprengel deformity‡	NA	4	11	22	NA	NA	NA	8
Pectus deformity‡	NA	23	13	NA	NA	23	NA	0
Syndactyly/ Polydactyly‡	47	7	24	5	3	NA	NA	21
Bridging of sella turcica‡	NA	26	68	24	21	NA	NA	30
Vertebral anomalies‡	NA	35	31	14	9	18	5.2	39
Ovarian fibroma‡	24	14	17	8	0	13	0	0
Medulloblastoma‡	4	1	4	0	3	13	0	0

Discussion

- **Multiple KCOTs with NBCCS**
  - **number from 1 to 30 with an average of 5**
  - **occur at an early age, usually first decade**
  - **CT revealed cortical perforation and additional small cysts that were not detected on OPG.**
  - **high recurrence (60%) as compared with nonsyndromic KCOT (28%).**
  - **Recurrence within 2 years to even 25 years after enucleation.**
    - **The friable cyst lining site of involvement**
    - **surgical accessibility, surgeon's expertise**
- **Multiple KCOTs with NBCCS**
- **Regular follow-up**
  - **every year for the first 5 years**
  - **and thereafter every 2 years**
- **Low-dose or nonionizing imaging modalities should be selected for surveillance**
  - **involve annual conventional radiographic**
  - **supplemented by preferably cone-beamCT or MRI**
- **Multiple BCC with NBCCS**
  - **mostly seen in younger patients**
  - **involve nonsun-exposed areas of the body.**
  - **incidence varies widely among ethnic groups.**
  - **100% of whites**
  - **38% of black**
  - **30% of Italian**
  - **probably owing to**
    - **Protective skin pigmentation.**
    - **Exposure to radiation therapy**
    - **Carcinogens (arsenic)**

- **Rib anomalies**
  - **are reported in 30% to 60% of patients with NBCCS**
  - **bifid ribs are more common, involving either the fifth, fourth, and third rib**
  - **high frequency(74%) in Indian patients**
- **Calcification of falx cerebri**
  - **is one of the most frequent radiological features(37% to 79%)**
  - **be more common in patients older than 20 years.**
  - **high frequency (92%) in the Australian**

in 56% of Indian at a mean age of 22.9 years

- **Ovarian fibromas and cysts**
  - **are seen in 25% to 50% of female patients with NBCCS and are often bilateral (75%).**
  - **were not seen in Indian women**
- **Medulloblastomas (now termed primitive neuroectodermal tumor)**
  - **are seen in 3% to 5%**
  - **usually within the first 2 years**
  - **Early-onset desmoplastic medulloblastoma**
  - **may be the first presenting sign of NBCCS in children**
  - **younger than 3 years, as other major criteria may not be evident at that age.**
  - **Molecular genetic studies for**
- **Medulloblastomas (now termed primitive neuroectodermal tumor)**
  - **studies for PTCH1 gene mutations in early diagnosis**
  - **Avoid Radiotherapy as they can develop BCC and other tumors**
  - **MRI**
    - **every 6 months until 3 years of age**
    - **annual follow-up until 7 years of age**
- **Diagnosis of NBCCS is made**
  - **screening for the syndrome and genetic counseling in other family members**
  - **NBCCS is usually a hereditary condition**
  - **mutations in the PTCH1 gene reported in members of same family**
  - **but 30% to 50% of the cases have also been reported to be sporadic in nature, presenting with new mutations**
  - **phenotypevariability in NBCCS is a complex event probably arising from genetic and environmental factors.**
- **Diagnosis of NBCCS is made,**
  - **Most cases in Indian are also apparently sporadic in nature, with the exception of cases 1 and 2 (father-son) reported in our case series.**
  - **Molecular genetic studies for PTCH gene mutations are expensive and not available everywhere. There are no such studies reported in Indian patients with NBCCS at present.**
- **Clinical and radiological criteria will continue to play an important role in diagnosis NBCCS. New findings are being added just like we found supernumerary teeth and Talons cusp**
- **NBCCS is rare in the Indian population and the clinical radiological features in NBCCS vary in different ethnic groups, this study has tried to determine the features that are characteristic in Indian patients.**

- **The presence of multiple KCOTs, bifid/fused ribs, and calcification of falx cerebri, often help in diagnosis of NBCCS in Indian patients.**

題號	題目
1	Which one are not major criteria of NBCCS (A) Multiple KCOT (3~5) (B) Alcidication of falx cerebri (C) Macrocephaly (D) Bifid rib (4^{th} and 5^{th})
答案(C)	出處：Table I
題號	題目
2	What can help in diagnosis of NBCCS in Indian patients by this paper? (A) Multiple KCOTs (B) Bifid/fused ribs (C) Calcification of falx cerebri (D) Above all
答案(D)	出處：Conclusion