A Possible Case of Metastatic Carcinoma From Gulf Coast

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ABSTRACT
The cranium of a mature female from the Galveston area of the Texas Gulf Coast exhibits multiple osteolytic carcinomic metastases. The diagnosis, based on macroscopic and microscopic examination and radiographic studies, documents numerous lytic lesions with full thickness destruction of both inner and outer cortical tables and intervening diploe. All lesions exhibit crenelated nonreactive borders. X-ray films revealed spotted shadows indicative of unerupted lesions. Diagnosis of metastatic carcinoma is more compatible with the lesions observed than with multiple myeloma which produces characteristically smaller, more numerous lytic lesions which often become confluent, producing scalloped margins.

The skeletal response to metastatic neoplastic foci may be solely osteolytic (Tkocz and Bierring, 1984), solely osteosclerotic with reactive new bone formation caused by osteoblastic stimulation (Tkocz and Bierring, 1984), or osteolytic and osteosclerotic mixed which, while considered rare (Sandritter et al., 1976), does occur (Ortner et al., 1991).

Very few cases of metastatic carcinoma have been reported in the paleopathological literature (Allison et al., 1980; Anderson et al., 1992; Blondiaux, 1984; Brooks and Melbye, 1967; Brothwell, 1967; Cassidy, 1977; Dastague, 1965; Fuste, 1955; Gejvall, 1960;

Gladykowska-Rzeczycka, 1991; Gregg et al., 1982; Grmek, 1976; Grupe, 1988; Hooten, 1930; Manchester, 1983; Moller and Moller-Christensen, 1952; Moller-Christenson, 1958; Morse, et al., 1974; Nemeskeri and Harsanyi, 1959; Nielson, 1970; Ortner and Putschar, 1985; Pahl et al., 1984; Satinoff, 1972; Soule, 1980; Steinbock, 1976; Strouhal, 1989, 1991; Strouhal and Vyhnanek, 1981; Tkocz and Bierring, 1984; Tyson and Dyer Alcauskas, 1980; Waldron, 1987; Wells, 1963; Wells, 1964). With the exception of Anderson et al. (1992), Ortner and Putschar (1985), and Tkocz and Bierring (1984), these cases all show purely osteolytic reaction. Indeed, Lichtenstein (1965) notes that "the great majority of carcinomic metastases in bone are lytic in their effect." Because of the paucity of reported cases, it is recommended that every new case be presented to the scientific audience (Tkocz and Bierring 1984).

Although the differential diagnosis of skeletal metastases may be difficult, cases do exist in which a reasonably certain diagnosis is possible (Grupe, 1988; Trokcz and Bierring, 1984). This paper describes the case of a probable pre-contact Native American calvarium that was recovered from Galveston County, Texas. The individual most likely suffered from a malignant carcinoma that metastasized to the cranium.

THE SKELETAL MATERIAL

220.90.AR is a well-preserved human cranium and mandible discovered on the Bolivar Peninsula in Galveston County, Texas

(Fig.). The skull was recovered by artifact collector Robert E. Lee, Sr. in 1955, near the site of the University of Texas "mound digs" and donated to the Brazos Valley Museum in Bryan, Texas by the collector's son Robert Lee, Jr. in 1990 (Brazos Valley Museum, 1994). The "mound digs" were, in reality, the site of the Caplen Cemetery (41GV1), originally excavated in 1932 by A.M. Woolsey, working under J.E. Pearce of the University of Texas (Aten et al., 1976). The archaeologists discarded all but 20 of the skeletons they discovered and provided no documentation except for the original field notes which were summarized by Campbell (1957).

The Caplen Cemetery consists primarily of a 15-meter-diameter oyster shell midden overlain by a dark soil and underlain by beach deposits (Aten et al., 1976). Woolsey's field notes describe three levels or "tiers" of burials at the site with some being located in the beach deposits, others in the shell midden, and the remainder in the overlying dark soil (Aten et al., 1976). While the entire skeleton of 220.90.AR was present, none of the post-cranial elements were collected (Robert E. Lee, Jr., personal communication, 1994). The skeleton was discovered buried in a layer of white sand covered with "large oyster shells" under approximately "3$_{1/2}$-4 ft of topsoil (Brazos Valley Museum, 1994). This would appear to correspond to Woolsey's burials within the beach deposits at the deepest portion of the cemetery.

Artifacts recovered from the site included grog-tempered pottery sherds of the Holly Fine Engraved variety which, according

to Aten et al. (1976) indicates a beginning date of occupation for the site in the Early Round Lake Period (ca. A.D. 1000). At least one grave was discovered with European trade artifacts indicating a continuation of the site as a cemetery into the Historic Period. Aten et al. (1976) suggests a general date of occupation between A.D. 1200 and A.D. 1800.

The majority of burials at Caplen were primary inhumations with occassional references to bundle burials which Aten et al. (1976) suggest were probably the result of post-depositional disturbances. The calvarium of 220.90.AR was part of a primary inhumation with the body buried in the flexed position (knees drawn up to the chest) (Robert E. Lee, Jr. personal communication, 1994). The remainder of the skeleton was not disturbed. Mr Lee (personal communication, 1994) also reported a single shell bead within the burial pit which he no longer has in his possession. Artifacts recovered from the Caplen excavations included materials "related to columella bead manufacture [which] were associated with females" (Aten et al., 1976). The presence of the shell bead in the burial may be an indicator of the sex of the individual.

The cranium was heavily glued and varnished before being donated to the museum, who, in turn, placed it on loan to Texas A&M University for this study. Based on recognized ageing and sexing criteria the skull is from an adult (25 - 50 years of age at death) and is probably female. Of course, having only the cranium makes this identification very tenuous and should only be

considered as a general statement. The teeth are heavily worn and indicative of Native American populations subsisting on a diet of stoneground shellfish along the Texas Gulf Coast.

There are xx of lesions of varying size present in the cranium and none in the mandible (Fig. XX).

RADIOGRAPHIC EVIDENCE

To support a diagnosis of metastatic carcinoma, x-rays were taken from the cranium at the Texas A&M University College of Veterinary Medicine. A study of x-rays for pathological conditions may be more sensitive in dry bones than similar studies on living bone (Micozzi, 1991; Ortner and Untermohle, 1981). Examination of the radiographs led to the discovery of what one radiologist has termed "unerupted cancerous lesions" (Michael Walker personal communication, 1993). These are lesions that appear as small, dark spots on the lateral projection in the tempoparietal region (Fig.) and provide good evidence for a cancer which has spread from a primary tumor foci through contiguous tissues or through lymphatic and blood vessels, and given rise to multiple metastases (Raven, 1990).

It should be noted that several other radiologists interpret this "mottled area" as "venous lakes" and not "additional destroyed areas," although noting that "the opinion is varied" (Cooke, 1994). Anderson et al. (1992) noted the evidence for

metastases "around the mouths of small veins on bone surfaces" in a medieval skeleton from Canterbury, England. Thus, the location of lesions near small veins would seem to be compelling evidence for venous dissemination of the tumor, and for a diagnosis of metastatic carcinoma.

SEM

Portions of the cranium were examined by scanning electron microscope (SEM) with the aid of high-resolution epoxy casts. Two areas were chosen for study, the large, lytic lesion on the right parietal and a broken and highly eroded area just left of vertex (Fig. 3). The areas cast included the edges of the inner and outer cortical tables as well as the intervening diploe. Both specimens were coated with latex rubber to form a negative impression mold. These molds were removed and cast using hysol epoxy resin. Casts were coated with 200 Å of gold palladium and examined using a JEOL scanning electron microscope at 15kev and a 30° beam angle. The diploe areas of each cast were photographed at x15, x100, and x150 magnifications and compared qualitatively.

DIFFERENTIAL DIAGNOSES

While a diagnosis of metastatic carcinoma is offered, it is not presented as a one hundred percent certainty. At the least, it is always best to offer at least one other possible interpretation for, as Lichtenstein (1965) so aptly put it, "not

infrequently even a skilled observer possessed of the essential clinical data must be content to record a tentative impression . . . or to suggest two or more plausible alternative possibilities."

With this in mind, a possible diagnosis of multiple myeloma is also offered. There is often difficulty in distinguishing between metastatic carcinoma and multiple myeloma, especially in paleopathological specimens. As Ortner and Putschar (1985) state, "in the skeleton these two types of cancer reflect a morphological gradient making differential diagnosis impossible in many cases."

Multiple Myeloma

A number of cases of multiple myeloma have been reported in the paleopathological literature (Brooks and Melbye, 1967; Fuste, 1955; Morse, 1969; Morse et al., 1974; Nemeskeri and Harsanyi, 1959; Ortner and Putscar, 1985; Ritchie and Warren, 1932; Steinbock, 1976; Wells, 1964).

Multiple myeloma is considered the most common primary malignant cancer in bone, affecting the plasma cells which, after varying time intervals, can affect significant portions of the skeleton (Ortner and Putschar, 1985; Zimmerman and Kelley, 1982). Myeloma is primarily derived from hemopoietic bone marrow and, while considered rare overall (Ortner and Putschar, 1985), occurs about twice as often in males as in females. Myeloma also predominates in individuals between 40 and 60 years of age (Lichtenstein, 1965), with nearly 90 percent over the age of 50

(End Results in Cancer, 1968). Steinbock (1976) notes that "this tumor is uncommon below the age of forty and is indeed rare in adolescence and children."

While the ribs, vertebrae, skull, and pelvis are the most commonly involved bones of the skeleton, almost any bone containing hematopoietic marrow may become involved (Lichtenstein, 1965; Zimmerman and Kelley, 1982). Dahlin (1967) notes that "the skull is usually involved by the time the myeloma has caused the patient's death."

Although Ortner and Putschar (1985) describe myeloma as "relatively rare," and Zimmerman and Kelley (1976) report that "less than 20 percent" of bone tumors in modern populations represent myeloma, it has been noted to be "much more common than is generally suspected" (Lichtenstein, 1965). Indeed, multiple myeloma comprised 43 percent of 1,286 malignant bone tumors in the Mayo Clinic surgical series (Dahlin, 1967). This confusin may be related to the difficulty in distinguishing multiple myerloma from metastatic carcinoma.

The appearance of multiple myeloma in the skeleton is predominately one of numeorus lytic lesions (Steinbock, 1976; Zimmerman and Kelley, 1982), although single lesions are not uncommon (Dahlin, 1967; Ortner and Putschar, 1985). "Solitary myeloma" may represent a single lytic focus, usually "associated with normal sternal marrow" (Dahlin, 1967), which may remain solitary for only a few months or for as much as five to ten years

or longer (Dahlin, 1967; Ortner and Putschar, 1985).

The most frequent form of multiple myeloma, however, is the disseminated variety (Ortner and Putschar, 1985). Lesion size varies greatly, although most are small when compared to those produced by metastatic carcinoma (Steinbock, 1976). Ortner and Putschar (1985) give an average size for the lesions of between three and ten millimeters, with the exception of the original ones, which may be considerably larger. Lesions as large as five centimeters are not uncommmon (Dahlin, 1967; Zimmerman and Kelley, 1982). The lesions appear as ralatively small, purely lytic defects with no reactive bony margins. Several small lesions may become confluent, and appear larger, although these confluent lesions will often show scalloped margins and can thus be distinguished from the larger, solitary defects (Ortner and Putschar, 1985). These confluent lesions may also be responsible for pathologic fractures (Ortner and Putschar, 1985; Steinbock, 1976). Snapper et al. (1953) found evidence for such fractures in 62 percent of their patients.

Metastatic Carcinoma

Metastatic carcinoma lesions in bone are produced when fragments of soft tissue cancers become disseminated in the body via the bloodstream and produce secondary neoplastic foci (Steinbock, 1976). The skeleton is one of the most common sites of cancer metastases. Sandritter et al. (1976) report that the most common tumors which metastasize to the bone include:

breast carcinoma (ca. 47%); prostate carcinoma (ca. 43%); thyroid carcinoma (ca. 31%); bronchial carcinoma (30%); hypernephroid renal carcinoma (ca. 30%); carcinoma of the skin (ca. 15%); and carcinoma of the cervix (ca. 12%) (Fig. xx).

See also Fig.X. (Figure 10.37/page 211 of Sandritter).

A general figure of 27% for bone metastases was discovered by Abrams et al. (1950) in 1000 consecutive autopsies of cancer victims. Their (Abrams et al. , 1950) analyses also showed that over two-thirds of the breast carcinomas, nearly one-third of the bronchial carcinomas, and one-fourth of the renal carcinomas had metastasized to one or more bones. Lichtenstein (1965) notes that "without detailing specific instances, suffice it to say that on occasion virtually every malignant neoplasm may do so [metastasize), some more often than others."

The bones most commonly involved in metastatic carcinoma, in order of frequency, are the vertebrae, sternum, ribs, femur, humerus, and calvarium (Sandritter et al., 1976). Steinbock (1976) adds the pelvis to this list and notes that "carcinomas rarely metastasize to bones distal to the elbow and knee." Lichtenstein (1965) states that "the calvarium is not infrequently involved and that sometimes it may be so riddled by osteolytic defects as to simulate the picture usually held to be typical of multiple myeloma." Brothwell (1967), however, offers that skeletons with multiple lytic lesions should be considered metastatic carcinoma until more compelling evidence can be

produced for a diagnosis of multiple myeloma.

DISCUSSION

In modern populations secondary cancers (metastases) are more common than primary bone malignancies (Anderson et al., 1992; Ortner and Putschar, 1985). In past populations the evidence for cancers is relatively scarce, and those that have been reported are almost always lesions in the skeleton (Zimmerman and Kelley, 1982). The sparse data on ancient cancers is often attributed to early death (Anderson et al., 1992) among individuals in past populations prior to the development of the "diseases of civilization." However, many other diseases commonly associated with old age such as arthritis, osteoporosis, and Paget's disease have been described in both preserved hard and soft tissue remains, indicating that some individuals lived to advanced ages (Zimmerman and Kelley, 1982).

Photographs and x-rays of the cranium were sent to Dr. William L. Hughes, an Oncologist and Hematologist in Oklahoma City for a medical opinion. Dr. Hughes states that his "best assessment would be that these were metastatic lesions to the bone and represent either multiple myeloma or metastatic carcinoma of the breast (*adenosarcoma*) (Hughes personal communication, 1994). This latter diagnosis is based on his assessment of the rapid spread of the cancer and the size and location of the lesions, as well as the probable sex of the individual. Zimmerman and Kelley

(1982) note that prostate cancer produces a solely osteoblastic response; while cancer of the breast may produce osteoblastic or osteolytic responses; and bronchial, renal, and thyroid cancers generally produce solely osteolytic responses. Ortner and Putschar (1985) state that "everybody aggres that the carcinomas most commonly metastasizing to the skeleton are those of the female breast and of the male prostate," while also taking note of the fact that males show a prevelance toward myeloma while females are more prone to breast cancer.

In macroscopic view, tumors appear as masses that replace or protrude from a normal structure (Zimmerman and Kelley, 1982). In microscopic view, malignancies appear architecturally disarrayed, with individual cells having large, irregular nuclei. In breast cancer, the tumor is characterized by an intrusion into the breast of sheets and rows of malignant cells (Fig. xx).

It was also Dr. Hughes' (1994) opinion that the lesions obove both orbits probably caused blindness before death and the area of destruction in the nasopaltine region would have casued serious respiratory problems. The actual cause of death may be linked to the lesion located in the right paraforamen magnum area. An infusion of metastasized cancer cells in this region may have blocked the spinal cord, causing respiratory arrest. In any event, it was Dr. Hughes (1994) belief that the lesion in this area "could not have occurred much before death." Carcinoma of the breast mostly shows osteolytic metastases, while carcinoma of

the prostate usually shows osteoblastic deposits. Solitary and relatively slow growing metastases are most often caused by renal cortical or thyroid carcinomas. These solitary lesions occur with prediliction in the shaft of the femur or the humerus, less commonly in the cranial vault. O & P 1985.

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