TECHNICAL REPORT
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業 績 報 告 書

IDIOPATHIC PULMONARY HEMOSIDEROSIS: A CASE REPORT HIROSHIMA

特発性肺臓ヘモシデリン沈着症: 1症例の報告 広島

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TABLE OF CONTENTS
目　次

LIST OF ILLUSTRATIONS
写真一覧表

IDIOPATHIC PULMONARY HEMOSIDEROSIS: A CASE REPORT
特発性肺臓ヘモシデリン沈着症　1症例の報告

INTRODUCTION

The diagnosis of idiopathic pulmonary hemosiderosis was made recently in a Japanese child referred to Atomic Bomb Casualty Commission (ABCC) because of abnormal radiologic findings in the chest. A search of recent Japanese medical literature failed to produce a report of idiopathic pulmonary hemosiderosis although the number reported from Europe and the United States is increasing.[1] Pathological features of this disease first were well described by Ceelen in 1931,[2] but it was not until ten years later that Waldenstrom[3] reported the first antemortem diagnosis of this condition. The main clinical features of this syndrome are anemia, cough, hemoptysis, dyspnea, and abnormal chest roentgenogram usually occurring in a child or young adult. The natural history of this disease is one of remission and exacerbation, and it usually terminates fatally. The diagnosis is confirmed by demonstrating hemosiderin laden macrophages in the sputum, fasting gastric contents, or in the lung parenchyma by means of needle aspiration.[4]

CASE REPORT

A seven year old Japanese female was referred to ABCC in Hiroshima because of anemia and abnormal radiologic findings of the chest. Her chief complaint was listlessness. The child was in good health until the age of four years nine months when she had an illness characterized by pallor, dyspnea, and malaise. There was no cyanosis or hemoptysis. She was anemic and

緒　言

胸部X線上異常があるため紹介を受けた日本人少女を最近原爆傷害調査委員会（ＡＢＣＣ）において診察した結果，特発性肺臓ヘモシデリン沈着症と診断したので報告する．日本における近年の医学文献を調べても，特発性肺臓ヘモシデリン沈着症の報告例を見ないが，欧米では本症の報告は増加している．[1] 本症の病理学的特徴は1931年に Ceelen によって詳細に報告されたが，[2] それから10年経過して初めて Waldenstrom [3] によって患者の生存中に本症の診断がつけられた．この症候群の主な臨床的特徴は，貧血，咳嗽，喀血，呼吸困難および胸部X線上の異常所見で，通常小児あるいは青年に生じる．この疾患の経過では緩解と増悪が繰り返され，通例死の転機をとる．喀痰，空腹時の胃内容物，あるいは穿刺によって得た肺実質の中にヘモシデリンを含む大食細胞を検出することによって診断は確立される．[4]

症例報告

７才の日本人女児は貧血および異常な胸部Ｘ線像のため，ＡＢＣＣに紹介された．主訴は元気がないことであった．患児は４才９カ月まで健康で，その頃，蒼白，呼吸困難および倦怠感を特徴とする疾病に罹患したが，チアノーゼや喀血はなかった．貧血があり，ツベルクリン反応が陽性で，胸部Ｘ線像の異常が認められたのでパス

was noted to have a positive tuberculin skin reaction and radiologic examination showed an abnormal chest. Because of these findings she was treated with para-amino salicylic acid and streptomycin for six months. She also received three blood transfusions during this period. A follow up chest film was reported as normal.

The patient was well until February 1960 when she developed hemoptysis and fever during a family and neighborhood epidemic of an influenza-like illness. Her illness lingered and pallor developed. She was found to be anemic and 500 cc of whole blood was given. The chest roentgenogram was abnormal at this time and on March 16, 1960, she was seen in the ABCC clinic for diagnostic evaluation.

She was the product of a normal delivery and weighed 2.65 kg at birth. There were no abnormalities noted at that time. Her mother had some kidney disorder during pregnancy. The child was breast fed; both nutrition and development were considered normal during infancy. In early childhood her appetite was poor. The primary constituents of her diet were boiled rice, seaweed, and occasional eggs. At six years of age she had measles and mumps. Her academic record has been below average.

A paternal uncle died of pulmonary tuberculosis prior to the patient's birth.

On physical examination the child appeared thin but not acutely ill. The oral temperature was 37.7°C; the pulse was 130/minute. Respirations were 22/minute and regular. Blood pressure was 90/56 mm of mercury. She was pale, but there was no icterus or cyanosis. Firm, easily movable, nontender, pea-sized lymph nodes were palpable in the axillae, inguinal areas, and the neck. Examination of the chest revealed the left lower thorax to be more prominent than the right. Respiratory excursions were equal. Harsh breath sounds were heard over the left upper lung field, but the rest of the pulmonary examination was normal. A grade I blowing apical

およびストレプトマイシンによる治療を6カ月間受けた．この間輸血を3回受けた．その結果，胸部X線再検査は正常といわれた．

その後，1960年2月まで健康であった．その頃，家族および近所の人々に流行性感冒に似た疾患が流行し，本患児は喀血および発熱を生じた．この疾患は長引き，次第に蒼白になり，貧血のために，合計 500cc の輸血を受けた．その際の胸部X線検査では異常があり，1960年3月16日，診断および検査のためにＡＢＣＣで診察を受けた．

本患児の出産状態は正常で，出生時体重は2.65kgであった．出生時に異常は認められなかった．母親は妊娠中腎疾患に罹患したことがあった．母乳栄養児で，乳児期の栄養および発育は正常といわれた．幼児期の食欲は不良で，主として御飯，海苔，時々生卵を食べるだけであった．6才の時麻疹と耳下腺炎を経験した．学業成績は平均以下であった．

父方の伯父は患児の出生前に肺結核で死亡した．

診察所見：痩身であるが，重症疾患のようには見受けられない．口腔体温37.7°C，脈搏 130，呼吸22で整，血圧90／56．蒼白であるが，黄疸やチアノーゼはない．腋窩部，鼠径部および頸部に堅い可動性の豌豆大のリンパ腺を触れるが圧痛はない．左下胸部は右側に比べて隆起している．呼吸運動は左右均等である．左上肺野に鋭利な呼吸音を聴取するが，その他の肺の診察所見には異常

systolic murmur was heard, but it disappeared when the patient assumed sitting position. The liver edge was palpable two fingerbreadths below the right costal margin in the midclavicular line, but it was not tender. The upper border of liver dullness was within normal limits. The spleen was not palpable. The rectal examination was unremarkable, and the remainder of the physical examination was within normal limits.

The laboratory results revealed a hemoglobin of 7.3 gm per cent and a hematocrit of 29.0 per cent. The reticulocytes were 29.2 per cent. There was a positive guaiac reaction in the stool. Other preliminary tests were normal with the exception of the routine radiologic examination of the chest (Fig. 1) which showed consolidation of the right middle lobe, probable atelectasis of the anterior portion of the right lower lobe, and parenchymal infiltrates in the left upper and left lower lobes. Five days later the patient was admitted to the diagnostic ward for further study.

はない．心尖部に第1度の吹鳴性収縮期雑音を聴取するが，これは坐位で消失する．肝縁を鎖骨中央線上で右季肋下2横指触れるが，圧痛はない．肝臓濁音界の上縁は正常範囲内である．脾臓は触れない．直腸診で異常はなく，その他の全身所見は正常範囲内である．

臨床検査所見：血色素量 7.3g％，ヘマトクリット29.0％，網状赤血球29.2％．便のグアヤック反応は陽性．その他の検査の結果はいずれも正常である．胸部X線検査で（図1），右肺中葉の硬化像，右肺下葉前部の拡張不全の疑い，および左肺上葉に実質性浸潤を認める．患者は更に検査のため5日後に入院した．

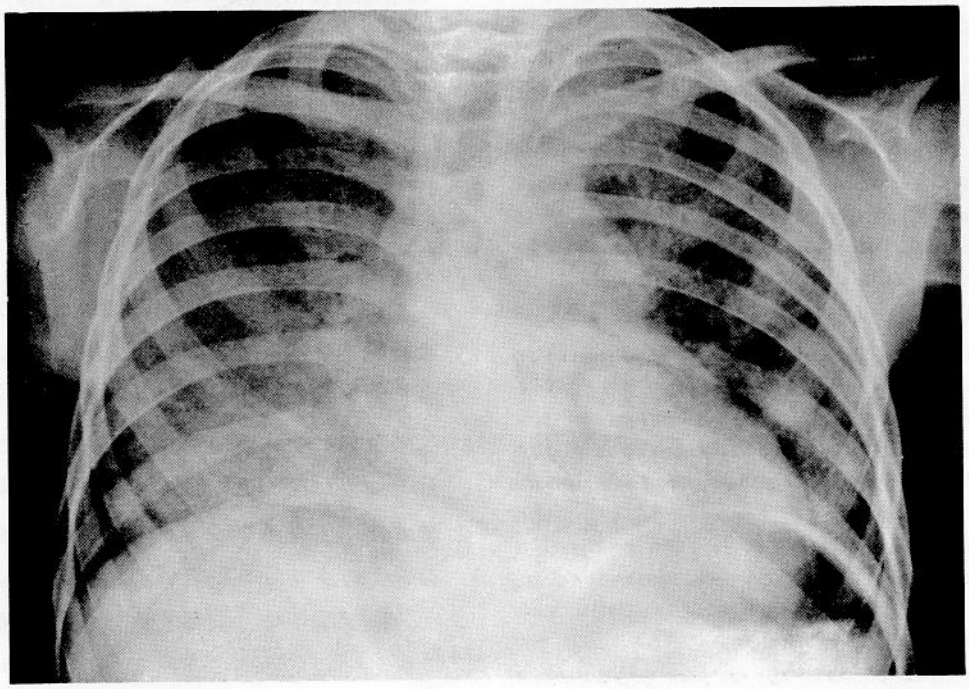

FIGURE 1 CHEST ROENTGENOGRAM MARCH 16, 1960 SHOWING DIFFUSE OPACIFICATION OF RIGHT LUNG FIELD AND MOTTLED LEFT LUNG FIELD DENSITIES

図1　1960年3月16日の胸部X線像．右肺野に瀰漫性陰影及び左肺野に斑状陰影を認める．

Additional laboratory studies showed the red cell indices to be hypochromic and microcytic with a reticulocyte count of 20.2 per cent. The erythrocyte sedimentation rate (Wintrobe) was 12 mm in one hour, and the platelet count was 152,500 per cu mm. The total leukocyte count was 6650 per cu mm with 82.0 per cent neutrophils, 14.0 per cent lymphocytes, 1.0 per cent monocytes, 1.5 per cent eosinophils, and 1.0 per cent basophils. The smear revealed moderate anisocytosis, basophilic stippling, and hypochromasia. The bleeding time, clotting time (Lee and White) and prothrombin time were normal. Sternal bone marrow was interpreted as moderate late erythroid hyperplasia. Erythrocyte osmotic fragility was normal. (Hemolysis began at .46 per cent NaCl and was complete at .38 per cent). Mechanical fragility of erythrocytes was normal (3.8 per cent). The serum iron was 7 mcg per cent with an unsaturated iron binding capacity of 286 mcg per cent. The nonprotein nitrogen and fasting blood sugar determinations were normal. The total serum protein was 6.5 gm per cent. The albumin was 4.3 gm per cent, and the globulin was 2.2 gm per cent. Total bilirubin was 5.91 mg per cent and the direct reacting fraction was 1.05 mg per cent. Bromsulphalein dye retention was 1.5 per cent after 45 minutes. The alkaline phosphatase was 8.97 Shinowara-Jones units. The thymol turbidity and cephalin flocculation tests were normal, and the serum glutamic oxaloacetic transaminase was 40 units.

The chest roentgenogram upon admission showed marked interval changes (Fig. 2). Complete resolution of the processes in the right middle and right lower lobes had occurred. The densities in the left upper and left lower lobes remained. On the second day of hospitalization the patient's temperature was 38°C. She was noted to be icteric, and the tip of the spleen was palpable but nontender. She had an episode of hemoptysis which was productive of bright red blood mixed with white sputum. During her three weeks' stay in the hospital she had a total of four

追加臨床検査所見：赤血球指数は低色素性小赤血球性で，網状赤血球は20.2%である．血沈1時間値12mm(Wintrobe法)，血小板152,500/mm³．白血球総数は6,650/mm³，好中球82.0%，リンパ球14.0%単球 1.0%，好酸球 1.5%，好塩基球 1.0%．血液塗抹検査では中等度の赤血球大小不同症，塩基性顆粒および血色素減少症を認める．出血時間，凝血時間（Lee-White法）およびプロトロンビン時間はいずれも正常．胸骨骨髄穿刺所見は中等度の後期赤血球系過形成を示すと解釈される．赤血球の滲透圧に対する抵抗検査は正常（溶血開始はNaCl 0.46%，溶血完結は0.38%）．赤血球の機械的作用に対する抵抗検査は正常（ 3.8%）．血清鉄 7 mcg%，不飽和鉄結合能 286 mcg%．残余窒素および空腹時血糖値はいずれも正常．血清総蛋白量 6.5 g%，アルブミン 4.3 g%，グロブリン 2.2 g%，総ビリルビン量5.91mg%，直接ビリルビン1.05mg%，ブロムサルフアレン滞溜45分後に 1.5%．アルカリ性フオスフアターゼは 8.97 Shinowara-Jones単位．チモール混濁反応およびセファリン絮状反応はいずれも正常．血清グルタミン酸・オキサロ醋酸トランスアミナーゼ40単位．

入院時の胸部X線検査では前回の検査に比べて著明な変化を認めた（図２）．すなわち，右肺中葉と下葉の陰影は完全に消失していた．しかし，左肺上葉と下葉の陰影は残存していた．入院２日目の体温は38°C で，黄疸を認めた．脾臓の尖端を触れたが圧痛はなかった．喀血が１回あり，白色の喀痰にまじって鮮紅色の血液があった．３週間の入院期間中に，同様な喀血が計４回生じたが，しばしば胸部診察を実施したにもかかわらず特記所見はなかった．入院中，黄疸は徐々に軽減した．入院後１週間たつと脾臓を触れなくなった．約２

similar episodes of hemoptysis, but frequent examinations of the chest were unrevealing. Her jaundice decreased gradually during her hospital stay. One week after admission the spleen was no longer palpable. The temperature gradually returned to normal after remaining slightly elevated for two weeks. The radiologic examination of the chest one week after admission showed mottled densities in the left lower lobe. The similar densities in the left apical region which had been noted one week previously were only faintly visualized. One week after admission the total bilirubin was 1.87 mg per cent, the hemoglobin was virtually unchanged, but the reticulocyte count was 8.8 per cent. Urinary urobilinogen which had been elevated upon admission returned to normal after ten days.

週間微熱が続いたが，その後体温は徐々に正常になった．入院1週間後の胸部X線検査では，左肺下葉に斑状陰影を認めた．1週間前の検査でこれに似た陰影が左肺尖部に認められたが，今回はかすかに残存していただけであった．入院1週間後の総ビリルビン量は1.87mg%．血色素量には実質上の変化はなかったが，網状赤血球は 8.8%であった．入院時に増加していた尿ウロビリノーゲンは10日後には正常に回復していた．

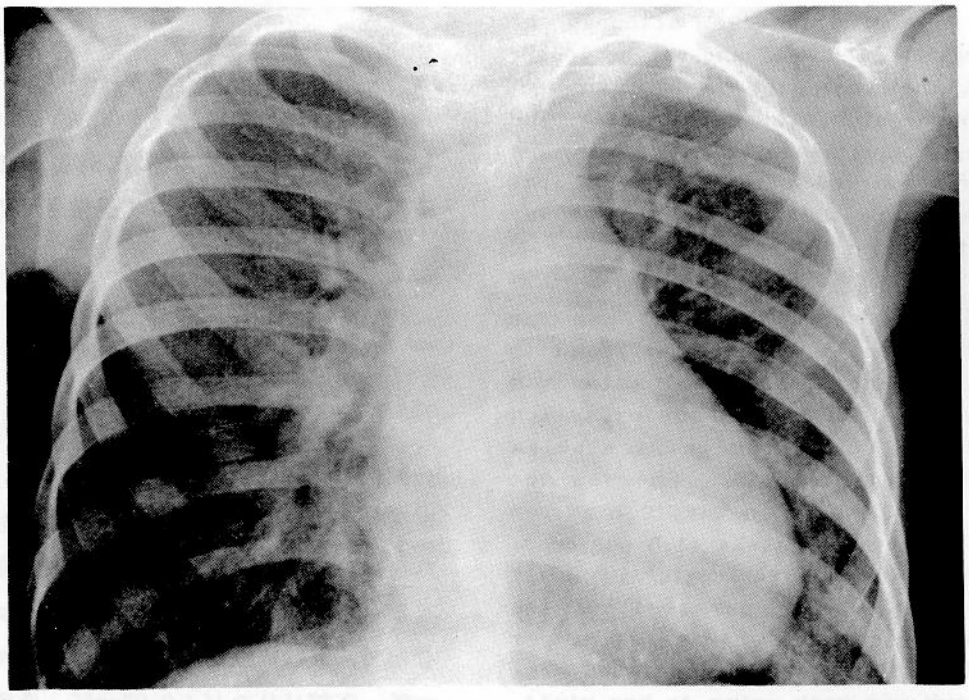

FIGURE 2 CHEST ROENTGENOGRAM MARCH 22, 1960 SHOWS RESOLUTION OF RIGHT LUNG FIELD OPACIFICATION

図2　1960年3月22日の胸部X線検査．右肺野の陰影の消失を認める

Pertinent negative laboratory results included the Coombs' test, heterophile agglutination test, and the cold agglutination test. The routine sputum culture revealed a mixed flora plus Candida *albicans*. Numerous sputum collections and

その他の臨床検査所見では，Coombs試験，異種抗体凝集反応および寒冷凝集反応は正常であった．喀痰培養検査では雑菌と白色カンジダを認めた．抗酸菌の有無について繰り返し喀痰および

gastric wash examinations for acid fast bacilli were negative. The PPD skin test of intermediate strength was positive. Numerous stool examinations revealed Enterobius and Trichocephalus ova, and on one occasion there was a strong positive guaiac reaction. Because of this finding an upper gastrointestinal series was performed, but this was interpreted as normal. The electrocardiogram revealed high voltage of the QRS complex.

胃液検査を実施したが，いずれも陰性であった．精製蛋白ツベルクリン皮内反応は陽性であった．繰り返し検便を行なった結果，蟯虫および鞭虫卵を認めた．グアヤック反応は1回強陽性であったので，胃腸のX線検査を実施したが，その所見は正常と解釈された．心電図検査ではQRSの高電位差を認めた．

The patient's history along with episodes of hemoptysis, and marked interval change of the chest roentgenograms suggested the diagnosis of idiopathic pulmonary hemosiderosis. Intracellular hemosiderin was demonstrated in macrophages recovered from both the sputum and fasting gastric wash specimens.

患児の病歴および喀血の事実と，胸部X線像にその後著明な変化があったことは，特発性肺臓ヘモシデリン沈着症の診断を示唆した．喀痰および空腹時の胃液から大食細胞中のヘモシデリンが検出された．

At the time of discharge, although the patient was feeling well and was no longer jaundiced, the hemotocrit was 23.0 per cent and the hemoglobin 6.2 gm per cent. The reticulocyte count was 7.8 per cent. The patient was started on a program of oral ferrous sulphate therapy, 0.6 gm per day and was discharged to her home.

退院時には患児の気分は良好で，黄疸も認められなかったが，ヘマトクリット23.0%，血色素量 6.2g%，網状赤血球 7.8%．1日 0.6g の硫酸第1鉄の内服を開始して退院させた．

One month after discharge from the ward the patient was seen and found to be well. The physical examination was within normal limits with the exception of a palpable liver, again 3 cm below the right costal margin. She was not icteric. The hemoglobin was 12.5 gm per cent and the hematocrit was 41.0 per cent. Reticulocytes were 4.3 per cent. The total bilirubin was 1.45 mg per cent and the direct reacting fraction was .07 mg per cent. The patient had discontinued oral iron therapy one week prior to her visit, and the serum iron was 57 mcg per cent. The unsaturated iron binding capacity was 190 mcg per cent. Radiologic examination of the chest revealed a decrease in the parenchymal densities in the left upper and left lower lobes. There was very faint opacification in the region of the right midlung field. Again the patient was discharged home on a similar therapeutic

退院後1カ月して患児の診察を行なったが，一般状態は良好であると認められた．その時の診察所見として右季肋下に肝縁を3cm触れたが，それを除いては正常範囲内であり，黄疸は認められなかった．血色素量12.5g%，ヘマトクリット41.0%，網状赤血球 4.3%，総ビリルビン量1.45mg%，直接ビリルビン0.07mg%．患児はこの診察の1週間前に鉄剤の内服を中止していた．血清鉄57 mcg%，不飽和鉄結合能 190mcg%．胸部X線検査では左肺上葉と下葉の実質性浸潤の減少を，また右中肺野に非常にかすかな陰影を認めた．前回と同様に鉄剤内服を継続するよう指示を与えて患児を帰宅せしめた．2カ月後に患者は再診察を

program. She was seen two months later at which time she reported no episodes of cough, icterus, or hemoptysis. She had failed to gain weight since her hospital admission. The liver edge was palpable, and at this examination the splenic tip was palpable and nontender. The hemoglobin was 10.8 gm per cent and the hematocrit was 33.0 per cent. Reticulocytes were 8.1 per cent. Urinalysis was normal. The total bilirubin was 2.25 mg per cent and the direct reacting fraction was .24 mg per cent. Again the patient had discontinued iron therapy one week prior to her visit and the serum iron was 25 mcg per cent. The unsaturated iron binding capacity was 270 mcg per cent. The patient's chest roentgenogram revealed no interval change in the two month period. She was discharged and advised to continue oral ferrous sulphate therapy and to return to the clinic if she developed symptoms of her disease.

She returned to the clinic ten weeks later. Her family reported that one month prior to the visit, there had occurred an episode of pallor, jaundice, dyspnea on exertion, nausea and vomiting without fever and hemoptysis. The patient was not examined at that time, but her illness was said to have lasted about ten days. She had discontinued iron therapy after this brief illness. On physical examination the liver was palpable 2 cm below the right costal margin; the spleen was not palpable. Examination of the chest was within normal limits. Again she had failed to gain weight. Laboratory studies revealed a hemoglobin of 11.2 gm per cent and a hematocrit of 38.0 per cent. The reticulocyte count was 2.4 per cent. The serum iron was 10 mcg per cent with unsaturated iron binding capacity of 369 mcg per cent. The stool and urine examinations were within normal limits. The total bilirubin was .83 mg per cent and the direct reacting fraction was .03 mg per cent. Radiologic examination of the chest revealed the previously described densities in the left lower and left upper lobes. Faint opacification of the right midlung field

受け，その間に咳嗽，黄疸あるいは喀血はなかったと述べた．入院以来，体重の増加は認められなかった．肝縁および脾臓の尖端を触れたが，圧痛はなかった．血色素量10.8ｇ％，ヘマトクリット33.0％，網状赤血球 8.1％．検尿は正常．総ビリルビン量2.25mg％，直接ビリルビン0.24mg％．患児はこの診察の１週間前に鉄剤内服を再び中止していた．血清鉄25mcg％，不飽和鉄結合能270mcg％．胸部Ｘ線検査では２カ月前の検査に比べて変化は認められなかった．患児は帰宅したが，硫酸第１鉄の内服を継続し，かつこの疾患の症状が生じた場合には診察を受けに来るよう勧めた．

患児は10週間後に再び訪れた．この時の家族の言によれば，診察の１カ月前に蒼白，黄疸，労作時呼吸困難，悪心，嘔吐および喀血があったが，発熱はなかったとのことであった．この病状は約10日間続いたが医師の診察を受けなかった．この短期間，症状のあった間は鉄療法を中止した．診察所見として右季肋下に肝縁を２cmふれ，脾臓はふれなかった．胸部検査は正常範囲内であった．この時も体重の増加は認められなかった．臨床検査所見としては，血色素量11.2ｇ％，ヘマトクリット38.0％，網状赤血球 2.4％，血清鉄10mcg％，不飽和鉄結合能 369mcg％，検便および検尿はいずれも正常範囲内．総ビリルビン量0.83mg％，直接ビリルビン0.03mg％．胸部Ｘ線検査では前回同様左肺上葉と下葉に陰影を，また右中肺野にかすかな陰影を，そのほかに横隔膜右葉前部の肋膜肥厚を認めた．心電図は正常範囲内．患者に以前と同じ療法を継続するよう指示し，３カ月に１回診察を受けに来るよう勧めて帰らせた．患児は７週間後に再び訪れた．この時，４日前より咳嗽，発

熱，呼吸困難，頻脈および倦怠感があると訴えた．祖母の言によれば，この間，患児に黄疸が生じたとのことであった．患児は蒼白で結膜の軽度の黄疸が認められた．口腔体温38°C，脈搏 102，呼吸促迫が認められたが，チアノーゼはなかった．右中肺野背面にラ音を聴取し肝縁を右季肋下に3 cmふれた．血色素量 8.7 g %，網状赤血球 9.9 %．尿ウロビリノーゲンは増加していた．総ビリルビン量3.98mg%，直接ビリルビン0.24mg%．血清鉄29mcg%，不飽和鉄結合能 223mcg%．胸部X線検査では前回にみられた肺実質性浸潤の増加を認めた．これは気管支構造の輪郭を明らかにし，また心臓右縁を不鮮明ならしめている（図3）．患児に入院を勧めたが，家族の希望で自宅で治療を行なうことになった．

again was noted along with pleural thickening of the anterior portion of the right leaf of the diaphragm. Electrocardiogram was within normal limits. The patient was discharged on the same therapeutic regimen as previously and advised to return to the clinic at quarterly intervals for examination. She returned seven weeks later complaining of cough, fever, dyspnea, tachycardia, and malaise of four days' duration. Her grandmother said the child was icteric during that period. She was pale and had slightly icteric conjunctivae. The oral temperature was 38°C; the pulse 102; and she was tachypneic, but there was no cyanosis. Rales were audible over the right midlung field posteriorly. The liver was palpable 3 cm below the right costal margin. The hemoglobin was 8.7 gm per cent and the reticulocyte count was 9.9 per cent. Urinary urobilinogen was elevated, and the total bilirubin was 3.98 mg per cent with a direct fraction of .24 mg per cent. The serum iron was 29 mcg per cent and the unsaturated iron binding capacity was 223 mcg per cent. The chest roentgenogram revealed an increase in the extent of the previously described parenchymal densities and showed the aerated bronchial structures and a lack of definition about the right cardiac border (Fig. 3). Hospitalization was advised, but the patient's family wished to keep her at home.

考　按

この患児の疾病には特発性肺臓ヘモシデリン沈着症の特徴が多い．その中で最も重要なことは，空腹時の胃液および喀痰中に細胞内ヘモシデリンを検出したことである．胸部X線の異常像，喀血，黄疸，臨床的に明白な心疾患の欠如，貧血等を認め，全般的病像は本症の特徴を指摘する．本患児の正確な発病の時期を決定することは困難であるが，4才の時に認められた胸部X線像上の異常と貧血は肺結核であったのかも知れない．肺結核であろうとの考えを裏付けるものとしては，ツベルクリン皮内反応の陽性および結核化学療法実施後

DISCUSSION

There are many features of this illness which indicate that the patient has idiopathic pulmonary hemosiderosis. The most important of these is the demonstration of intracellular hemosiderin in the fasting gastric wash and sputum specimens. Combined with anemia, an abnormal chest roentgenogram, episodes of hemoptysis and jaundice, and the absence of clinically evident heart disease, the overall picture is characteristic. It is difficult to date the precise onset of this patient's disease for the episode of anemia in association

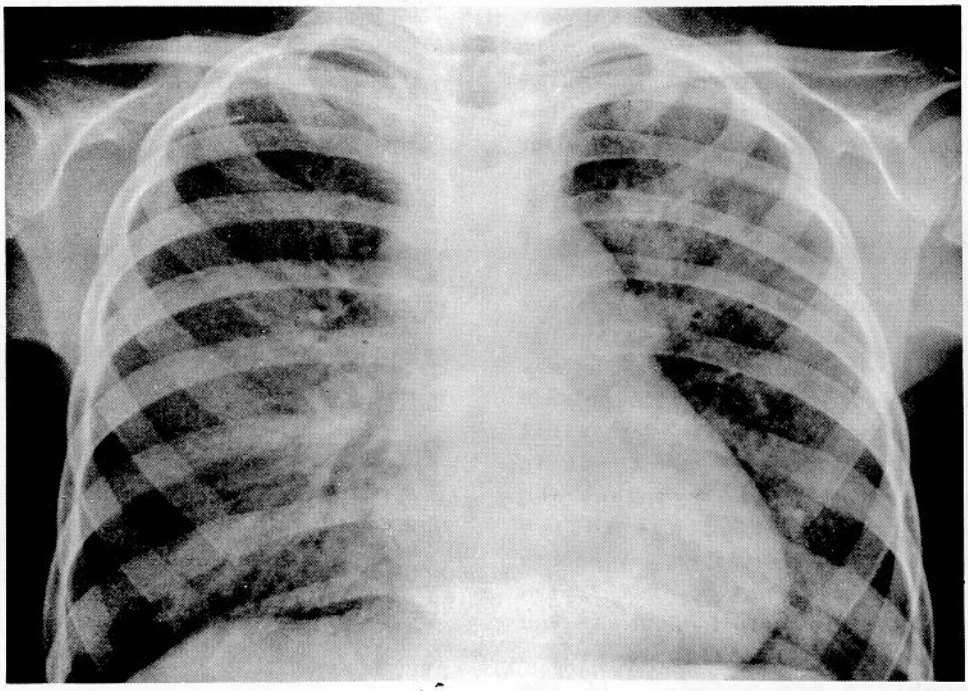

FIGURE 3 POSTEROANTERIOR CHEST ROENTGENOGRAM OCTOBER 31, 1960 SHOWING INCREASE IN PARENCHYMAL DENSITIES IN LEFT UPPER AND RIGHT LOWER LOBES

図3　1960年10月31日の背腹方向胸部X線検査．左肺上葉及び右肺下葉に実質性浸潤の増大を認める

with radiologic demonstration of pulmonary abnormalities at age four may have represented pulmonary tuberculosis. Other features in favor of this are the positive tuberculin skin test and the change in radiologic findings in the lungs after the course of antituberculous chemotherapy. No bacteriological studies or tests for hemosiderin were performed at that time. However, in retrospect, it is felt that this was the first episode of intra-alveolar bleeding. The patient's most recent episodes again represented mild bouts of intrapulmonary hemorrhage.

Until recently, idiopathic pulmonary hemosiderosis was thought to be a disease virtually limited to children and with a uniformly bad prognosis. However, as more cases have been reported,[1] adults are seen to be afflicted[5] with this syndrome, and prolonged[6] and suspected complete[7] remissions have been described. The age of onset usually is in early childhood, but a few of the adult cases have been described

における胸部X線所見の変化である．その際，ヘモシデリンに対する検査および細菌学的検査は行なわれていない．しかしながら，振り返ってみると，この時に最初の肺胞内出血があったのかも知れない．本患児の極く最近の発病も軽度の肺内出血を示すものである．

最近まで特発性肺臓ヘモシデリン沈着症は元来小児に限定された疾患であり，その予後は一様に不良であると考えられてきた．しかしながら，症例報告が増加するにしたがって，[1] 成人もこの症候群に罹患することが認められ，[5] 長期の緩解[6]や完全な緩解[7]があったと思われる例が報告されている．発病年齢は通常幼児期であるが，少数の成人の症例では発病の時期が30才以後であることが報告されている．[6] 男女別の罹患率は小児期と

with onsets at age greater than 30 years.[6] The sex incidence changes from the childhood to the adult form. In the younger patients, the disease is more common in females than in males; whereas in adults the ratio is reversed. A recent review has documented 37 cases with onset at age 16 or older.[5]

Classically, the acute attack consists of dyspnea, cough, hemoptysis, cyanosis, tachycardia, fever, and pallor. These are the effects of the acute intra-alveolar hemorrhage. After a few days icterus may appear and within a week or two the episode will be terminated. The lack of physical signs on auscultation of the chest is impressive in view of the symptoms and abnormal radiologic findings in the chest. The chest roentgenogram may become progressively clearer, or the infiltrates may remain stationary. Marked anemia and reticulocytosis; sometimes leukocytosis and eosinophilia are noted.[8] If the acute episode progresses, acute cor pulmonale may develop, and death will ensue. Hepatosplenomegaly, clubbing of the fingers and toes, and hematemesis from swallowed blood may be observed. The subacute episodes may be difficult to detect since the symptoms are limited to cough, mild anemia, dyspnea, and minimal hemoptysis.

Bronson[5] recently has reviewed the radiologic findings in this disease. Small nodular infiltrates frequently are bilateral and predominantly in the perihilar and lower lung field areas. However, all parts of the lung are susceptible, and pleural effusion has also been described in an adult patient. The infiltrates may vary in size from a few millimeters to 3 cm in diameter and sometimes will have radiolucent centers. The large areas of homogenous densities seen during acute attacks often clear and sometimes are replaced by a pattern quite similar to interstitial fibrosis or granulomatosis. In fact, radiologic findings often are confused with hemosiderosis secondary to sustained pulmonary

成人では異なっている．若年患者では，この疾患は男性よりも女性に多く，成人ではこの割合が逆になっている．文献の再検討を行なって症例をまとめた最近の報告によれば，発病期が16才ないしそれ以上であった症例数が37例あった．[5]

典型的な例では，急性発作では呼吸困難，咳嗽，喀血，チアノーゼ，頻脈，発熱および蒼白が認められる．これは急性肺胞内出血の影響である．数日後に黄疸が現われることがあり，１，２週間内にこの症状は終る．症状および胸部Ｘ線像に異常があるにもかかわらず胸部打診上，理学的所見が欠如することは印象的である．胸部Ｘ線上の陰影は漸次消失するか，あるいは浸潤が停止性の場合もある．著明な貧血および網状赤血球増多症，時には白血球増多症および好酸球増多症が認められる．[8] 急性発作が進行すれば，急性肺性心が生じ，その後に死亡する．肝肥大，棍棒状指趾および嚥下された血液による吐血が観察されることもある．亜急性の発病では，症状が咳嗽，軽度の貧血，呼吸困難および極く少量の喀血に限定されるので，発見が困難である．

Bronson[5]は最近この疾患の放射線学的所見を再検討した．小さな結節状浸潤がしばしば両肺に認められ，これは主として肺門周囲および下肺野に認められる．しかしながら，これは肺の各所に起り得る．また成人では肋膜滲出液を伴なうことも報告されている．浸潤はその大きさが様々であって，直径数mmから３cmにおよび，時には中心がＸ線透過性のものもある．急性発作期間中に認められる大きい均質性陰影部位はその後消失することがしばしばあり，時にはそれに代って間質性線維症あるいは肉芽腫症に極めて類似した像が現われる．事実上，Ｘ線像は僧帽弁狭窄，粟粒結核，

hypertension as in mitral stenosis, miliary tuberculosis, other granulomatoses, or carcinomatosis. Multiple pulmonary hemangiomata with recurrent bleeding may cause similar radiologic and clinical findings.[9]

The etiology of the anemia has been puzzling because of the coexistent features of iron deficiency and hemolysis. Recently Apt *et al*[10] by using radioisotopic techniques have demonstrated that the anemia is caused by blood loss into the alveoli, and for still unknown reasons the iron is sequestered in the lungs. Apparently the amount of blood destroyed in the lungs is sufficient to account for the observed hyperbilirubinemia. Unlike a hemolytic anemia the erythrocyte survival is normal when corrected for blood loss, the serum iron is low, and most of the sequestered iron is unavailable for reutilization in hemoglobin synthesis. These excellent studies also demonstrated that during remission, erythropoiesis and erythrocyte survival were normal.

As the pulmonary lesion becomes more extensive, anoxemia develops and because of embarrassed oxygen diffusion, compensatory erythrocytosis may be observed. Thus, a normal hemoglobin in a late stage of the disease occasionally is seen.

Pathological findings are limited to the lungs, mediastinal lymph nodes, and occasionally the myocardium. The lungs are heavy, firm, and dark red in color, and there is enlargement of the tracheobronchial nodes. There may be right ventricular hypertrophy, and in four reported cases there has been an associated myocarditis.[11] The alveoli are crowded with red blood cells and hemosiderin laden macrophages. There may be hemosiderin granules lying free in the alveoli as well as in the tracheobronchial nodes. There is a markedly increased amount of hydrolyzable iron in the lungs.[12] Hemosiderin seldom is found in the liver, spleen, or other lymph nodes. Pulmonary interstices are thickened and contain

その他の肉芽腫症あるいは癌の場合のように，持続性肺循環系高血圧に続発したヘモシデリン沈着症としばしば混同される．また，たびたび出血を伴なう多発性肺血管腫が類似したX線像および臨床所見を生じることがある．[9]

貧血の病因は明らかでなく，鉄欠乏と溶血現象という特徴が共存している．最近，Apt 等[10]が放射性同位元素を用いた検査で，貧血が肺胞内への失血によって惹起され，かつ原因は不明であるが鉄が肺内で分離されることを証明した．肺内で破壊される血液の量は，臨床的に観察される過ビリルビン血症の原因となるに十分であるように思われる．溶血性貧血とは異なり，血液損失を補正した場合には赤血球寿命は正常であり，血清鉄は低く，分離された鉄の大部分は血色素合成に利用されない．これらの優れた研究によって，緩解中は赤血球造血および赤血球寿命はいずれも正常であるということも証明された．

肺病変が一層広範囲になるにつれて無酸素血症が生じ，不十分な酸素拡散のため代償性赤血球増多症が観察されることがある．したがって，この疾患の末期では血色素量が正常であることが時折認められる．

病理学的所見は肺，縦隔洞リンパ節，時には心筋に限定される．肺は充実し，堅く，暗赤色を呈し，気管気管支リンパ節の肥大がある．右心室肥大が認められることもあり，報告の4例では併発性心筋炎があった．[11] 肺胞には赤血球とヘモシデリンを含む大食細胞が詰まっている．気管気管支リンパ節のほかに，肺胞内にもヘモシデリン顆粒が遊離していることがある．肺内では水解性鉄

hemosiderin as do the elastic fibers of the alveolar septa and smaller blood vessels. Since the elastic fibers are frequently fragmented and deficient in number, in the past some authors[3,8] have felt that this is the primary lesion of the disease. However there are well documented reports[13] that show normal elastic fibers in the presence of acute cases. Now it is considered a result rather than a cause. There may be a diffuse interstitial pulmonary fibrosis as a result of long standing disease. Recently an acute fatal nephritis has been observed in a few young adults with the disease.[14]

Concepts are plentiful, but the true pathogenesis has yet to be delineated. Steiner[15] has championed an auto-immune mechanism with the lungs being the 'shock' organ. He has had inconsistent results using splenectomy in treatment of the disease. In 1939, Anspach[16] noted necrotising arteritis of the lungs at the autopsy of one patient with the syndrome. The occasional therapeutic response to adrenal steroids and ACTH[17] also supports the immunologic theory. Lendrum[18] believes that diapedesis of red blood cells at the junction of pulmonary artery radicals and the bronchial vasculature is the source of intra-alveolar bleeding. Some authors postulate a defective vasomotor control of the pulmonary vascular bed causing episodes of transient pulmonary hypertension,[1] whereas others feel that a change in the permeability of the capillary bed is responsible.[5] Newer theories are those of Propst[19] who has demonstrated excessive acid muco polysaccharide in the elastic fibers, thus weakening them and causing bleeding. One might speculate that it is this increased muco polysaccharide which binds the iron and sequesters it in the lungs. Herzog[20] has demonstrated proliferation of pulmonary capillary argyrophil fibers, and he considers this to be the primary lesion of idiopathic pulmonary hemosiderosis.

As may be expected in diseases which are poorly understood, the treatment for this

の量が著明に増加している.[12] ヘモシデリンは肝臓，脾臓あるいはその他のリンパ節中にはほとんど認められることはない．肺胞間質は肥厚し，肺胞中隔および細小血管の弾力線維も同様にヘモシデリンを含む．弾力線維はしばしば離断し，その数が不足しているので，ある著者は[3,8] これがこの疾患の原発性病変であると考えた．しかしながら，急性症例において弾力線維が正常であることを示した詳細な報告がある.[13] 現在ではこれは原因というよりもむしろ結果であると考えられている．長期にわたる疾患の結果として，瀰漫性間質性肺線維症が認められることがある．最近本症を伴なう数名の青年患者に致命的な急性腎炎が認められた.[14]

この疾患に対する考え方は種々あるが，真の病因はなお解決の余地がある．**Steiner**[15] は肺が主な病変器官（**Shock organ**）であるとして，自己免疫機構を主張した．彼はこの疾患の治療に脾剔出術を用いたが，その結果は一様ではなかった．1939年に **Anspach**[16] はこの症候群のあった１名の患者の剖検で壊死性動脈炎を認めた．副腎皮質ステロイドおよびＡＣＴＨ療法[17] が時折有効であることは免疫説を支持するものである．**Lendrum**[18] は肺動脈基根部と気管支血管系の連結部における溢血が肺胞内出血の原因であると考えている．数名の著者は肺血管壁の血管運動調節に欠陥があり，それが一過性肺循環系高血圧の原因になると仮定するが,[1] 他の者は毛細血管壁の透過性の変化がその原因であると考えている.[5] 最新の学説としては，**Propst**[19] の説があり，彼は弾力線維内に過剰の酸性ムコ多糖類を認め，それにより弾力線維が弱まって出血を生じることを証明した．この増加したムコ多糖類が鉄と結合し，肺内で鉄が分離するのであると推測されるかも知れない．**Herzog**[20] は肺の毛細血管の好銀性線維の増殖を証明し，これが特発性肺臓ヘモシデリン沈着症の原発性病変であると考えた．

syndrome leaves a great deal to be desired. Some newer modes of therapy have been mentioned, but basically the treatment consists of supportive measures for the anemia, hemoptysis, and episodes of pulmonary and cardiac decompensation.

本症の本態が不明であるために，この症候群に対する治療についてはなお不十分な点がはなはだ多い．最新の治療法のいくつかに言及したが，基本的には治療は貧血，喀血および肺と心臓の代償不全に対する対症療法である．

SUMMARY

A case of idiopathic pulmonary hemosiderosis in a Japanese child has been investigated and described. The diagnosis was confirmed by the demonstration of hemosiderin in phagocytes of the sputum and gastric juice. The clinical course, pathology, radiologic findings, and concepts of pathogenesis have been discussed. It is unlikely that the lack of case reports in the literature represents the true incidence of the disease in Japan.

総　括

日本人小児における特発性肺臓ヘモシデリン沈着症の1症例を報告した．診断は喀痰および胃液の大食細胞中にヘモシデリンを検出して確認した．臨床経過，病理学的，放射線学的所見および病因論の概念に考察を加えた．日本に本症例の報告はないが，このことは日本におけるこの疾患の真の発病率を示しているとは思われない．

REFERENCES
参考文献

1. Soergel, K.H.: Idiopathic pulmonary hemosiderosis; review and report of two cases, Pediatrics 19:1101-1108, 1957.
(特発性肺臓ヘモシデリン沈着症，2症例の検討と報告)

2. Ceelen, W.: Die Kreislaufstoerungen der Lungen, in Handbuch der speziellen pathologischen Anatomie und Histologie, edited by Henke F. und Lubarsch, Springer-Verlag, Berlin, 1931, Band 3, Teil 3, p. 20.
(肺の循環障害，特殊病理学的解剖学および組織学便覧)

3. Waldenstrom, J.: Relapsing, diffuse, pulmonary bleedings or hemosiderosis pulmonum - new clinical diagnosis. Acta Radiol 25:149-162, 1944.
(再発生瀰漫性肺出血すなわち肺臓ヘモシデリン沈着症—新しい臨床診断)

4. Gellis, S.S., Reihold, J.L.D. and Green, S.: Use of aspiration lung puncture in diagnosis of idiopathic pulmonary hemosiderosis. AMA Amer J Dis Child 85:303-307, 1953.
(特発性肺臓ヘモシデリン沈着症の診断における吸引肺穿刺法の利用)

5. Bronson, S.M.: Idiopathic pulmonary hemosiderosis in adults; report of a case and review of the literature. Amer J Roentgenol 83:260-273, 1960.
(成人における特発性肺臓ヘモシデリン沈着症，1症例の報告と文献の検討)

6. Boyd, D.H.A.: Idiopathic pulmonary haemosiderosis in adults and adolescents. Brit J Dis Chest 53:41-51, 1959.
(成人および思春期児童における特発性肺臓ヘモシデリン沈着症)

7. Browning, J.R. and Houghton, J.D.: Idiopathic pulmonary hemosiderosis. Amer J Med 20: 374-382, 1956.
(特発性肺臓ヘモシデリン沈着症)

8. Wyllie, W.G., Sheldon, W., Bodian, M. and Barlow, A.: Idiopathic pulmonary hemosiderosis (essential brown induration of lungs). Quart J Med 17:25-48, 1948.
(特発性肺臓ヘモシデリン沈着症（本態性肺臓褐色硬化症)

9. Stefanini, M. and Dameshek, W.: The Hemorrhagic Disorders. A Clinical and Therapeutic Approach. New York, Grune and Stratton. 1955, p. 62.
(出血性疾病，その臨床および治療方法)

10. Apt, L., Pollycove, M. and Ross, J.F.: Idiopathic pulmonary hemosiderosis. A study of the anemia and iron distribution using radioiron and radiochromium. J Clin Invest 36: 1150-1159, 1957.
(特発性肺臓ヘモシデリン沈着症：放射性鉄および放射性クロムを用いて行なった貧血と鉄分布の研究)

11. Campbell, S. and Macafee, C.A.: A case of idiopathic haemosiderosis with myocarditis. Arch Dis Child 34:218-222, 1959.
(心筋炎を伴なう特発性ヘモシデリン沈着症の1症例)

12. Jonsson, B., Vahlquist, B. and Agner, K.: Essential pulmonary hemosiderosis. Blood 6: 665-671, 1951.
(本態性肺臓ヘモシデリン沈着症)

13. Nancekievill, L.: Acute idiopathic pulmonary haemosiderosis. Brit M J 1:431-432, 1949.
(急性特発性肺臓ヘモシデリン沈着症)

14. MacGregor, C.S., Sleigh Johnson, R. and Turk, K.A.D.: Fatal nephritis complicating idiopathic pulmonary haemosiderosis in young adults. Thorax 15:198-203, 1960.
(青年における特発性肺臓ヘモシデリン沈着症を併発した致死性腎炎)

15. Steiner, B.: Essential pulmonary haemosiderosis as an immuno-haematological problem. Arch Dis Child 29:391-397, 1954.
(免疫血液学的課題としての本態性肺臓ヘモシデリン沈着症)

16. Anspach, W.E.: Pulmonary hemosiderosis. Amer J Roentgenol 41:592-596, 1939.
(肺臓ヘモシデリン沈着症)

17. Irvin, J.M. and Snowden, P.W.: Idiopathic pulmonary hemosiderosis; report of case with apparent remission from cortisone. AMA J Dis Child 93:182-187, 1957.
(特発性肺臓ヘモシデリン沈着症, コーチゾン投与によって緩解が生じたと思われる症例の報告)

18. Lendrum, A.C.: Pulmonary haemosiderosis of cardiac origin. J Path Bact 62:555-561, 1950.
(心臓に起因する肺臓ヘモシデリン沈着症)

19. Propst, A.: Morphologie und Pathogenese der essentiellen Lungenhamosiderose. Arch Path Anat 326:633-663, 1955.
(本態性肺臓ヘモシデリン沈着症の形態学と病理学)

20. Herzog, G.: Zum Wesen der sogenannten idiopathischen Hemosiderosis Pulmonum. Ber d Oberhees Ges f Natur u Heilkunde zu Giessen, Naturw Abtlg 27:199-214, 1954.
(いわゆる特発性肺臓ヘモシデリン沈着症の本質)