

# Melanuria in the melanoma with reference to the urinary bladder: Brief history

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## Abstract

The far famed, weighty work of Willis on metastasis contains two statements on melanuria on the basis of the urinary bladder and even the liver. Therefore, this paper considers further evidences based on collating sufficient materials from *The Transactions of the Pathological Society of London*. The findings included wide ranging discussion of melanuria by the old masters themselves as well as at present.

**Keywords:** Cancer; Melanoma; Metastasis; Melanuria; History

## Introduction

Willis [1] left a legacy in his monograph, "The Spread of Tumours in the Human Body." According to his style, historical information was usually provided. For example, there was his slant thus: In the cases of Eberth and Mariconda, both of melanotic tumours, the kidneys appeared normal to the naked eye but, many glomerular emboli were found microscopically. From these glomerular deposits, Eberth saw extension of pigmented tumour cells into the tubules and he believed that this must be the usual cause of melanuria.

### Another angle was provided as follows:

Melanuria is seen chiefly in cases with extensive melanotic disease of the liver; in cases of melanomatosis without involvement of the liver, melanuria rarely occurs [2]. This probably means that melanuria is not essentially a sign of hepatic disease but, merely that it is a sign of very extensive melanomatosis, A condition in which the liver is frequently the seat of massive deposits.

A wider view needs to be obtained from *The Transactions of the Pathological Society of London* an Institution with the following interesting guidelines thus: Instituted for the cultivation and promotion of Pathology, by the exhibition and description of Specimens, Drawings, Microscopic Preparations, Casts or Models of Morbid Parts.

## Historical Texts

There were no growths in the urinary bladder according to Beadles [3] and Legg [4]. Single deposit was detected by Bryant [5], his observation being as precise as "One black nodule growing

from the anterior wall of the mucous membrane of the bladder." In the words of Mackenzie [6], "there is only a speck of the smaller size seen here and there." He added that the bladder contained about 2 oz. of bile-stained urine. Calvert and Pigg [7] were specific as regards the lesion: "On the mucous surface ... as one small black growth, a little bigger than a pin's head."

The case of Target [8] was so unique as to be in the museum at Guy's Hospital from 1859. The full description merits citation: On opening the bladder a soft pigmented polypus was found attached to the mucous membrane by a slender peduncle. It was situated on the posterior wall about an inch from the orifice of the left urethra. It was about the size of a filbert and its smooth surface was marked with patches of brown pigmentation giving it a stippled appearance. The pedicle was composed merely of mucous membrane, and was about one third of an inch in length. Histologically, the tumour was composed of small round and oval sarcomatous cells with granules of pigment scattered among them; the pigment was a light-brown colour and was arranged in clumps outside the cells. The tumour was thickly permeated with capillary vessels.

Fagge [9] contributed two cases: The more straightforward case displayed deposits as black spots in the lining of the pelvis of each kidney and that of the urinary bladder. The urine of the other patient was described fully: The urine contained in the bladder was of a dark brown colour, between Nos. 8 and 9 of Vogel's standard tints, but looking rather greenish in comparison with them. When set aside it deposited a loose flocculent material, which was very dark in hue and the super-natant liquid being much paler.

Under the microscope I found that the deposit consisted mainly of deeply pigmented casts of the uriniferous tubules, some almost black, others appearing to be uniform brown colour or containing scattered brown granules. There were also some colourless casts, partly hyaline, partly epithelial. In addition to the pigment in the casts, there was a large quantity of it in the form of granules, partly scattered over the field and partly aggregated together in clumps. Finally, there were certain rounded translucent bodies of a light brown colour with apparently pigmented nuclei for some of them were surrounded by masses of protoplasm. And some of the usual polymorphous epithelial cells from the urinary passages also contained much pigment.

## Discussion

The above historical material actually contained colorful conclusions. Therefore, it suffices to add what transpired before the recognition of melanuria as being basically specially tinged urine! Indeed, that stage revealed the failure of Virchow to appreciate the metastasis angle cited thus [9]: Virchow himself however, rather discredits these observations for he quotes Hoppe-Seyler as having shown that the urine in such cases is very rich in indicant and merely possesses to an exaggerated extent the property of turning black, which belongs in a less degree to healthy urine likewise. He even suggests that the presence of pigment in the renal secretion may have nothing to do with the melanosis as such, but may simply depend upon the fact that the liver is among the organs secondarily affected by the disease; that the colouring matter in the urine is of the same nature with that which exists in the new growths is he says unproven and he thinks that it is rather improbable than otherwise.

This failure of the “Father of Cellular Pathology” is reminiscent of another such misconception. Incidentally, I pointed this out back in 1962 as “The paradox of Virchow’s views on cancer metastasis” [10]. In it, the mistake again rested on his failure to reason along the lines of the cellular nature of cancer spread!

Actually, Fagge [9] himself came near to taking a correct stand. Note how he unfortunately dismissed the right theory as follows: And I may observe that the modern theory appears to me very doubtful, according to which a pigment-mole in any part of the body which shows no sign of having taken on an active growth is regarded as the source of infection from which melanotic sarcomatous growths have started. In my second case, I searched all over the body with the greatest care for a primary nodule and could find nothing and I have of course, no intention of denying that the affection very often spreads by infection from a tumour in the skin or in the eyeball. But, it does seem to me essential that any mole or mark which is to be regarded as its starting-point should

itself have increased in size towards the end of the patient’s life or at least that it should contain embryonic tissues like those of the supposed secondary growths.

## Conclusion

Nowadays, the simple position of melanuria is not only well established but also of continuing interest. For instance, Gambichler and his associates [11] presented a case report in which there was acute kidney injury in a patient with melanuria, diffuse melanosis and metastatic melanoma. Another case report centered on the sudden onset of melanuria in a patient with metastatic melanoma complicated with toxic epidermal necrolysis [12]. Yet another recent case is that of Eide [13] it presented thoroughly described disseminated malignant melanoma with generalized melanosis of the skin and other tissues, melanuria, melanoptysis and a dark brown blood serum. In his view, the appearances were in keeping with the relevance of “the glomerular melanoma cell emboli” recorded by previous authors.

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