Pineal Gland And Choroid Plexus Calcifications On CT: A Retrospective Study In A Brazilian Subtropical City

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Citation

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Abstract

Introduction: Pineal gland and choroid plexus calcifications (PGC and CPC, respectively) are the most frequent sites of intracranial calcifications incidentally discovered among head computed tomography (CT) examinations. While recent publications have partially elucidated the mechanisms involved in the calcification process, there is still lack of evidence and therefore insecurity, when considering PGC and CPC as normal or abnormal findings.
Methods: The authors aimed to retrospectively analyze non-contrasted head CT scans of patients between 0 and 40 years old. Parameters including sex, age, month of CT performance, presence or absence of PGC and CPC and – if so – their respective dimensions, were collected. Statistical analyses of datasets were then sought, in order to assess potential interactions between variables. A p-value achievement of 0.05 or less was interpreted as significant for crossing tests.
Results: PGC was present in 183 (51.7%) of people. Also, CPC of any type occurred in 151 (42.6%) cases, most times bilaterally. As expected, age progression and PGC were intimately related ($p < 0.0001$). If PGC was found to be strongly associated with men ($p = 0.01$), no difference between gender and CPC was detected ($p = 0.531$). Either, no correlation was demonstrated between month of CT realization and PGC occurrence ($p = 0.357$).
Conclusions: Both PGC and CPC are likely to be identified in around 50% of head CT examinations, with an increasing percentage among aging progression. Rather than the presence of symptoms, there is no suggested age threshold to enforce malignant suspicion. PGC is more common in men, and should be understood as an active, reversible and multifactorial phenomenon. Otherwise, CPC shows and unique and definitive degenerative mechanism that affect sexes equally and constitutes a passive process.

INTRODUCTION

The initial evaluation of a patient presenting neurological symptoms will occasionally include a non-contrasted head computed tomography (CT) performance [1-3]. Despite the reason of CT examination seeking, intracranial calcifications (physiologic or not) are very commonly observed [4]. Pineal gland calcification (PGC) and choroid plexus calcification (CPC) are the most prevalent areas of calcifications, followed by basal ganglia, cerebellum, habenula, and other sites (Figure 1).
Both PGC and CPC usually denote the development of a degenerative process, which includes calcium and magnesium salts deposition, and increases with age progression. This fact justifies an historical concern about an age threshold, below which especially PGC occurrence would be abnormal [5]. Although, more recent studies have partially faded away that preoccupation, suggesting that PGC process is active, regulated and also reversible [6] – rather than CPC, which is still a passive event.
The purpose of our work was to assess, by a retrospective evaluation of head CT scans, the prevalence of PGC and CPC in general population. Moreover, we aimed to correlate those data with age, sex and season of CT acquisition, and to discuss this issue towards the results of contemporary relevant publications.

MATERIALS AND METHODS

Study design and patient population
The authors conducted a retrospective non-interventional study in order to determine the presence or absence of PGC and CPC in general population. All patients between 0 and 40 years old, who have performed head CT for numerous purposes, between February 2012 and September 2012, were included in our study. Such age threshold was established considering the apparent stability in PGC and CPC

development after reaching adulthood [7]. Only CT scans with a 512 x 512 matrix of data and without contrast medium injection were selected. The institutional ethical board review committee has previously approved this research.

CT examinations parameters
All CT scans images were acquired in a single-slice Shimadzu scanner SCT 7000ts (Shimadzu Medical Systems, Kyoto, Japan). As habitually, seeking the avoidance of imaging artifacts determined by petrous regions of temporal bones, different parameters were applied for infra and supratentorial structures. For posterior fossa structures (infratentorial), a table speed of 45 mm per tube rotation (5.0 pitch), 150 mAs, 120 kV, and slice thickness of 3 mm. Parameters for supratentorial region included a table speed of 90 mm per tube rotation (1.0 pitch), 130 mAs, 120 kV and slices of 10 mm each. The CT scanner was calibrated periodically, following manufacturer recommendations.

Imaging analysis
One radiologist (CH), with 15 years of experience in general radiology, analyzed examinations separately. Measurements were taken using freely available workstation software (eFilm workstation Brazil, version 3.3.5; Merge Healthcare, Chigado, IL, USA). Images were assessed in DICOM (Digital Imaging Communications in Medicine) format, enabling the use of gray tone and zoom adjustment tools. All scans were analyzed for the following variables: a) sex; b) age; c) month of CT performance; d) presence or absence of PGC; e) extension and mean Hounsfield units (HU) of PGC (if present); f) presence of absence of CPC; g) extension and mean HU of each plexus (if calcified). Information of each included patient was tabulated in Microsoft Office Excel version 2007 (Microsoft Corporations, Redmond, WA, USA) for further statistical analysis.

Statistical analysis:
Data were analyzed by using Statistical Package for Social Science 15.0 (SPSS) software (IBM Corporation, NY, USA). Descriptive analysis was performed for all categorical (month of CT performance, sex, presence or absence of PGC and CPC) and continuous variables (age, PGC and CPC extensions and mean HU). After, all possible comparative (crossing) tests between each variable were conducted. For categorical data, the Chi-squared test was applied. For study purposes, a p-value of 0.05 or less ($p < 0.05$) was adopted for significance consideration. When categorical variables were crossed with non-categorical data, the Shapiro-Wilk test was initially performed in order to rule out normal distribution, finally followed by Mann-Whitney (non-parametric) test, once variables were not normally distributed.

RESULTS

This retrospective study included a total of 354 head CT examinations. On sex distribution, a majority of male population (246, 69.5%), versus 108 women (30.5%) was observed. The mean age obtained was 19.8, and a median of 12.6 years old, ranging from 0 to 40.
The presence of PGC was present in 183 (51.7%) of the whole study population. Also, CPC of any type occurred in 151 (42.6%) cases, often bilaterally (124 patients, 82.1% of all CPC, Figure 2). Descriptive analyses of categorical and non-categorical data are summarized in Tables 1 and 2, respectively.

Table 1

Descriptive analyses of month of examination performance, sex and presence or absence of calcifications. CT = Computed tomography. PGC = Pineal gland calcification. CPC = Choroid plexus calcification.

Variables	Frequency (N)	Percentage (%)
CT scan month		
2 (February)	2	0.6
3 (March)	23	6.5
4 (April)	59	16.6
5 (May)	61	17.2
6 (June)	51	14.4
7 (July)	72	20.3
8 (August)	55	15.5
9 (September)	32	9.0
Sex		
Male	246	69.5
Female	108	30.5
Presence of PGC		
Yes	183	51.7
No	171	48.3
Presence of CPC		
Bilateral	124	35.0
No	203	57.3
Right only	16	4.5
Left only	11	3.1

Table 2

Descriptive analyses of age, pineal gland and choroid plexus (of each lateral ventricle) extensions and mean density of each structure (in Hounsfield units). PG = Pineal gland. HU = Hounsfield units. RCP = Right choroid plexus. LCP = Left choroid plexus.

Variables	Mean	Standard Deviation	Median	Minimum	Maximum
Age	19.8	21.0	12.6	0.0	40.0
PG extension	0.5	0.4	0.2	0.1	1.1
Pineal HU	101.0	91.0	52.3	41.0	367.0
RCP extension	0.5	0.5	0.2	0.1	1.2
RCP HU	66.2	62.0	22.2	37.0	178.0
LCP extension	1.2	0.5	7.0	0.1	82.0
LCP HU	66.6	62.5	23.9	37.0	189.0

There was no significant association when comparing the presence of PGC with month of examination performance ($p = 0.357$). On the other hand, sex and the presence of PGC were strongly related, being the male population more likely to present such calcification than the female one ($p < 0.05$). As well, significant association was demonstrated between the presence of PGC and CPC ($p < 0.05$).

When analyzing non-categorical data by Mann-Whitney test, an association between age and PGC was demonstrated ($p < 0.05$). Even though, PGC was seldom present in younger patients examinations (Figure 3). The presence of PGC was not correlated to CPC extensions, or a possible predominance of one side upon another. Additionally, no association between sex and CPC occurrence was observed in our study ($p = 0.531$). These results are summarized in Tables 3, 4 and 5.

Table 3

Comparative analyses between the presence or absence of PGC and month of CT performance, sex and presence or absence of CPC. Note the significant correlations between PGC and male patients ($p < 0.05$) and the concomitance of PGC and CPC occurrence ($p < 0.05$). No association was observed between PGC and the month or season of CT performance. PGC = Pineal gland calcification. CT = Computed tomography. CPC = Choroid plexus calcification.

Variables	Presence of PGC		p-value
	Yes N (%)	No N (%)	
CT scan month			
2 (February)	0 (0.0)	2 (1.2)	0.357
3 (March)	10 (5.5)	13 (7.6)	
4 (April)	32 (17.5)	26 (15.2)	
5 (May)	36 (19.7)	25 (14.6)	
6 (June)	24 (13.1)	27	
7 (July)	42 (23.0)	30 (17.5)	
8 (August)	25 (13.7)	30 (17.5)	
9 (September)	14 (7.7)	18 (10.5)	
Sex			
Male	138 (75.8)	108 (63.2)	0.010
Female	44 (24.2)	63 (36.8)	
Presence of CPC			
Bilateral	96 (52.5)	28 (16.4)	<0.0001
No	67 (36.6)	136 (79.5)	
Right only	14 (7.7)	2 (1.2)	
Left only	6 (3.3)	5 (2.9)	

Table 4

Appliance of Mann-Whitney (non-parametric) test, crossing the presence or absence of PGC and age, choroid plexus extensions and mean density (in Hounsfield units). Note the strong correlation demonstrated between the increase of age and presence of PGC ($p < 0.05$). PGC = Pineal gland calcification. RCP = Right choroid plexus. LCP = Left choroid plexus. HU = Hounsfield units.

Variables	Presence of PGC		p-value
	Yes Median (1°Q-3°Q)	No Median (1°Q-3°Q)	
Age	28 (22 – 34)	7 (1 -20)	<0.0001
RCP extension	0.5 (0.4 – 0.7)	0.5 (0.4 – 0.7)	0.395
RCP HU	62.5 (52.00 – 74.00)	59 (48 – 83)	0.903
LCP extension	0.5 (0.4 – 0.7)	0.5 (0.4 – 0.7)	0.459
LCP HU	63 (50.75 – 75.25)	61.5 (54 – 94.25)	0.553

Table 5

Appliance of Mann-Whitney (non-parametric) test, crossing the presence or absence of CPC and sex. Note that no correlation was observed between these variables ($p > 0.05$). CPC = Choroid plexus calcification.

Variables	Presence of CPC				p-value
	Bilateral N (%)	No N (%)	Right only N (%)	Left only N (%)	
Sex					
Male	91 (73.4)	139 (68.5)	10 (66.7)	6 (54.5)	0.531
Female	33 (26.6)	64 (31.5)	5 (33.3)	5 (45.5)	

Figure 1

A head CT scan of a 34-year-old asymptomatic man demonstrates the presence of bilateral choroid plexus, pineal gland and posterior falx calcifications.

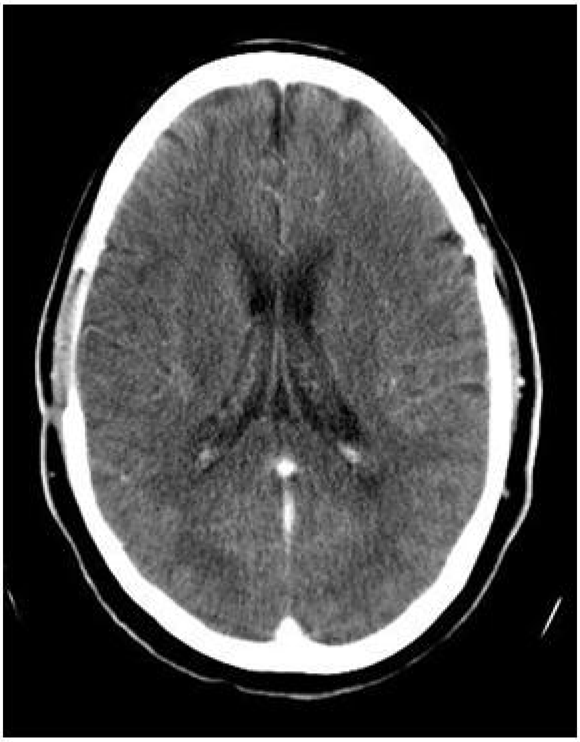

Figure 2

Computed tomography (CT) examination of a 24-year-old woman complaining of headache revealing bilateral choroid plexus calcification (CPC). Minor calcifications at the pineal gland are also seen in this section.

Figure 3

Axial view of a head computed tomography (CT) scan of a two-days-old boy showing pineal gland calcification (PGC) and an extensive area of intracranial hemorrhage.

DISCUSSION

PGC reveals to be a well-described and quite common finding on CT examinations worldwide. Besides the benign and probable age-related behavior of PGC, not only its precise etiologies, but also the effects regarding the calcification mechanism remain unclear. Since its first description, by Schuller in 1918 [8], the occurrence of PGC has been associated with aging progression, and – just as the current research - several studies have statistically proved that correlation [9-11]. Even though, once melatonin is a product of pineal gland activity, and takes part in the circadian cycle inversely with sun light exposure, PGC has been currently understood as a regulated and reversible process, which could potentially differ in populations living in different altitudes and seasons (latitudes), rather than merely meaning a passive phenomenon [6]. However, a definite mechanism involving melatonin production and PGC occurrence hasn`t been achieved yet [12,13]. Finally, other studies [14-17] have tried to include PGC in the pathophysiology of many disorders, such as schizophrenia, Alzheimer`s dementia and sleep disorders, but no association was consistently demonstrated until now.

Along with the correlation between age and PGC, the authors aimed to assess possible seasonal differences. Santa Maria is a city located in the center of the south-most state of Brazil (Rio Grande do Sul), with coordinates of 29° 45' South latitude and 53° 42' West longitude. It is considered a subtropical city, as sunlight exposure varies significantly during the year. Therefore, we have divided examinations by month. Months from February to May are known for a high sunlight exposure (40,8% of all scans), and those from June to September with a lower one (50,9% of all scans). Besides no correlation was proved, as other authors have already reported [18], we postulated that the incidence of PGC would be higher in months with higher sunlight exposure, considering the primary balance between melatonin secretion and sunlight during the circadian cycle. However, literature data is still conflictive, since other publications have suggested that even a deprival in sunlight exposure could be a risk factor for PGC, indicating that this is a complex, controversial and multifactorial issue [12].

The presence of PGC was consistently higher in men ($p = 0.01$), a fact that is in agreement with the vast majority of studies in literature. If such difference hasn`t been minimally explained until today, most authors agree that it is secondary to the relation between melatonin and sexual hormones, which is also challenging. In that context, it is believed that melatonin determines an antagonist effect through estrogens by stimulating progesterone activity [19], justifying the low prevalence of PGC in pre-menopausal female population when comparing to men.

On the other hand, the discussion about CPC occurrence is much less complex, while choroid plexus may only present degenerative alterations with aging, play no hormonal role and show no difference between sex and ethnics as PGC does. Such degeneration is usually composed by calcium and magnesium salts, and is often referred as “acervuli”, “corpora arenacea” or “brain sand”, and may also occur at the pineal gland [4]. We decided to include CPC analysis in our study because, together with PGC, these are far the most common calcifications on non-contrasted CT examinations. Nonetheless, while PGC and CPC are both affected by a degenerative process, we shall consider their high statistical association ($p < 0.0001$) partly occasional – due only to the high prevalence of both – and so the presence of one cannot safely predict the occurrence or absence of another.

Some limitations of our work must be prudently highlighted. Despite the significant size sample included, examinations were performed using a single-slice helical CT scanner, what could have diminished the diagnostic accuracy in detecting calcifications, especially for younger subjects [20]. Further, both age and extension of calcifications were collected as continuous variables (non-categorized), which precluded a statistical crossing between them. Also, an enquiry for patient`s ethnic was not performed, and some studies have consistently proved differences regarding it and PGC [18,21]. Finally, patients were not asked for occupation (indoor/outdoor), for recent travels or living elsewhere, and this may have influenced the comparison between season of CT scan and PGC occurrence.

CONCLUSIONS

The incidental findings of PGC and CPC reveal to be very prevalent, no matter the requesting cause, occurring in around 50% of all non-contrasted head CT examinations. Once both PGC and CPC share a common degenerative mechanism with age progression, they are more frequent in the elderly population. However, there is no age threshold for calcification development, and they shall securely be interpreted as occasional features in asymptomatic patients. PGC is more likely to affect men, due to a complex interaction between melatonin and sexual hormones. While not statistically proven in our research, PGC may also vary for different ethnics, latitudes and altitudes. Therefore, PGC should be understood as an active, reversible and multifactorial phenomenon, rather than CPC, in which the degenerative process role is unique and definitive.

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