Mechanisms of Fatal Pulmonary Hemorrhage in Tuberculosis

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Fatal hemorrhage is not an uncommon mode of exitus in patients afflicted with pulmonary tuberculosis. Perhaps the most disturbing feature is that many of the individuals who are stricken have passed the acute phase of their illness and apparently are on the road to recovery.

The incidence of fatal hemorrhage has been estimated by different authors to be from 1 to 5 per cent.¹ A survey of 2,500 autopsies at the Municipal Tuberculosis Sanitarium revealed that 109 cases (4.36 per cent) died in this manner. Of this total, 70 were men and 39 were women, and the greatest incidence was in the age group 20 to 29 years (Figure 1). The youngest and oldest individuals to suffer fatal hemorrhage were 11 and 65 years of age respectively. Of the 109 only 49 gave a history of having had any previous bleeding or hemorrhage. The chronicity of the disease was certainly a factor, the interval of time varying from one month to 21 years, and 33 patients gave a history of having had the disease for a period of four years or over. Twenty-two had pneumothorax for varying lengths of time, the maximum being four years, however, their disease was of such a nature that in only a few instances was any beneficial effect noted clinically, and no relationship to hemorrhage could be shown. The most common complication was amyloidosis—24 cases (22 per cent), showed gross and/or microscopic evidence of amyloid degeneration (this is about the same percentage as is seen routinely in our autopsy work). There was one case each of hypertensive heart disease, chronic glomerulonephritis, syphilis, and silicosis.

There is no chronological pattern as to the occurrences of these fatal hemorrhages. For example, in the years 1933, 1934 and 1935 several were recorded, and the next comparable number was in the middle 1940's; however, the highest total for any single year occurred in 1949. In spite of the chemotherapeutic and surgical measures employed in the past few years the incidence of fatal hemorrhage has remained about the same. Since chronicity is a fact it stands to reason that procedures which prolong the course of the disease also increase the likelihood of sudden fatal hemorrhage. This is especially true in cases which are far-advanced at the time of admission to the sanitarium. (During the last five years this group comprised 75 per cent of all admissions to our institution.) One cannot discount the observations of Petersen² in which he correlated hemorrhagic episodes in the tuberculous patient with conditional changes in the meteorological environment. These episodes he associated with blood pressure increases attributable to pressor changes.

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One usually associates fatal pulmonary hemorrhage with the rupture of an artery adjacent to or a part of a parenchymal cavity wall following an aneurysmal dilatation. These dilatations have been termed Rasmussen's aneurysms as Doctor Vald Rasmussen was the first to describe them in 1868. The number of these lesions identified in different institutions varies greatly and perhaps to some extent in proportion to the time spent dissecting the specimens. Proliferative and reparative processes usually prevent aneurysmal formation within tuberculous cavities by occluding the blood vessels before their walls are destroyed. Because of the magnitude of the hemorrhage and the destructive and/or reparative processes going on in the lung, it is almost impossible to demonstrate the site of bleeding; this is especially true in those cases in which the bleeding apparently results from the rupture of an aneurysm; whereas bronchial lesions which perforate or erode the adjoining vessel can be demonstrated with relative ease. Rasmussen pointed out in his article that many men before him had attempted to explain the causes and mechanisms of fatal pulmonary hemorrhage but had been rather unsuccessful in their attempts. Laennec supported the idea that frequently pulmonary hemorrhage came about by a diapedesis of blood through the bronchial mucus membranes. A factor favoring this theory was that vessels in the vicinity of the cavity, especially in the fibrous wall, were usually obliterated. This was true also for vessels which traversed the cavity, however, we know now that many of these vessels remain open. Andral was of the opinion that there were three possible sources of pulmonary hemorrhage: first, that seen in conjunction with a tuberculous endobronchitis, however, he was not in a position to demonstrate the actual bleeding point; second, bleeding in cases of pulmonary apoplexy (it is assumed that by this he meant vascular disturbances such
as hemorrhagic infarctions) and third, hemorrhage from a cavity. In this instance Andral was able to demonstrate a bleeding vessel in only one case—a vessel that was enclosed in a trabeculum crossing the cavity. Rokitansky was about the only writer who had described cases such as simulated those of Rasmussen. According to Rokitansky the copious hemorrhages seen in tuberculosis easily arose from branches of the pulmonary arteries situated in the condensed walls of cavities, especially bronchlectatic cavities. He was of the opinion that the vessel walls became macerated, jelly-like and soft due to exposure to the contents of the cavity and necrotic processes in the wall of the cavity so that finally they would burst into the cavity and a massive hemorrhage would take place. The lesion he described as either a split-like fissure in the vessel or the separation of a portion of the vascular wall gave rise to a punched-out defect. Very frequently this punched-out defect was seen in an aneurysmal dilatation of the vessel towards the cavity.

Rasmussen's observations were based on the examination of 11 cases who died during a violent hemoptysis. Eight of these were patients in whom there was a rupture of a vessel running in the wall of the cavity and the other three were instances of rupture of an aneurysm of the aorta into the bronchus or into the pulmonary tissue itself. Of the eight cases in which hemorrhage was due to a rupture of a vessel adjacent to a cavity, four demonstrated rupture of a small sac-like aneurysm which had developed on a branch of a pulmonary artery running in the wall of the cavity, and four showed dilatation or ectasia of a branch of the pulmonary artery with operculated rupture. These aneurysms varied in size from that of a pea to a walnut. The wall varied in thickness and in those which had not ruptured the wall was seen to be two or three times thicker than the rest of the vessel. The lesions were sometimes multiple and the vessels on which the aneurysms were located averaged from one to three millimeters in diameter.

Plessinger and Jolly studied a series of 667 cases from the years 1938 to 1947 and of these 49 died of massive pulmonary hemorrhage. In 29 of these cases they were able to demonstrate an aneurysmal dilatation of a vessel. On the basis of their histological studies, they describe the incriminative vessel as usually running tangential to the wall of the cavity. As the vessel broached the wall of the cavity it passed through its own diseased pulmonary tissue and started to dilate slightly. Concomitantly a variable degree of endothelial thickening usually occurred so that the lumen of the vessel was slightly constricted. Similar obliteratorative endothelial changes were observed in the other large vessels in the vicinity of the cavity wall. Serial sections revealed that the vessel wall proper dilated eccentrically; the dilatation taking place only on the side toward the lumen of the cavity. Finally a point of rupture of the media was encountered. A great deal of emphasis is placed on the presence of a fibrin clot in every unruptured aneurysm and in some of the ruptured aneurysms. They are in agreement with Rasmussen's theory that this clot may occasionally plug the rent in the aneurysmal sac and thus prevent a fatal hemorrhage for some time.
O'Leary\textsuperscript{5} reported a death occurring in a nine month old infant in which instance a recently ulcerated cavity eroded a large vessel. Certainly some of the cavities seen appear to be so rapidly excavating that proliferative changes in the neighboring blood vessels do not take place.

Codina Suque and Mansilla Delicado\textsuperscript{6} felt that bleeding might be the result of a profuse diapedesis of blood into the alveolar spaces quite removed from an active tuberculous process, or at least from an ulcerating lesion. They were of the opinion that what was commonly considered to be post-hemorrhagic “seeding” probably represented hemorrhagic areas complicating preexisting tuberculous foci. The preexisting tuberculous involvement we would assume to have been a recent bronchogenic or hematogenous dissemination from a “spilling” lesion elsewhere in the parenchyma or lymph nodes. These workers emphasize that it is not necessarily the amount of blood lost but the impingement on functional lung parenchyma which accounts for death.

Quiroga\textsuperscript{7} points out that fatal hemorrhage may be the result of a rapidly ulcerating caseous pneumonia (necrotic pneumonia of Sabourin) or from a rupture of small vessels constituting the vascular make-up of cavity walls. However, we have not seen sufficient evidence of bleeding from granulation tissue such as lines most tuberculous cavities to account for a fatal hemorrhage in any of the cases studied. Klosk\textsuperscript{8} reported a case of fatal hemorrhage due to rupture of a large branch of the pulmonary artery without aneurysmal formation—a circumstance he considered unique.

The inconsistency of the mechanism of fatal hemorrhage can best be illustrated by the following case reports:

\textbf{Case 1:} H.G., a 23 year old white man born in Chicago, contracted a severe cold with pleurisy and about 10 months later pulmonary tuberculosis was diagnosed. Pneumothorax was instituted and abandoned after a few treatments. He had

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure2.png}
\caption{Sagittal sections through the lungs showing two aneurysms filled with laminated blood clots and a huge cavity in the left apex filled with recently clotted blood.}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure3.png}
\caption{A Section through the left lung showing a large cavity in the apex filled with clotted blood and a small cavity in the mid-portion with a probe extending from the branch of the right pulmonary artery into the cavity.}
\end{figure}
frequent small hemorrhages and succumbed to a massive hemorrhage approximately 18 months after the onset of illness.

Pathology: There was considerable involvement of the left lung, as seen in Figure 2, and in the lower portion of the upper lobe cavity a huge laminated blood clot was found, and a small circular cavity in the lower lobe also contained a laminated blood clot. Infiltrations were noted in the opposite lung and there was considerable involvement of the pleura covering the organ. Here, we are dealing with two aneurysmal dilatations both filled with clotted blood and a rent in the wall of the larger one was responsible for a massive hemorrhage.

Case 2: M.J., a 35 year old foreign-born white woman whose husband had died from pulmonary tuberculosis one year before her admission. Her health was good, she maintained, until one month before coming to the sanitarium. Physical examination was essentially normal except for the chest which revealed dullness to percussion over the left lung and harsh breath sounds over both apices. X-ray film inspection revealed considerable involvement of the left lung and the sputum was positive for acid-fast bacilli. Her course was progressively downhill and she died six months after admission to the sanitarium with laryngeal and intestinal complications. Death, however, was sudden with a massive pulmonary hemorrhage. Pathology: Examination of this lung (Figure 3) revealed a 7 cm. cavity in the apex which was filled with a dark red blood clot. There was a smaller cavity measuring 2.5 cm. in diameter in the upper part of the lower lobe which was filled with what appeared to be an older clot and into this cavity protruded a 1.5 cm. aneurysmal dilatation of the pulmonary artery. Careful dissection revealed a rent in the wall of this aneurysmal dilatation which was the source of the bleeding.

Case 3: A.P., a 35 year old Negro woman entered the sanitarium approximately six months after the onset of illness. She had been coughing and expectorating considerable material prior to admission and there was occasional blood streaked sputum. She was known to have had hypertension for some time and her blood pressure on admission was 195/120. Previously induced pneumothorax on the right obscured the physical findings but x-ray film revealed considerable disease in the right lung with most involvement apparently in the mid-lung field. In spite of supportive therapy her disease progressed and was complicated by severe tuberculous laryngitis. Approximately 16 months after admission to the sanitarium she expired suddenly with massive pulmonary hemorrhage.

**Figure 4:** Sagittal sections of the lungs showing a large cavity in the left lower lobe filled with dark red clotted blood and scattered collections of blood throughout the opposite lung along with a large clot in the right main bronchus.—**Figure 5:** Close-up of the right lower lobe to show the flooding of the acini with blood.
Pathology: A middle section of the lungs (Figure 4) showed a large cavity in the left lower lobe with a heavy fibrous wall surrounding it and pneumonia consolidation in the adjacent parenchyma. The remainder of the lungs showed a flooding of the acini with blood (Figure 5). No residue of an earlier infection could be found and because of the nature of this lesion it was considered a young adult primary infection. Dissection failed to reveal any aneurysmal dilatation of a vessel; the source of hemorrhage was apparently the erosion of a branch of the pulmonary artery.

Case 4: W.N., a 43 year old white man whose mother had died from pulmonary tuberculosis when he was seven years of age. He was in fairly good health until four years before admission, at which time he had a severe cold with a cough and pulmonary tuberculosis was diagnosed. He had been in and out of the sanitarium on numerous occasions, usually leaving against medical advice. Six months before final admission he suffered severe pulmonary hemorrhage and continued to have blood-streaked sputum afterwards. He was a known alcoholic and physical examination revealed a poorly nourished white male who showed evidence of marked weight loss (50 pounds) with physical findings of a markedly enlarged liver, dullness over the right lung field and many rales over the entire right lung and the mid-portions of the left lung. During his six months stay in the sanitarium his lung picture did not change significantly but he had marked albuminuria, positive congo red test for amyloidosis, evidence of liver malfunction and sputum positive for acid-fast bacilli. He had a sudden massive pulmonary hemorrhage and expired.

Pathology: There was a huge dark red blood clot projecting out of the larynx (Figure 6) and on sectioning the lungs one saw that there was cavitation in both upper portions, that on the right being more extensive and most of the cavities were filled with dark red clotted blood. Extensive dissection failed to reveal the point of rupture of the pulmonary artery. The cyst-like cavities in the upper portion of the right lung communicated with bronchi and apparently represented old tuberculous cavities which had re-epithelialized (Figure 7).

**FIGURE 6**

*Figure 6:* Close-up of the larynx and upper portion of the trachea with a huge blood clot in place as was found at the time of post mortem examination.—*Figure 7:* Close-up of the anterior portion of the right apex showing the epithelialized cavities and revealing the smooth glistening nature of the lining with the exception of a portion of the cavity laterally situated which showed considerable ulceration and may have been the source of bleeding.
Case 5: S.F., a 43 year old Negro man who was born in Memphis, Tennessee, and had worked as a sand blaster for 14 years. The onset of his illness was approximately one year before admission to the sanitarium. His chief complaint was weakness; there had been one episode of hemoptysis. Approximately two weeks after entering the sanitarium he suffered a massive fatal hemorrhage.

Pathology: Sagittal sections revealed a large cavity in the right lung surrounded by consolidated parenchyma (Figure 8). Small firm nodulations were felt in portions of the lung. The left lung showed a cavity in the mid-portion and there were several caseous infiltrates noted in the lung parenchyma, especially in the upper portion. Smaller ulcero-caseous lesions were noted throughout the right lung.

Figure 8: Sagittal section through the lungs showing bilateral cavitation and the huge blood clot in the trachea and main stem bronchi. The hilar lymph nodes were markedly enlarged and showed caseous infiltrations. The peribronchial nodes on the left showed calcified lesions.—Figure 9: Sagittal section of the lungs demonstrating ulceration of the right main bronchus and its secondary branches and multiple fibrocaseous lesions in the parenchyma of the right lung.

Figure 10: Close-up to illustrate the ulceration of the right main bronchus showing the clot in place and the elliptical defect superior to it.—Figure 11: The reverse side of the lung showing the defect in the right pulmonary artery through which the blood escaped into the bronchial tree.
Figure 12: Sagittal section through the lungs showing both major bronchi and secondary bronchi filled with dark red clotted blood and darkly pigmented lymph nodes. Figure 13: Close-up to show the black peribronchial node projecting through the anterior wall of the right main bronchus.
The lymph nodes were hard and rubbery in consistency and on section showed whirls of fibrous tissue indicative of some degree of silicosis. None of the cavities showed a definite limiting fibrous wall and careful dissection failed to reveal a bleeding point. This undoubtedly represents a case of erosion of a vessel wall by one of these rapidly ulcerating lesions.

**Case 6:** T.L., a 61 year old white foreign-born woman who was known to have pulmonary tuberculosis for at least nine years before admission to the sanitarium. During that time she had three or four acute febrile episodes but at no time did she require sanitarium care. Her husband had died from tuberculosis about six years before and x-ray films were taken periodically to determine the status of her pulmonary lesion. A febrile episode two months before admission was accompanied by high temperature, pain in the chest, cough, fatigue, and weight loss, and she expectorated a few cc. of yellowish sputum which was positive for acid-fast bacilli. Sanitarium care was recommended. Aside from a blood pressure of 170/100 physical findings upon admission were limited chiefly to the right lung which revealed slight dullness on percussion and limited excursions. No rales were heard in the chest at the time of admission. During her stay in the sanitarium she was given a course of streptomycin for approximately 90 days with some improvement. Bronchoscopy revealed a tuberculous endobronchitis on the right with bronchostenosis. Because of this finding, right pneumonectomy was considered but she refused surgery. She was ambulatory for the most part during her stay in the sanitarium and occasionally showed some blood streaking of the sputum. Approximately 18 months after admission to the sanitarium she experienced a massive pulmonary hemorrhage.

**Pathology:** A mid-section of the lung showed several fibrocaseous infiltrations scattered throughout the right lung with some fibrosis and retraction of the right apex (Figure 9). A rather large solitary fibrocaseous lesion was noted at the periphery of the right mid-lung field. There was marked ulceration of the mucosa of the mainstem bronchus and the secondary bronchi on the right. In the anterior portion of the lower lobe bronchus, a few centimeters from its origin, a large oval defect was noted (Figure 10); this defect was almost entirely filled by an organized blood clot, however, there was a small elliptical opening superior to the clot through which a probe could be passed to communicate with the adjacent pulmonary artery. This case demonstrates well the erosion of a main vessel (Figure 11) by a long standing tuberculous endobronchitis.

**Case 7:** M.P., a 61 year old white woman, foreign born, gave a history of having had the “flu” several times. For one year prior to admission she had slow progressive loss of weight and a few days before suffered a rather severe hemoptysis with streaking of the sputum every day thereafter. She entered a private hospital where a diagnosis of tuberculosis was made. Her sputum was positive for acid-fast bacilli and other laboratory examinations were negative with the exception of low grade hypochromic anemia. On bed rest over a period of six months she gradually improved but suddenly expired with a massive pulmonary hemorrhage.

**Pathology:** At autopsy a defect was found in the left upper lobe bronchus. This defect measured 6 mm. in diameter and the base of it was formed by a firm peribronchial lymph node (Figures 12 and 13). In the right main bronchus the mucosa was extremely thin and transparent and pigmented peribronchial nodes could be seen shining through. The hemorrhage arose from the bronchial artery which was eroded by the hard tuberculous node.

**Case 8:** H.Z., a 26 year old white man was visiting friends in the city when he suffered a pulmonary hemorrhage and was admitted to the sanitarium as an emergency. He had never been treated in a tuberculosis sanitarium but he stated that at the age of two years he had whooping cough which necessitated hospitalization for 24 months. Subsequently, when he was admitted to grammar school
Figure 14: Sagittal section of the lung showing the small, round necrotic area in the right upper lobe branch. Only small fibrocaseous foci are apparent. No evidence of cavitation was found. Figure 15: Close-up showing the necrotic lesion and the slightly enlarged hilar lymph node. The node contains some small caseous infiltrations.
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A chest x-ray film was taken and his parents were informed that there was considerable scarring of his lungs compatible with healed tuberculosis. In the years following he was hospitalized frequently because of his "weakened" condition. He stated that recently he had developed slight cough with a very small amount of expectoration, experienced some chest pain, and had mild dyspnea on exertion. Occasionally there were evening temperature elevations up to 101 degrees F.

Physical examination revealed a well developed and well nourished white man apprehensive and acutely ill. Examination of the chest showed impaired resonance and bronchial breathing over the right base. Sputum specimen was negative for acid-fast bacilli. Three days after admission to the sanitarium he suffered a severe pulmonary hemorrhage and expired.

Pathology: A mid-section of the lung disclosed a few small fibrocaseous tubercles in the upper portion of each lung. These tubercles appeared to be fairly well encapsulated. At a point in the right bronchus where the upper lobe bronchus takes its origin there was a necrotic area approximately 1.0 cm. in diameter (Figures 14 and 15) and a section of this lesion revealed that the entire bronchial wall was involved in this necrotizing process. This lesion eroded a branch of the bronchial artery and was responsible for the massive hemorrhage that was seen. The parenchymal disease was quiescent.

Discussion

Probably a massive hemorrhage produces death by suffocation, although in some instances, the loss of blood itself may be sufficient to terminate a cachectic individual. An estimation of the actual blood loss is difficult, as one must consider the amount of blood coughed up and expelled and that found in the lung and gastro-intestinal tract at the time of post-mortem examination. There is not much doubt that, in some cases, the total volume approximates 1,000 cc. Most patients die suddenly following a massive hemorrhage, and do not present the picture of exsanguination. The amount of blood necessary to produce death by suffocation probably varies greatly and is dependent upon several factors. When the main airways are filled to overflowing (as seen in Figures 7 and 8) undoubtedly the individual is asphyxiated by his own blood. On the other hand, collections of blood in the functional parenchyma in a lung partially destroyed by a previous disease (as seen in Figure 5), and with limited reserve may likewise asphyxiate an individual even though the volume of blood is not so great.

The presence of a definite aneurysm has been the exception instead of the rule in the routine examination of lungs from fatal hemorrhage cases at this institution. It was impossible to identify the bleeding vessel in many cases, however, this is true in instances of hemorrhage from other organ systems. A compilation of the findings in 50 consecutive cases is listed below:

<table>
<thead>
<tr>
<th>Bleeding Point</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>None identified</td>
<td>36</td>
</tr>
<tr>
<td>Pulmonary artery (no aneurysm)</td>
<td>8</td>
</tr>
<tr>
<td>Rasmussen aneurysm</td>
<td>4</td>
</tr>
<tr>
<td>Bronchial artery</td>
<td>2</td>
</tr>
<tr>
<td>TOTAL</td>
<td>50</td>
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Even though the caliber of the involved vessels varied considerably in different cases no correlation could be made between the size of the vessel and the magnitude of the hemorrhage or the rapidity of death. Profuse
hemorrhage from the small bronchial arteries correspond to hemorrhages from the larger pulmonary artery branches because of the differences in pressure. The pressure in the lesser (pulmonary) circulation is estimated to be about one-sixth (mean value) that of the greater (systemic) circulation. Since the bronchial artery is derived from the aorta the pressure, no doubt, is consistent with systemic pressure. When the lung has wide spread involvement, the amount of blood flowing through the pulmonary arteries to the affected parts is proportionately reduced and the pressure is correspondingly less. Recent work by Marchand et al. has shown that the pattern of the bronchial arteries varies considerably in disease, however, the pressure within the vessels probably is not altered to any appreciable degree. In the two instances (Cases 7 and 8) where the bronchial artery was the source of bleeding, the lesion was located near the main trunk of the vessels. Whether the smaller ramifications of the vessel are ever involved is questionable; it is our feeling that a branch of the pulmonary artery is the most likely source of hemorrhage at any point in the lung distal to the secondary bronchi.

The cases presented emphasize the multiplicity of mechanisms involved in fatal massive hemorrhage. It is true that many cases show a ruptured Rasmussen’s aneurysm (and the incidence of this lesion varies with different institutions) but the majority reveal only an erosion of a branch of the pulmonary artery without any significant aneurysmal dilatation.

SUMMARY

A survey of 2,500 autopsies at Municipal Tuberculosis Sanitarium, Chicago, was made and a report of 109 cases whose deaths were attributable to pulmonary hemorrhage were analyzed. Selective cases were described in detail to illustrate the different mechanisms of massive hemorrhage and a review of the literature given.

RESUMEN

Se hizo una revisión de 2,500 autopsias en el Sanatorio Municipal de Chicago, entre ellas 109 muertes, fueron atribuidas a la hemorragia pulmonar. Se describen casos seleccionados en detalle para ilustrar los mecanismos diferentes de la hemorragia voluminosa y se revist la literatura al respecto.

RESUME

L’auteur à fait l’étude de 2,500 autopsies au Sanatorium Municipal de Chicago, et rapporte 109 cas dont la mort est imputable à une hémorragie pulmonaire. Il retient des cas significatifs pour illustrer les différents mécanismes de l’hémorragie massive, et fait la revue de ce qui a été publié sur ce sujet.

REFERENCES

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