MALIGNANT MELANOMATOSIS

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Malignant melanomata without a discoverable primary site are unusual. To be designated as such, a case must be subjected to complete autopsy and exhaustive search made of the skin, eyes, meninges, rectum, and other tissues in which primary tumors of this variety have been reported. Unusual, too, are cases of this neoplasm which show extensive involvement of bone. The case here reported combined both these features and because of them presented peculiarities of interest both clinically and pathologically. The difficulties presented to the clinician by such a case are shown by the fact that this individual was a patient in three different large hospitals with three different diagnoses, the correct conclusion being reached only on biopsy.

CASE REPORT

History: R. W., male, thirty-eight years of age, single, Scotch, was admitted to the Toronto General Hospital Dec. 14, 1934, and died Jan. 13, 1935. The Wassermann reaction was negative.

Complaining of severe aching pain in the left hip since July, the patient had been admitted to a hospital in October 1934. A diagnosis of tuberculosis of the left sacro-iliac joint was made, chiefly on the x-ray picture. A plaster spica was applied and the patient was transferred to a sanatorium for treatment. Here, further study and the rapid progress of the lesion resulted in a diagnosis of osteogenic sarcoma, osteolytic type. Subsequently a biopsy was performed on a mass in the right iliac fossa which projected from the wing of the ilium. This was reported "secondary melanotic sarcoma" (S-34/5277).

Many innocent appearing pigmented moles covered the skin. No history regarding their onset or any change in them could be obtained. The patient denied that any had given him trouble or had been removed. In front of the sacrum was a large mass palpable by rectum, firm, nodular, and somewhat tender. A smaller rounded mass fixed to the ilium was palpated abdominally in the right iliac fossa. The left leg was paralyzed and sensation was lost over the left foot. The rectal sphincter was lax. X-rays showed extensive destruction of the left lateral mass of the sacrum and a rounded mass partially calcified lying in front of the promontory. The patient had lost over 50 lbs. in weight during the previous six months. In spite of radiation therapy, weakness increased.

Autopsy (A-19/35: Drs. Belt and Plewes): The body was very emaciated, 169 cm. in length and weighing only about 80 lbs. Chronic decubitus ulcers were present over the sacrum and right great trochanter. The skin of the chest, upper and lower limbs and back was irregularly spotted by about 25 pigmented moles, varying in size from a pin-point to 6 mm. in diameter, and in color from pale pink to brownish black. A few were slightly hairy, the majority were just palpable, and all had a smooth rounded surface. None of the moles invaded the surrounding skin or was ulcerated. Ophthalmoscopic examination of the fundi of both eyes showed no tumor.

Three brownish-black, softened areas involved the outer aspect of the skull, two of which infiltrated the inner table and the outer aspect of the dura in the left parietal and right cerebellar regions. The pia arachnoid and brain were free of discoloration and tumor. The pericardium and parietal and visceral pleura were studded with rounded, inky-black blobs, which were often confluent. The lungs were irregularly consolidated and in the left
lungs was a large creamy-pink tumorous area with a softened center. The peribronchial lymph nodes were large with both anthracotic and melanotic pigmentation. The adventitia of the aorta and the intimal surfaces of the inferior vena cava andazygos vein showed multiple paint-like plaques of black tumor, which frequently were confluent.

A large tumor was present in the pelvis behind the peritoneum, invading the musculature and deeply infiltrating the left lateral mass of the sacrum, the ilium, andischium near the sacro-iliac joint. This measured 10 × 8 × 4 cm., was irregular in shape, black, and semi-fluid in consistency. The left acetabulum was completely eroded through, as were the cartilage and bone about the left sacro-iliac joint. The left half of the bony pelvis was freely movable separate from the sacrum, and the head of the femur was easily palpable from the pelvic cavity.

On the mucosal surface of the proximal jejunum a dark brown nodule 1 mm. in diameter was barely palpable and had a smooth surface. Several small dark brown tumors were present in the mesentery. The cecal mucosa was discolored a diffuse dark brown, but not the rectum. The large, distorted liver was involved in multiple masses of tumor measuring up to 8 cm. in diameter, which varied in color from white to sooty black. Where they reached the surface the masses appeared as rounded protuberances with umbilicated centers.

Several of the bodies of the thoracic and lumbar vertebrae were infiltrated by secondary pigmented growths which reached 2 cm. in diameter. A few of the pedicles and heads of ribs showed similar nodules and were softened. The adrenals, kidneys, spinal cord and its membranes were not invaded.

An ulcerating necrotic cystitis, acute ureteritis and pyelitis were related to obstruction by tumor. Bilateral bronchopneumonia was the probable terminal event.

Microscopic Examination: The pelvic tumor had much the same character in all sections. The cells were large, elongated or polyhedral, with a tendency to parallel arrangement. There were many distortions, whirls and herring-bone formations being prominent. The nuclei were mostly large, elongated, hyperchromatic, with bizarre forms. Mitotic figures were numerous. Often there were prominent single nucleoli. Some tumor cells were diffusely impregnated with finely granular golden brown pigment, especially where they were degenerating or necrotic. The greater part of the pigment was contained in large mononuclears, and some lay free interstitially. Perle's stain for iron in the brown pigment was negative.

Sections of lung showed an irregular filling of the alveolar spaces with acute inflam-
matory exudate. An area about a venule contained tumor cells laden with brown pigment. The large tumor was composed of whorl-like invasions of melanin-free polyhedral cells of irregular size and distribution and its center was necrotic. In some sections there was increased interstitial tissue congested with blood and endothelial cells containing melanin and anthracotic pigment. A melanin-laden tumor nodule was adjacent to a pulmonary arteriole.

The liver masses were composed of irregular-shaped cells with vacuolated cytoplasm and long processes which formed a fibrillar background. Pigment was distributed among the cells in varying amounts and varied in color from golden to dark brown. The liver cords were often compressed into capsule-like coverings for masses of malignant cells. The uninvolved parenchyma was congested and necrotic about central veins. In the spleen were a few isolated, pigment-bearing phagocytes but no malignant masses.

The mesenteric, aortic, and iliac lymph nodes contained both melanin-laden phagocytes and masses of tumor cells loaded with golden-brown pigment. Recent hemorrhages into tumor masses were noted in some hypogastric lymph nodes. In one mesenteric node the malignant cells were rounded and appeared like epithelium though many contained pigment. The hypophysis, suprarenal glands, and heart contained no tumor. The tubules of the kidney were often filled with casts of brownish bland matter.

Twenty sections from brown pigmented cutaneous moles were examined. Though pigmentation varied greatly, and the basement layer sometimes contained melanin, no evidence of a malignant invasion was found. Sections from the anorectal region were free of tumor. Five sections from the eye failed to disclose any malignancy, and showed no invasion or hyperplasia, though the usual amount of melanotic pigment was present. The dura mater showed melanin-laden tumor tissue on its outer surface only.

Anatomical Diagnosis: Secondary melanotic sarcoma of left hip, sacrum, ilium, spine, ribs, skull, lungs, pleura, liver, kidneys, inferior vena cava, azygos vein, and mediastinal aortic, iliac, pelvic, and inguinal lymph nodes; emaciation (extreme); serous atrophy of fat; acute confluent bronchopneumonia (bilateral); multiple abscesses of lungs; acute fibrous pleurisy; acute bronchitis; obsolete tuberculosis of lung and peribronchial lymph nodes; acute ulcerative cystitis; acute suppurative pyelonephritis; abscesses of kidneys; peri-urethral abscesses (prostatic); multiple benign melanomata of skin.

Résumé: In a clinical case of sacro-iliac disease of rapid onset, the diagnosis was finally established by biopsy as secondary melanotic sarcoma. Search of numerous cutaneous moles, eyes, rectum, and other possible sites for primary malignancy failed. There was widespread dissemination of malignant tumors, sometimes non-pigmented, which especially invaded the pelvic bones as well as the spine, ribs, and skull, the large veins and serous surfaces, and lymph nodes.

Discussion

Among 41,984 surgical specimens examined by the Department of Pathology of the Toronto General Hospital during the period January 1928 to June 1935, there were 93 (0.2 per cent) reported “melanotic sarcoma.” The primary sites of these tumors were as follows: skin 48 per cent, eye 41 per cent, unknown (clinically) 5 per cent, “melanotic whitlow” (3) 2 per cent, with single cases of primary lesions in nasal mucosa, brain, and glans penis. A similar order of frequency is obtained from the autopsy records, in which, over a period of ten and one half years, 4 out of 3,756 (0.1 per cent) cases were diagnosed as malignant melanoma. A search of all of the cases revealed only two instances of secondary tumor in bone: in one of these the primary site was the skin of the forearm and a mass attached to the humerus was later palpated; the other was found at autopsy in the spine.

The following table presents a résumé of these autopsies and includes one done by Dr. Heaton at the Hamilton Sanatorium, of which specimens were
presented to the museum with a complete report. These cases illustrate the variation in even a short series of malignant melanomata and include the case here reported.

**Malignant Melanomata**

*(From Specimens and Autopsy Records, Toronto General Hospital)*

<table>
<thead>
<tr>
<th>Reference</th>
<th>Primary Tumor</th>
<th>Bone</th>
<th>Other Organs</th>
<th>Duration</th>
<th>Age</th>
<th>Sex</th>
<th>Other Diagnoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hamilton Sanatorium, Dr. Heaton, Museum 162</td>
<td>Skin of back</td>
<td>None</td>
<td>Subcutaneous nodules, heart, spleen, pancreas, kidneys, adrenals, ovaries, mediastinal and abdominal nodes</td>
<td>3 1/2 years (surgical excision)</td>
<td>30</td>
<td>F</td>
<td>Bronchiectasis (generalized skin pigmentation)</td>
</tr>
<tr>
<td>A-232/29</td>
<td>Meninges</td>
<td>None</td>
<td>Brain, stomach, adrenal, lung, peritracheal lymph nodes</td>
<td>5 months</td>
<td>60</td>
<td>M</td>
<td>Melanomata of skin; syphilitic aortitis</td>
</tr>
<tr>
<td>A-355/31(10)</td>
<td>Adrenals</td>
<td>None</td>
<td>Subcutaneous nodules, urinary bladder</td>
<td>13 months</td>
<td>65</td>
<td>M</td>
<td>Chronic epididymitis; arteriosclerosis; cardiac hypertrophy</td>
</tr>
<tr>
<td>A-285/33</td>
<td>Eye</td>
<td>Spine</td>
<td>Subcutaneous nodules, liver, gallbladder, spleen, heart, adrenals, lungs, pancreas, prostate, peritoneum</td>
<td>4 years (enucleation)</td>
<td>75</td>
<td>M</td>
<td>Melanomata of skin; urethral stricture</td>
</tr>
<tr>
<td>A-19/35</td>
<td>?</td>
<td>Sacrum, ilium, ischium, spine, skull, ribs</td>
<td>Dura, pleura, peritoneum, liver, kidneys, lungs, lymph nodes, vena cava, azygos vein</td>
<td>7 months (radiation)</td>
<td>38</td>
<td>M</td>
<td>Bronchopneumonia; melanomata of skin; cystitis and urethritis</td>
</tr>
</tbody>
</table>

Besides the primary sites represented by the surgical specimens and autopsies above recorded, various authors have reported primaries in the conjunctiva (19), optic nerve, breast, esophagus (21), vulva, clitoris, uterus, vagina (7), maxilla (20), urethra, peripheral nerves (17), hard palate, small intestine (5), and rectum (6). Månsson (11) reports an autopsy on a boy of fourteen years in which the liver only was occupied by melanosarcoma. Miller (8) discusses the ovary as a primary site. These sites were all considered in the study of this autopsy. As already pointed out, the most common sites, skin and eye, were ruled out by macroscopic and microscopic search. The first symptoms were referable to the sacro-iliac joint, and the largest tumor at autopsy was found in this region. Whether the malignant tumor arose from the sheaths of the lumbar plexus, which was surrounded and infiltrated by it, could not be determined. If this was the primary tumor,
the fascia, muscle, cartilage, and bone must also be considered as possible sources, though primary malignant melanomas of these tissues have not been recorded. Geschickter and Copeland (18) state that in only 3 out of 169 cases were there metastases in bone and these were at the sites of nutrient vessels. Considering these facts, it seems useless to speculate further on the origin of this neoplasm. It is possible that the patient had had a mole removed from his skin sometime previously and had forgotten about it and that his terminal illness was the result of metastases only. Cases have been reported in which from the removal of the malignant growth even twenty years (12) have elapsed before generalized secondaries caused death. A case in our series was diagnosed melanotic sarcoma of the skin of the forearm by biopsy in 1922 and the patient is still well in spite of a recurrence in 1932.

**SUMMARY**

An autopsy is reported in which careful search failed to reveal the origin of a malignant melanoma. Clinically, the earliest manifestations were those of sacro-iliac disease. There was unusually extensive bone involvement as well as generalized metastasis.

A list of primary sites in cases of malignant melanoma examined as surgical specimens and at autopsy is given. The most common origins are the skin and eye. The peri-ungual tissues, nasal mucosa, glans penis, adrenals, and meninges are also represented as primary sites by specimens in this Department. Other primary malignant melanomas are mentioned as reported in the literature.

**Note:** The author is indebted to Dr. R. I. Harris for the clinical details of this case.

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16. **Smith, D. T.**: Evidence showing the existence of two distinct types of pigment cells capable of giving rise to melanotic tumors, Bull. Johns Hopkins Hosp. 36: 185, 1925.


