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STUDY SUBJECTS

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SUMMARY

Tracheobronchial calcification is reportedly more frequent in women than in men. Ten cases of extensive tracheobronchial calcification were identified on chest radiographs of 1,152 consecutively examined Adult Health Study subjects, for a prevalence of 0.87%. An additional 51 subjects having this coded diagnosis were identified among 11,758 members of this fixed population sample. Sixty of the 61 subjects were women. The manifestations and extent of this type of calcification and its correlations with clinical and histopathologic features, which have not been previously reported, are described here.

INTRODUCTION

Tracheobronchial calcification is considered a physiological process and has been reported to be more frequent in women than in men.^{1,2} Edge et al³ described 37 such cases among 100 elderly persons. According to Harasawa et al,⁴ it occurs in 1.5% of men and 4.1% of women. The extents of such calcifications and their correlations with clinical, histopathologic, and other radiological findings have not been reported. The present study established the frequency of this type of calcification among apparently healthy members of a fixed pop-

要 約

気管気管支の石灰化は女性に多いとされている。一定期間に受診した成人健康調査対象者1,152名のうち10例(0.87%)に気管気管支石灰化が認められた。また、この固定集団11,758名中、診断コードにより51名にも認められた。これら61名中60名が女性であった。これまで報告例のないこれらの石灰化の特徴、範囲とその臨床所見・病理所見との関連について述べた。

緒 言

気管気管支石灰化は生理的現象と考えられ、男性よりも女性に頻度が高いとされている。^{1,2} Edge ら³は、100名の高齢者中37例にこの所見を認めている。原澤ら⁴によれば、男性で1.5%、女性で4.1%とされている。このような石灰化の範囲並びにその臨床所見、病理組織学的所見、及び放射線学的所見との関連については報告されていない。本研究では、健康と思われる固定集団に見られるこの種の石灰化の

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ulation sample according to age, and assessed for possible correlations with clinical, other radiological, and histopathologic findings.

MATERIALS AND METHODS

The Adult Health Study (AHS)⁵ conducted by RERF, formerly ABCC, consists of a fixed population sample originally numbering 20,000 persons drawn at random from the A-bomb exposed and nonexposed members of the Hiroshima and Nagasaki populations. Biennially, all AHS subjects receive physical and laboratory examinations and any other diagnostic studies which are indicated. They routinely received chest radiography with 14 × 17-inch posteroanterior (PA) stereoscopic and lateral projections. All chest radiographs are exposed at about 100 kVp and 5 mAs.

At the time of this investigation, 11,758 Hiroshima AHS subjects had undergone chest radiography at least once. The age and sex distribution of these subjects is shown in Table 1.

年齢別頻度を確認し、臨床所見、放射線学的所見及び病理組織学的所見との関連について検討した。

材料及び方法

放影研(元 ABCC)の成人健康調査(AHS)⁵は広島及び長崎の被爆者及び非被爆者から任意に抽出された当初20,000名の固定集団に対して行われている。すべてのAHS対象者は2年に1回、理学検査及び臨床検査を受け、必要な場合には他の検査も行われる。通常検査として、対象者は14×17インチフィルムを用いた背腹方向(PA)立体及び側方向胸部X線撮影を受ける。すべての胸部X線撮影は約100 kVp及び5 mAsで行われる。

この調査が行われた際、11,758名の広島のAHS対象者が少なくとも1回の胸部X線撮影を受けていた。これらの対象者の年齢及び性別の分布を表1に示す。

TABLE 1 DISTRIBUTION OF SUBJECTS AT INITIAL CHEST RADIOGRAPHY BY AGE AND SEX

表1 初回胸部X線撮影時の対象者の分布、年齢及び性別

Age at examination in years	Men	Women	Total
10-19	262	270	532
20-29	387	640	1027
30-39	1137	2027	3164
40-49	657	1434	2091
50-59	857	1555	2412
60-69	731	1042	1773
70-79	292	369	661
80+	30	68	98
Total	4353	7405	11758

All chest radiographs of 1,152 AHS subjects who were consecutively examined from April to September 1986 were reviewed for the presence of tracheobronchial calcification. Using this coded radiological diagnosis, all AHS subjects who had been diagnosed as having tracheobronchial calcification were identified, and all of their chest radiographs were carefully scrutinized.

1986年4月から9月の間に逐次検査を行った1,152名のAHS対象者の胸部X線写真すべてについて気管気管支石灰化の有無を調べた。更に、放射線学的診断コードを用い、気管気管支石灰化があると診断されたすべてのAHS対象者を確認し、その胸部X線写真を慎重に読影した。

Tracheobronchial calcification was categorized as extensive or partial in degree, "extensive" being that located in the cartilaginous rings of the trachea from the level of the second thoracic vertebra to throughout the entire main-stem bronchus; "partial" calcification being that of any degree less than extensive. All subjects with partial calcification were excluded from this study.

The sites of onset of calcification, the times at which calcification became extensive, its progression and resolution, any resulting luminal narrowing or protrusions into the lumina, and any calcification located in other than the tracheobronchial rings were identified during scrutiny of the radiographs. The lung fields and mediastinum were reviewed for evidence of old inflammatory diseases, such as tuberculosis, pleural thickening and adhesions, calcifications of the lung parenchyma and lymph nodes, and any interval changes therein. The past histories and clinical findings were reviewed for any medical therapy they had received, and for any admissions to hospitals. The data collected were assessed for this entity's correlation with the latter items, with age and A-bomb exposure.

RESULTS

Ten cases of extensive tracheobronchial calcification were identified during the review of the chest radiographs of the 1,152 consecutively examined subjects, for a prevalence of 0.87%. Fifty-one additional cases were identified by retrieval of this coded diagnosis (Appendix). All radiographs were carefully scrutinized. Sixty of the 61 cases were women, whose mean ages were 66.3 years (SD 7.5) at initial chest radiography and 79.0 years (SD 5.2) at the last.

Thirty-four of the 61 subjects had extensive calcification throughout the trachea and main-stem bronchi at initial chest radiography. Their mean age at initial radiography was 69.3 years (SD 7.6) with a range of 55 to 93 years. Twenty-seven subjects showed no extensive calcification at initial radiography; their calcifications became extensive during follow-up examinations, and at a mean age of 72.9 years (SD 6.6). The age distributions of the 61 subjects at the diagnosis of extensive calcification are shown in Table 2.

気管気管支石灰化の程度は、広範囲にわたるものと限局性のものに分類した。“広範囲”とは、第2胸椎レベルの気管から主気管支全体にまでわたる軟骨輪に認められるものとし、“限局性”石灰化とは“広範囲”にまでいたらない程度のものとした。限局性石灰化のみ認められる対象者は本研究では除外した。

石灰化の発生しはじめる部位、石灰化が広範囲に認められた時期、石灰化の進行及び消退、石灰化に伴う内腔の狭窄、あるいは内腔への突出、及び気管気管支軟骨輪以外に位置する石灰化をX線写真で観察した。結核などの古い炎症性疾患の有無、胸膜肥厚及び癒着、肺実質及びリンパ節の石灰化、及び検査間に認められた変化を確認するために、肺野及び縦隔を観察した。既往歴及び臨床所見を調べ、何か治療や入院がなされたかをみた。これらの情報をもとに、この所見と治療・入院歴、年齢及び原爆被爆との関連を調査した。

結 果

広範囲にわたる石灰化は、逐次検査を受けた1,152名の対象者の胸部X線写真中10例に認められ、有病率は0.87%であった。更に、コード化した診断からの検索によって、新たに51例が確認された(付録)。すべてのX線写真を慎重に検討した。61例のうち60例は女性で、平均年齢は初回胸部X線撮影時で66.3歳(SD 7.5)、最終撮影時で79.0歳(SD 5.2)であった。

初回胸部X線撮影時に気管及び主気管支の広範囲にわたる石灰化が認められたのは、61名の対象者中34名であった。その初回時平均年齢は69.3歳(SD 7.6)で年齢幅は55歳から93歳であった。27名の対象者には初回時に広範な石灰化は認められず、追跡期間中に石灰化が広範なものとなり、その時点での平均年齢は72.9歳(SD 6.6)であった。これら61名の対象者の広範囲にわたる石灰化があると診断された時点の年齢分布を表2に示す。

TABLE 2 DISTRIBUTION OF 61 SUBJECTS WITH EXTENSIVE TRACHEOBRONCHIAL CALCIFICATION BY AGE

表2 広範囲にわたる気管気管支石灰化が認められた61名の対象者の年齢別分布

Age in years	Subjects with extensive calcification at initial radiography	Subjects whose calcification became extensive during follow-up period
<50	0	0
50-59	3	0
60-69	14	11
70-79	16	13
80+	1	3
Total	34	27

Among 27 cases whose calcification became extensive during follow-up, partial calcification occurred in the main-stem bronchi and interlobar bronchi before becoming extensive in 19 cases (Figures 1 and 2). Calcification first appeared in the tracheae of five subjects; and simultaneously in the tracheae, main-stem and interlobar bronchi of three additional subjects. In no case was there resolution of calcification. Nor was there luminal narrowing of the trachea or bronchus, protrusion of calcification into the lumen, or calcification outside the cartilaginous rings (Figures 1 and 2).

追跡期間中に石灰化が広範囲と認められた27例中19例において、石灰化が広範囲にわたる前に主気管支及び葉間気管支に限局性石灰化が認められた(図1及び2)。5名の対象者では最初に気管に石灰化が発生し、別の3名の対象者では気管、主気管支及び葉間気管支に同時に発生した。石灰化が消退した例はなく、気管及び気管支の内腔の狭窄、内腔への石灰化の突出像、あるいは軟骨輪以外の部位での石灰化も認められなかった(図1及び2)。

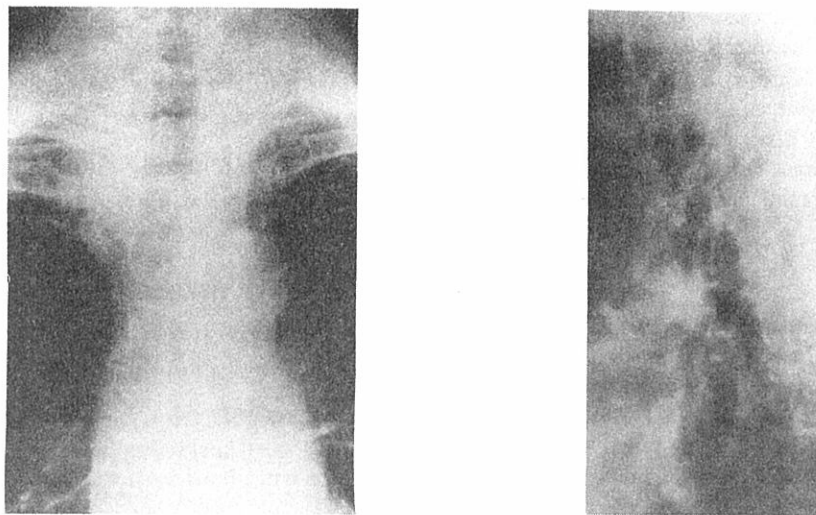


Figure 1. Posteroanterior (A) and lateral (B) chest radiographs show an example of calcification in the main-stem bronchi and more peripherally, but not in the trachea. (MF# [redacted])

図1 背腹(A)及び側方向(B)のX線写真は、主気管支及びその周辺部に発生した石灰化の1例を示しているが、気管には石灰化は見られない。(MF# [redacted])

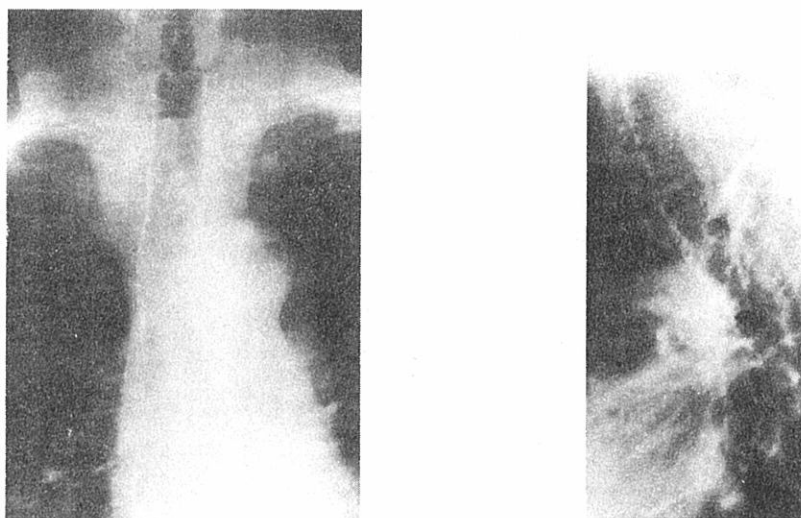


Figure 2. Posteroanterior (A) and lateral (B) chest radiographs of the same case as Figure 1, 12 years later, showing that the calcification has become very extensive.

図2 図1と同一人物の12年後の背腹(A)及び側方向(B)のX線写真で、石灰化が広範囲に及んだことを示している。

Postinflammatory manifestations were observed in the lung fields and mediastina of eight subjects at their initial chest radiographies, and of nine subjects at their last radiographies. Calcification of the lung parenchyma or lymph nodes was observed in six at their initial, and in seven at their last radiographies. Pleural thickening and adhesions were observed in 8 at their initial, and in 10 at their last radiographies. Interval radiographic changes included those of one person with active pulmonary tuberculosis who was treated during the observation period; another with diffuse pulmonary fibrosis secondary to rheumatoid arthritis; and a third with multiple calcifications, each several millimeters in diameter in one lung field peripherally, probably in postinflammatory granulomas.

Concerning clinical findings and diagnoses, four subjects each developed pneumonia once during the observation period, all of which resolved completely. One subject had chronic bronchitis; another, asthma treated elsewhere as an outpatient.

Eleven subjects were deceased and 4 of these had been autopsied. Histopathologically, the tracheal mucosa of these four subjects was smooth. All four had prominent calcifications in their tracheal

初回胸部X線撮影時に8名、最終撮影時に9名の対象者の肺野及び縦隔に炎症後の変化が認められた。肺実質あるいはリンパ節の石灰化は初回撮影時に6名、最終撮影時に7名に認められた。胸膜肥厚及び癒着は初回撮影時に8名、最終撮影時に10名に認められた。検査間にX線写真上変化が認められたのは、観察期間中に治療を受けた活動性肺結核の1例、慢性関節リウマチに伴う慢性肺線維症1例、及び片側肺末梢に認められた炎症後の肉芽腫によると思われる数mm径の多発性石灰化1例であった。

臨床所見及び診断によれば、4名の対象者が観察期間中に1回肺炎を起こしていたが、これらは全例完治していた。その他に、1名の対象者は慢性気管支炎で、もう1名は喘息で外来患者として他院で治療を受けていた。

11名の対象者は死亡しており、そのうち4名については剖検が行われていた。病理組織学的には、これら

rings, more dense in the cartilaginous centers (Figure 3A). Normal cartilaginous tissue was observed at the edges of the rings, and calcification was of nearly uniform density throughout each cartilaginous ring on cross section. Minimal ossification was observed in the tracheal rings of three of the four autopsied subjects (Figure 3B), but no calcification or ossification occurred outside the cartilaginous rings, all of which retained their normal shapes.

4名の気管粘膜は滑らかであった。4名すべてにおいて気管軟骨輪に著明な石灰化が認められ、それは軟骨中心でより濃厚であった(図3A)。気管軟骨輪の辺部では正常な軟骨組織が認められ、石灰化は軟骨輪横断面でほぼ同一濃度であった。4名の剖検中3名の気管軟骨輪に小規模の骨化が見られたが(図3B)、軟骨輪外部には石灰化も骨化も生じておらず、正常な形態を維持していた。

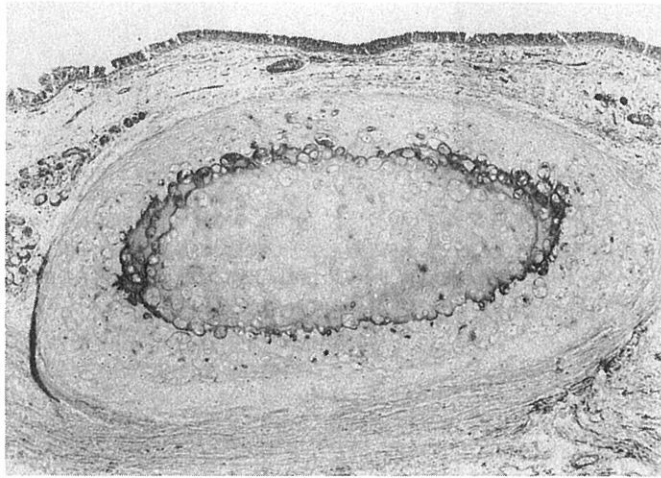


Figure 3A. Histologically, tracheal calcification is seen in the center of the cartilaginous ring (dark area). Hematoxylin and eosin stain, original magnification $\times 55$. (MF# [REDACTED])

図3A 病理組織学的には気管石灰化は軟骨輪の中心部(黒い部分)に認められる。ヘマトキシリン及びエオジン染色55倍(MF# [REDACTED])

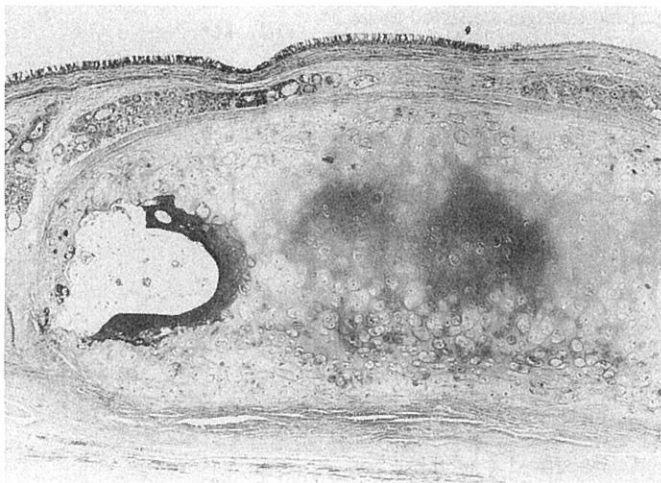


Figure 3B. Ossification is also seen in the cartilaginous ring. (MF# [REDACTED])

図3B 骨化も軟骨輪に認められる。(MF# [REDACTED])

The data were assessed to estimate prevalence and incidence, and for any evidence of effects attributable to A-bomb radiation exposure. The effect of age was significant ($p < .001$). The age effect was largely an increasing incidence among women in their 50s to 60s with the incidence being relatively constant for women over 60 years of age. No evidence of a dose effect was observed ($p > .2$).

DISCUSSION

There are few reports of tracheobronchial calcification in the scientific literature. This condition is extremely rare in children, but not rare among the elderly.^{6,7}

Partial tracheobronchial calcification is sometimes difficult to image because of variations in radiographic techniques, and because of the physical statures of examinees. Tracheal ring calcification is especially difficult to visualize on PA chest radiography because of superimposed mediastinal structures. Considered a physiological process, tracheobronchial calcification is usually excluded from examinees' medical records. For these reasons, only extensive calcification was selected for observation in this study. Tracheobronchial calcification is relatively easily imaged by computed tomography; Gamsu and Webb⁸ reported that 9 (10.1%) of 89 subjects had such calcifications, all of whom were over 40 years of age. No detailed descriptions of the extents of such calcification appear in the literature; the majority may have been partial in degree.

Edge et al³ reported 37 of 100 elderly persons with tracheobronchial calcifications on chest radiography. Harasawa et al⁴ reviewed the chest radiographs of 2,496 persons, and reported that 1.5% of the men and 4.1% of the women had tracheobronchial calcifications. Even in these reports, the extents of calcifications were not described. Among the 1,152 consecutively examined subjects in the present study, 10 (0.87%) had extensive tracheobronchial calcification. Prevalence rates in the present study were relatively low compared to those of other studies because only cases with extensive calcifications of the trachea and bronchi were included in the present study. The calcifications of 27 subjects became extensive during follow-up; and those of 19 were limited to the bronchial region before becoming extensive. The calcifications of five other subjects were limited to the trachea before becoming extensive. Tracheobronchial calcification seemed to arise pre-

有病率及び発生率を推定し、原爆放射線被曝に起因する影響を探知するために、データを評価した。年齢の影響は有意であった ($p < .001$)。年齢の影響は、おおむね50歳代から60歳代の女性において大幅に発生率が上昇するという形で認められ、60歳以上の女性では発生率は比較的一定していた。線量の影響の証拠は認められなかった ($p > .2$)。

考 察

気管気管支石灰化に関する報告は少ない。石灰化は子供ではごく稀れであるが、高齢者では珍しくない。^{6,7}

X線撮影上の条件の変動、及び被検者の体格のために、限局性気管気管支石灰化は撮影されにくい場合がある。特に、気管軟骨輪の石灰化は縦隔構造物と重なるために、背腹方向の胸部X線撮影の場合、描出が困難である。気管気管支石灰化は生理的な現象とみなされて、通常、被検者の医学記録から除外される。これらの理由から、本研究では広範囲にわたる石灰化のみを観察対象として選択した。コンピューター断層撮影法を用いると、気管気管支石灰化を比較的容易に描出することができる。Gamsu及びWebb⁸の報告によれば、89名の対象者中9名(10.1%)にこのような石灰化が認められ、全員が40歳以上であった。石灰化の範囲についての詳細な記述はなされていないが、大半は限局性石灰化の段階であろう。

Edgeら³は、100名の高齢者中37名に胸部X線撮影で気管気管支石灰化が認められたことを報告した。原澤ら⁴は、2,496名の胸部X線写真を検討した結果、男性の1.5%、女性の4.1%が気管気管支石灰化の所見を有したと報告した。これらの報告でさえも石灰化の範囲については述べていない。本研究においては、逐次検査を受けた1,152名中10名(0.87%)に広範囲にわたる石灰化が認められた。本研究では気管及び気管支に広範囲にわたる石灰化のある者のみを取り上げたため、その有所見率は他の報告と比較すると低いものとなった。27名の対象者は追跡検査中に石灰化が広範囲に広がり、そのうち19名については石灰化は最初気管支領域に局在し、その後広範囲に及んだ。他の5名の対象者の場合は、石灰化は最初気管に局在し、その後広範囲に及んだ。気管

dominantly from the main-stem bronchi or the interlobar bronchus to the trachea.

Extensive tracheobronchial calcification was observed at initial chest radiography in 34 subjects whose mean age was 69.3 years. Calcification became extensive during the follow-up in 27 subjects at a mean age of 72.9 years. Extensive tracheobronchial calcification was usually observed after 60 years of age; and it most frequently became extensive in persons in their 70s. Tracheobronchial calcification is reportedly more frequent in women than in men; in the present study, it was overwhelmingly so. This contrasts with the rates of calcification in other sites such as rib cartilage.⁹

No subject in the present study had narrowing of the trachea or bronchi, or protrusion of calcification into their lumina, either radiographically or histologically.

Tracheal dimensions can be altered by a variety of conditions, including dilatation in tracheobronchomegaly and tracheomalacia; narrowing in tracheopathia osteochondroplastica (TO), relapsing polychondritis, and "saber sheath" trachea. In TO, multiple protruding nodular calcifications or ossifications in the walls of the trachea and bronchi can cause luminal narrowing. TO is reportedly unrelated to calcification within tracheal rings,¹⁰ the nodules being formed in tissue other than cartilaginous rings. TO can cause varying degrees of obstructive pneumonia.^{11,12} This did not occur in subjects in the present study.

By chest radiography this entity did not correlate with any abnormality of the lung fields or mediastinum. All 61 cases were elderly and the observation period spanned 13 years, suggesting there was no correlation between extensive tracheobronchial calcification and any respiratory disease.

Ectopic calcification may be metastatic or dystrophic, the former due to hypercalcinemia secondary to destructive processes in bone (e.g., bone metastases), hyperthyroidism, and processes such as hypervitaminosis D. Serum calcium levels were not determined for all subjects in the present study, but there were no other finding to suggest the presence of any such diseases. In dystrophic calcification, calcium is deposited in atrophied, degenerative, necrotic tissue, and in foreign bodies. The process of calcification in our subjects appeared to

気管支石灰化は、主に主気管支あるいは葉間気管支から気管の方向に進展するようである。

広範囲にわたる気管気管支石灰化は初回胸部X線撮影時に34名に認められ、その平均年齢は69.3歳であった。27名の対象者については、石灰化は追跡調査中に広範囲に広がり、その平均年齢は72.9歳であった。広範囲にわたる気管気管支石灰化は通常60歳以上の人に見られ、広範囲に至るのは70歳代の人に最も多いようである。気管気管支石灰化は男性よりも女性に多く発生すると報告されているが、本研究ではその傾向が非常に顕著であった。これは肋軟骨などの他の部位の石灰化と対照的である。⁹

本研究では、放射線学的あるいは組織学的に見て、気管あるいは気管支の狭窄、あるいは石灰化の内腔への突出を認めた対象者はなかった。

気管の形態は、種々の疾患により変化するが、気管気管支肥大症及び気管軟化症においては拡張し、軟骨骨形成性気管症、relapsing polychondritis及び"saber sheath" tracheaにおいては狭窄を起こす。軟骨骨形成性気管症においては、気管壁及び気管支壁に多くの石灰化が結節状に突出し、内腔の狭窄を引き起こすことがある。軟骨骨形成性気管症は、気管軟骨輪内の石灰化とは無関係であるとされており、¹⁰軟骨輪以外の組織に形成されると考えられている。軟骨骨形成性気管症には種々の程度の閉塞性肺炎が併発する。^{11,12}これらの所見は、本研究における対象者には認められなかった。

胸部X線撮影写真上、石灰化と肺野、あるいは縦隔に認められる異常との間に関連はなかった。61例すべてが高齢者で、観察期間は13年間にも及んだが、このことは広範囲にわたる気管気管支石灰化と呼吸器疾患との関連は認められないことを推察させる。

異所性石灰化は転移性あるいは異栄養性のもので、前者は骨の破壊過程(骨転移など)、甲状腺機能亢進症及びビタミンD過剰症に伴う高カルシウム血症が原因である。本研究では、対象者の血清カルシウム値は測定されていなかったが、このような疾患を示唆する臨床所見は指摘されなかった。異栄養性石灰化では、カルシウムは萎縮・変性・壊死を起こした組織及び異物中に沈着する。本研究の対象者の石灰

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