Localised Myeloma with Osteogenesis and Russell Body Formation

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SUMMARY

A case of an osteosclerotic myeloma of the mandible is described. Bone formation took the form of prominent sunray spiculation and radiologically mimicked an osteosarcoma. No other well-documented solitary lesion of this type could be found in the English literature. In addition, this tumour contained an abundance of intracytoplasmic Russell bodies and also produced a paraprotein. The paraprotein peak disappeared after resection.


Osteogenesis in myeloma is an infrequent but well-documented phenomenon. The least common pattern is sunray spiculation which has been described only in patients with otherwise typical lytic lesions of multiple myeloma at other sites. We wish to describe a unique case in which prominent sunray spiculation occurred within an apparently solitary myeloma of the mandible. Radiologically this was confidently interpreted as an osteosarcoma. This case presents two additional interesting features, viz. an abundance of intracytoplasmic Russell bodies with unusual ultrastructural features and the production of a paraprotein which disappeared after resection of the tumour.

CASE REPORT

A 64-year-old White male gave a 6-month history of a progressively enlarging, painless swelling of his jaw. He had no complaints other than cosmetic. Examination showed a bony-hard, non-tender, 5 x 5 cm mass, which involved the posterior half of the left horizontal ramus of the mandible. There were no other clinical features of note. Radiologically, a radio-opaque, rounded mass was noted. It had a prominent sunray spiculation throughout and was diagnosed as an osteogenic sarcoma (Fig. 1). A complete skeletal survey showed no significant abnormality.

Special investigations revealed a haemoglobin of 14.7 g/100 ml, a white cell count of 8700/μl with a normal differential count, a platelet count of 200,000/μl, and an erythrocyte sedimentation rate of 50 mm in the first hour (Westergren). The serum protein concentration was 8.8 g/100 ml with an albumin concentration of 5 g/100 ml. The serum calcium concentration was 10.3 mg/100 ml, serum phosphorus 6.5 mg/100 ml and the alkaline phosphatase 90 units (normal 30-85). Serum electrophoresis revealed a monoclonal band in the γ-globulin region (Fig. 2). Serum immunoglobulin studies showed an IgG of 1648 mg/100 ml (normal 510-1600), an IgA of 368

Fig. 1. Roentgenogram showing tumour with sunray spiculation at angle of mandible.

Fig. 2. Serum electrophoretogram. Note monoclonal band (arrow) in patient's serum pre-operatively (A) and disappearance postoperatively (B). Control sera (C).
mg/100 ml (normal 60-310) and an IgM of 149/100 ml (normal 30-230). Bence Jones protein was not detected in the urine.

Histological examination of a drill biopsy specimen indicated a myeloma or lymphoreticular tumour, and a left hemimandibulectomy was performed. Postoperatively, the monoclonal serum protein component was no longer detectable by electrophoresis (Fig. 2), and the patient is alive and well 9 months later.

**MATERIALS AND METHODS**

Tissue for light microscopy was fixed in a 10% formaldehyde solution and sections were stained with haematoxylin and eosin, phosphotungstic acid haematoxylin, PAS, methyl green-pyronine (Unna-Pappenheim), ninhydrin-Schiff stain, Nile blue sulphate and luxol fast blue by standard techniques. Only tissue which had been fixed in formaldehyde for several days was available for electron microscopy. Minced fragments were transferred to phosphate-buffered glutaraldehyde and were postfixed in Palade’s solution. After dehydration in graded acetone, the tissue was embedded in Spurr’s epoxy resin. Sections were stained with uranyl acetate and lead citrate and were examined with an AEI-GEC 6B electron microscope.

**RESULTS**

**Macroscopic Findings**

The resected specimen consisted of the left half of the mandible. In the region of the angle and ramus there was a bony-hard, rounded mass which measured 5 × 4 × 0.5 cm with a smooth outer surface (Fig. 3). The entire cut surface of the mass was composed of close-set, pale, bony lamellae, orientated at right angles to the surface of the mandible (Fig. 4). These lamellae were separated by soft, brownish-coloured tissue. The outline of the mandible as it appeared before development of the tumour was faintly discernable.
TABLE I. COMPARISON OF RUSSELL BODIES AND HYALINE GLOBULES

<table>
<thead>
<tr>
<th>Location</th>
<th>Russell bodies</th>
<th>Present case</th>
<th>Hyaline globules</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal plasma cells, myeloma, lymphoma, leukaemia, light chain disease</td>
<td>Apparently solitary plasmacytoma of mandible</td>
<td>Normal adrenal medulla and liver, carcinoma cells of liver, breast, lung</td>
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<tr>
<td>Staining characteristics</td>
<td></td>
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<tr>
<td>Phosphotungstic acid</td>
<td></td>
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<tr>
<td>haematoxylin</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>PAS</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Unna-Pappenheim</td>
<td>+</td>
<td>+</td>
<td>-</td>
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<tr>
<td>Ninhydrin-Schiff</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Nile blue sulphate</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Luxol fast blue</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Ultrastructure</td>
<td>Finely granular matrix, surrounded by rough endoplasmic reticulum</td>
<td>Filamentous, arciform sub-units and dense areas within matrix surrounded by rough endoplasmic reticulum</td>
<td>Coarsely granular matrix surrounded by rough endoplasmic reticulum</td>
</tr>
</tbody>
</table>

luxol fast blue. These histochemical stains indicated the presence of ribonucleic acid, protein and phospholipid. We performed the same staining reactions on Russell bodies associated with inflammatory plasma cells, and these showed an identical picture except for a diastase-labile PAS reaction.

Electron Microscopic Findings

Ultrastructural examination supported the diagnosis of myeloma. The cells showed characteristic peripheral nuclear chromatin distribution and scattered profiles of rough endoplasmic reticulum (Fig. 7). The hyaline bodies were composed of moderately electron-dense, rounded inclusions of varying size within the cytoplasm. These were intimately surrounded by profiles of rough endoplasmic reticulum (Fig. 8). They showed a substructure of arciform filaments which were densely packed and haphazardly arranged (Fig. 8, inset). Individual filaments were of constant size and measured about 1000 Å in length. In addition, intensely electron-opaque granular structures were present within the rounded inclusions (Fig. 8). These varied in size and appeared to coalesce to form large geographically outlined aggregates.

DISCUSSION

The myeloma described in this article presents several unusual and interesting features, viz. the radiological presentation as an osteoblastic lesion with sunray spiculation mimicking an osteosarcoma, the profusion of hyaline bodies within tumour cells, and the clinical presentation.
as an apparently solitary myeloma with paraprotein production.

Osteosclerosis in multiple myeloma is well recognised. This phenomenon has been most commonly encountered in pathological fractures as a healing process following irradiation or urethane therapy. However, new bone formation without such a background has been reported in only 36 cases. This usually takes the form of sclerosis within or at the periphery of a lytic lesion. Rarely, spiculation has been described at one site in patients with otherwise typical lytic lesions of multiple myeloma. Although osteosclerosis has also been described in solitary myeloma, we are unaware of any previous example in the English literature of a solitary myeloma with sunray spiculation. This reactive bone formation was an integral part of the tumour and not merely a surface periosteal...
reaction. In the presence of diffuse disease, it is unlikely that this feature would be misinterpreted radiologically as an osteogenic sarcoma. However, a solitary lesion with a sunray pattern invites such a misdiagnosis. Similar bone spiculation may occur in tuberculosis and fungal osteomyelitis, thyroid acropathy, haemangioma, meningioma, Ewing's sarcoma, metastatic neuroblastoma and other metastases.

The presence of round eosinophilic bodies within inflammatory plasma cells is a common occurrence. They are referred to as Russell bodies after eosinophilic bodies observed by Russell in 1890 in a variety of tumours, and were subsequently considered to have been located within plasma cells bordering on these malignant tumours.

Similar bodies have occasionally been seen in myeloma cells. They were noted in the plasma cells of 4 out of 19 patients with paraproteinaemia. They are referred to as Russell bodies in inflammatory plasma cells that are similar to the staining reactions noted in the myeloma cells of the present case. However, PAS staining of Russell bodies is variable. Eosinophilic hyaline globules similar in appearance to Russell bodies have been described in normal adrenal medulla and liver, in carcinoma cells from the lung, breast and liver, and in lymphoma and leukaemia cells. They differ from Russell bodies in that they are negative for phospholipid and ribonucleic acid.

Ultrastructurally, Russell bodies within non-neoplastic plasma cells are located within the rough endoplasmic reticulum, they are rounded and electron-dense and are sometimes described as having a granular substructure. They vary in size, the largest exceeding that of the nucleus. They are considered to result from condensation of secretory material within dilated endoplasmic reticulum and have been shown to fluoresce with antigammaglobulin. Similar large, electron-dense, rounded bodies were demonstrated by Maldonado and Brown, both intra- and extracisternally. Smaller, electron-dense, intracisternal rounded bodies in myeloma cells have been considered to represent early stages of Russell body formation. The hyaline globules described in a variety of normal and neoplastic tissues are also granular, rounded bodies surrounded by rough endoplasmic reticulum.

A remarkable feature of the present case was the abundance of these Russell bodies. Ultrastructurally, they were large, electron-dense, rounded bodies, bordered by profiles of rough endoplasmic reticulum. They differed from those previously described in that they have a substructure of arciform filaments and intensely electron-dense granular structures. However, the nature of the substructure may have been influenced by formalin fixation. The only other Russell bodies which bear some resemblance to those of the present case were observed in the neoplastic plasmacytoid cells of Waldenstrom's macroglobulinaemia. The large, electron-dense, granular bodies in those cells also had intensely dense rounded structures within them but did not have a filamentosubstructure.

 Apparently solitary skeletal myeloma occurs most commonly in the vertebral column but has also been described in the skull, rib, mandible, maxilla, clavicle, sacrum, ilium,ibia, femur, humerus and sternum. A small number of well-documented cases have shown prolonged survival without dissemination after resection. Survivals of 16 years, 16 years, 22 years, 24 years and 35 years have been reported in patients with lesions in the mandible,ibia, femur, clavicle and upper limb, respectively. Of particular interest in our case was the presence of a paraprotein peak which disappeared after resection of the lesion. Potter documented a similar occurrence. The presence of such a peak should not negate a diagnosis of apparently solitary plasmacytoma, and reappearance of the peak would be a valuable index of recurrence or dissemination.

Dr Eric Harley, Department of Chemical Pathology, performed the electrophoretic study. Drs Lauren V. Ackerman and Juan Rosai reviewed the biopsy specimen.

REFERENCES