On the Importance, in Post-Mortem Diagnosis of Yellow Fever, of the Microscopic Lesions described by ROCHA LIMA and HOFFMANN

by

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(With Plate 1.)

Not all of the more commonly known macroscopical lesions of yellow fever: jaundice, the appearance of the liver, usually slightly enlarged, with a diffuse yellow colouring like a dead leaf and similar to that seen in poisoning by phosphorus, cloudy swelling and fatty degeneration of the heart and kidneys, congestion of the digestive apparatus and contents of stomach looking like coffee dregs, need be apparent or even necessarily existent. This feature has been recently pointed out by ROCHA LIMA.

Of all these lesions, those of the liver undoubtedly appear to be the most constant, but even these may fail.

I was able to convince myself of this fact in a recent case of yellow fever, of a man coming from Fortaleza, State of Ceará, whose post-mortem examination I carried out at the Hospital PAULA CANDIDO in 1923.

Besides the appearance of the liver, which differs from what used to be considered as always present in the disease, the case was of interest on account of the haemorrhagic lesions seen in the lungs, which are rare in yellow fever, and, beside on account of the microscopic lesions, some of them occurring in the liver and described by ROCHA LIMA as characteristic for the disease, and others in the kidneys which HOFFMANN recently showed to be typical of yellow fever.

The finding of these two microscopi-
cal lesions was decisive, in the present instance, in assuring the post-mortem diagnosis of yellow fever, which indicates the practical importance they must have.

The clinical observation of the case, due to the courtesy of Dr. JOÃO PEDRO DE ALBUQUERQUE and Dr. TA VARES DE MACEDO JUNIOR, and the Protocol of autopsy are given.

*Observation. I. S., of Brazilian nationality, born in the state of Minas Gerais, 27 years of age, white, single, business man, 1rst. Class passenger of Brazilian S. s. Bahia.

Admitted to Hospital PAULA CANDIDO at noon on March 1.1923, on the fourth day of his illness (according to paper brought) in a serious condition, the outcome of which was death at 11.25 p. m. of the same night.

He had gone on board at Fortaleza (State of Ceará), where yellow fever was, at the time, epidemic; he became ill after the ship had left Recife (Pernambuco) and must therefore have gone on board while the disease was at its stage of incubation.

The following notes are taken from the clinical observation made in the hospital.

March 1.1923. Temperature 37° C., pulse 82. In the afternoon temp. 38° C., pulse 94. Clinical features: Jaundice. Feeling of uneasiness in epigastric region. Urine scanty and retained until 200 c. c. were removed which proved to contain a great deal of albumin, Singultus. Black vomit towards the end. After enterocolysis, colourless faeces are expelled.

Clinical Diagnosis. Yellow fever.

Protocol of Autopsy. (*) (N°.1943 of Pathologic Department of Instituto OSWALDO CRUZ).

The body is that of an adult male white Brazilian, well nourished and exhibits marked rigor mortis. The pupils are equal, moderately dilated, circular. The cornea are cloudy and dry. The skin, the buccal mucous membrane and the conjunctivae shows a diffuse yellowish discoloration, more accentuated on conjunctivae; the skin along the abdomen and the back of the thorax and arms shows extensive petechiae. The superficial lymphatic glands are not enlarged. There is no oedema.

A longitudinal incision is seen in right cervical region, giving passage to a rubber cannula which is in connection with the right common carotid.

Peritoneum is glistening and moist. In its dependent parts a few cubic centimetres of clear yellow fluid are found. Liver does not reach the costal margin. Fat of omentum preserved. Cecal appendix free and permeable. Diaphragm is at the fourth interspace on the right and fifth rib on the left.

On section there is a moderate amount of subcutaneous fat. The muscles are well-developed, dark-red, and moist.

Thorax. On removal of the sternum the precordial area appears normal. On opening the pericardium, there is a small amount of clear yellowish fluid.

Right lung shows some adhesions, not extensive to wall of thorax.

Mucous membrane at base of tongue reddened and showing some dots of a bright red colouring occupying the apex of the papillae. Small patches of a bright red colour are also seen along epiglottis and pharynx.

Mucous membrane of oesophagus pale. Trachea shows a mucous membrane of a dark red colouring and very moist. From the bronchi there flows a good deal of blood-stained fluid.

Left lung enlarged weighing 660 grams. Pleura shows at its base different-sized purplish-red patches. Crepitation reduced in both lobes. Palpation reveals ill-defined nodules of a not very firm consistence in upper lobe.

On cut section of superior lobe the surface shows a wedge-shaped zone with its base towards the pleura and prominent, irregular and of a very deep red almost black colour, other smaller zones of a very dark red colour are seen spread over the surface of section and are found on the surface of all sections made through this lobe.

No areas of consolidated lung tissue are to be seen.

In the inferior lobe the cut surface is of a dark red colour, very moist and giving upon pressure plenty of a dark red fluid.

The right lung is increased and weights 880 grams. In limited zones of the upper lobe the pleura is covered with firm, yellow membranes.

The inferior lobe shows a surface of section which may well be compared to that of the superior lobe of the other side. Areas of a deep red colour, slightly prominent, irregular and separated by zones of lung tissues of a lighter colour are present. There is no consolidation of the lung tissues.

Superior and middle lobes shows a cut surface of a

(*) One liter of formaldehyde solution was injected by the left carotid, at noon on March 2. Autopsy was undertaken at 3 p. m. on March 2.
deep red colour very moist which exsudes freethelys fluid on pressure, which is large in amount.

Heart not increased in size; epicardial fat pronouncedly yellow. On epicardium there are a few small points of a bright red colour. They are seen principally along the interventricular groove. Apex formed by left ventricle.

Cavities of heart not increased. Endocardium smooth and shining in its whole extension, with a slight yellowish tinge. Valves flexible and free. Intima of sorta shows a yellow colour and a smooth and shining surface.

Spleen increased in size and weighing 270 grams. Upon section areas, dry and brownish, are seen (partial fixation by formalin). Owing to the state of preservation of the organ (partial fixation) the lesions of the parenchyma can not be appreciated; connective tissue recognisable.

Adrenals apparently without lesion. Medulla of adrenals unsoftened (partial fixation by the formaldehyde).

Kidneys. Both kidneys of normal size. Right kidney weighs 170 grams and left 200 grams. Upon section areas, dry and brownish are seen (partial fixation by formaldehyde). The state of preservation of the organ (partial fixation) does not permit of a study of macroscopic lesions.

Bladder distended by urine of a yellow colour and slightly turbid. Great quantities of albumin are shown. In the urine by an albumin-test; a test for biliary pigments gives positive results, Mucous membrane of bladder pale.

Prostata and seminal vesicles without lesion.

Stomach contains a rather thick fluid of a black colour.

Folds little pronounced. Mucous membrane pale showing three small spots of about 2 millimetres of diameter of a bright red colour.

Mucous membrane of duodenum, jejunum, ileum and large intestine are pale along their whole extension. A few Ascaris were found in the jejuno-ileum.

Liver diminished in size, weighing 1100 grams. Righlobe globular. Left very much reduced. Anterior border rounded. Capsule thin and smooth. Consistence of organ more or less firm. Surface of organ of a pinkish-yellowish coloration, with areas in which the yellowish tone predominates. Vessels of capsule are turgent and form discretely distributed areas.

On section the cut surface is smooth with fairly distinct lobular markings. Small areas of a pinkish yellow colour and about the size of a liver lobule are to be seen separated from each other by grooves of a light red colour. Disseminated in an irregular fashion are other areas of the size of a liver lobule of a light yellow which stand out very clearly from the dominant pinkish-yellowish colour of the parenchyma. There is no evident increase of connective tissue. No areas of partially fixed tissue are seen like in the spleen and kidneys the formation does not appear to have penetrated much, which must be owing to the small amount injected (1 litre). The appearance is the same on all sections; the lobular markings are everywhere fairly distinct.

Biliary vesicle distended by fluid bile of a yellow colour.

Mesenteric lymph-nodes not increased.

Pancreas without macroscopic lesions.

Head. Bony parts normal. Dura-mater adherent on a normal extension. Inner surface smooth and shining. Vessels of the con vexitly are turgid. Leptomeninges containing fluid in their meshes, and with a jelly-like aspect which is more pronounced in the dorsal half of the brain. Vessels of base normal.

Upon section the little vessels appears like blood-se points. Areas of softening o r other macroscopical lesions are absent.


MICROSCOPIC STUDY

Liver:—Small pieces of liver treated with Sudan III and Scharlach R showed the existence of pronounced fatty degeneration.

Sections of material imbedded in paraffin showed very clearly the type of lesion described by ROCHA LIMA (Cf. Plate 1 fig. 2).

Fatty degeneration is marked, and is found without any other lesion round the portal spaces. In the intermediate portin of the liver lobule, besides fatty degeneration, there is necrosis of liver cells, which shows the peculiarity of of affecting discontinuously the cells of a liver trabeculae; the isolated cells affected by the necrosis are reduced in size, retracted, show a very eosinophile protoplasm and a nucleus in karyolysis or pyknosis. This type of necrosis is quite different from the one seen in chronic passive congestion and from a special type of necrosis, of embolic origin, which I have described elsewhere.
Blood capillaries are dilated, but not specially so. I did not see deposits of biliary pigments, nor inclusions in KUPFFER's cells. There is also no haemosiderin in the liver cells.

Kidney.—The sections showed the presence of edema of the capsular space, degeneration and desquamation of the capsular epithelium. Edema and extensive fatty degeneration of the renal epithelium occur, the lesion involving chiefly the cells lining the convoluted tubules.

Hyaline and hemorrhagic casts are present.

Extensive necrosis of the epithelial cells occur in other portions of the tubule (loops of HENLE, collecting tubules). The lumina became filled with necrotic desquamated cells surrounded by endothelial leucocytes; in some places one finds formless masses, which are deeply stained by the hematoxylin an appearance highly suggestive of calcification.

The process has not, in our material, the extension of the tubular lesions produced by mercuric bichloride; in fact, the calcified casts are rather scanty and escaped notice until our attention was specially directed towards its research.

CONCLUSIONS

Many of the macroscopic lesions usually seen in yellow fever may be missing or insufficiently clear to allow of a confirmation of the disease merely from the post-mortem macroscopic lesions.

Microscopic study is indispensable and will show two lesions which are considered typical for the disease.

One of them, described by ROCHA LIMA, consists in necrosis of liver cells, occurring in isolated cells of a trabeculae, chiefly midway between centre and periphery of a liver lobule, together with a more or less intense fatty degeneration. This lesion may be found in other diseases such as septic peritonitis, gangrenous appendicitis, acute yellow atrophy of liver, but its constancy and dispersion in the liver of cases of yellow fever, is, according to ROCHA LIMA's experience, one of the best characteristics of the disease, from the histological point of view.

In the present case it was very clear as can be seen from the illustration printed.

Another microscopic lesion, is one which HOFFMANN has recently called attention to, and which he was able to observe in 24 cases of yellow fever examined during the epidemic of 1906-08 in Havana, by such men as FINLAY, GORGAS, GUITERAS and others. It consists in the presence of calcified casts within the tubuli contorti and loops of HENLE, as is often seen in nephritis caused by mercuric bichloride. An acute diffuse nephritis has been demonstrated a long time ago, with parenchymatous degeneration and necrosis of the tubular epithelium in the different segments of the tubules and the formation of casts. LUTZ (personal communication) advises looking for urinary casts in all suspected cases of yellow fever, for, in this disease they have never been missed in his experience. The interesting point in HOFFMANN's observation is the frequency of these casts, which are made up of desquamated cells, fibrin and wandering cells, to become impregnated by an acute process, with lime salts, so that they appear a deep blue in hematoxylin preparations.

This lesion also occurs accidentally in various infectious diseases, but inconstantly and infrequently; it has not been observed in WEIL's disease.

At first examination I allowed HOFFMANN's lesion to pass unnoticed, which is what must have happened to a great number of pathologists who studied material of yellow fever. However, as soon as my attention had been called to the subject by reading HOFFMANN's paper, I was able to demonstrate the lesion in the first section examined. This alone shows, that in the case studied, it was discrete, though clear. By a minute study of the granular casts found in the tubuli contorti and principally in the terminal segments of the unifibrous tube (loops of HENLE and tubes of BELLINI), I was able to find in some of them irregular masses, structureless and staining with haematoxylin in the same way as tissues incrusted with lime salts; at times the little fragment incrusted with lime salts would take up the whole lumen of the tube, at other times several smaller masses would be formed, with the staining reactions of calcified tissues and lying in the midst of desquamated epithelial cells and wandering cells.
EXPLANATION OF PLATE 1.

Fig. 1 Macroscopic section of liver (case of yellow fever) showing preserved lobular outline.

Fig. 2 Section from the same liver (case of yellow fever) showing fatty degeneration and necrosis of liver cells, affecting often scattered cells of a trabeculae, chiefly midway between centre and periphery (ROCHA LIMA's lesion).

Fig. 3 Section of a convoluted tubule (case of yellow fever) showing calcified cast (HOFFMANN's lesion).

Fig. 4 Section of a loop of HENLE (case of yellow fever) showing desquamation and necrosis) of epithelial cells and a calcified cast (HOFFMANN's lesion).
1924—HOFFMANN, W. H., Los cilindros de cal en los riñones, un nuevo signo diagnostico de la fiebre amarilla. Sciencia Medica, Anno II, no. 6, pg. 284.


