CASE REPORT

Alveolar soft-part sarcoma presenting with eosinophilia and shunt

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Alveolar soft-part sarcoma (ASPS) is a rare soft tissue tumour found in young adults that usually arises in skeletal muscle and occurs most frequently in the lower limbs. Radiological and pathological findings of ASPS in a 34-year-old man who presented with increasing shortness of breath over a period of four to six weeks with peripheral blood eosinophilia, hypoxemia and a significant arteriovenous shunt are reported. The present article is the fourth report of eosinophilia in association with sarcoma, and the first involving ASPS.

Key Words: Eosinophils; Sarcoma; Shunt

CASE PRESENTATION

A 34-year-old, previously healthy man presented with a six-week history of dyspnea and a mass on the left leg that had been present for six months. Clinical features included a cough, hemoptysis and a 18.1 kg weight loss. His oxygen saturation was 86% with room air and 93% with supplemental oxygen (5 L/min by nasal cannula). He had a 5 cm × 8 cm fluctuant mass on the lateral aspect of his left leg, just below the knee.

The patient's blood count showed eosinophilia (1.3 × 109/L [normal 0.0/L to 0.7 × 109/L]), with a normal total white blood cell count of 8.3 × 109/L. Electrolytes, renal function and liver enzymes were normal. Plain films (Figure 1A) and computed tomography (CT) of the thorax (Figure 1B) showed numerous (more than 100) well-circumscribed nodules in the lower and mid-lung zones ranging from 2 mm to 16 mm in diameter.

Pulmonary function tests showed mild obstruction, with a forced expiratory volume in 1 s of 3.13 L (71% predicted), a forced vital capacity of 4.86 L (91% predicted) and no change in the forced expiratory volume in 1 s of 3.13 L (71% predicted). A chest radiograph showed a 20% shunt. CT of the chest did not show feeding vessels to any of the nodules. An echocardiogram was not performed.

The patient's leg mass was confirmed on plain film to be of soft tissue origin. Ultrasound confirmed this to be a vascular mass. Magnetic resonance imaging (MRI) showed this lesion to be located within the deep musculature of the lateral compartment of the lower left leg, just below the knee (Figure 2), with heterogeneous signalling (intermediate-decreased T1 with increased T2 signal intensity). It was a highly vascular lesion.

A needle core biopsy of the left lower leg lesion (Figure 3A) showed malignant cells arranged in an alveolar/organoid pattern. Tumour aggregates were separated by thin-walled endothelial-lined vascular channels, and exhibited small-to-intermediate, rounded-to-polygonal nuclei. The cytoplasm was abundant and exhibited an acidophilic, granular appearance. Intermediate, rounded-to-polygonal nuclei. The cytoplasm was abundant and exhibited an acidophilic, granular appearance. Myoglobin, cytokeratin, myogenin, desmin, actin and s-100 protein. CD34 staining highlighted the vascular channels within the tumour lobules, but the tumour cells were negative; staining with vimentin was weakly positive. This pattern of staining was consistent with alveolar soft-part sarcoma (ASPS) (see Discussion). High-power examination (100x under oil) revealed numerous granules and crystals that were further identified by electron microscopy.

The patient complained of severe headaches, for which he was evaluated using CT and MRI of the brain, but no abnormalities could be identified and a lumbar puncture was negative for malignant cells.

The patient received one cycle of chemotherapy (MAID-G protocol [mesna, ifosfamide, doxorubicin dacarbazine and granulocyte colony-stimulating factor]) (1,2), which was discontinued due to lack of response. He died of respiratory failure four months following the initial diagnosis. The eosinophilia persisted throughout.

DISCUSSION

Soft tissue sarcomas are cancers of connective tissue including muscle, tendon, fat, fibrous tissue, synovial tissue, vessels and nerves. Sixty per cent of soft tissue sarcomas arise in the extremities, with the lower extremities being three times more likely to be involved than the upper extremities. Thirty per cent of soft tissue sarcomas arise in the trunk, with a large proportion of these arising in the retroperitoneum. Fewer are seen in the head and neck region.
The most common presentation of soft tissue sarcomas is an asymptomatic mass. Mechanical symptoms referable to pressure, traction or entrapment of nerves or muscles may be present (3). In 1952, Christopherson et al (4) described a unique soft tissue tumour composed of cells with granular cytoplasm arranged along delicate fibrous septa, giving rise to an alveolar or organoid pattern. For this reason, they named the lesion ‘alveolar soft-part sarcoma.’ The tumour contained numerous vascular channels around the clusters of tumour cells, reminiscent of a paraganglioma or an endocrine neoplasm.

ASPS is usually a disease of young adults (mean age 25 years) (5). One report (6) demonstrated a chromosomal translocation in association with this tumour (t[X;17] [p11;q25]). The disease has an indolent clinical course with relatively low rates of local and distant recurrence. The lung and brain are common sites of metastases. Brain metastases were only observed as part of a more disseminated disease (7).

High signalling on T1-weighted MRI images of our patient’s leg and numerous signal voids were highly suggestive of ASPS (8). ASPS is a highly vascular tumour and, on enhanced CT of the chest, some of the masses contain dilated and tortuous intratumoural vessels (9). These vessels likely account for the 20% shunt noted in the pulmonary function tests.

Most sarcomas metastasizing to the lung produce large nodules (‘cannon balls’). The chest radiograph of our patient was unusual, showing much smaller lesions.

Cytological detection of characteristic crystalloids using a Papanicolaou smear from a needle core biopsy is characteristic of ASPS (10,11), and facilitated the final pathological diagnosis of our patient.

Eosinophilia has been found in patients with lymphomas and a variety of other solid tumours. Along with its substantial role in immunomodulation, we are beginning to recognize the importance of eosinophils in neoplastic disorders (12). Eosinophilia may be associated with a positive prognostic significance in some tumours (13,14) and a negative influence in others (15,16). In addition, eosinophilia has been associated with a good response to treatment in some malignancies (17). Removal of the primary neoplasm sometimes corrects the eosinophilia, and tumours have been found that produce eosinopoietic cytokines such as interleukin-5 and granulocyte/macrophage colony-stimulating factors. Eosinophilia could be a marker of a patient’s immune system activation (18).

Three other cases of sarcoma causing eosinophilia have been recently reported (19-21). One case reported an undifferentiated embryonal sarcoma arising in a pediatric patient with mesenchymal hamartoma of the liver (19). Another case
reported eosinophilia associated with a cardiac rhabdomyosarcoma (20). A third case involved a 67-year-old woman with a uterine leiomyosarcoma in which the tumour was heavily infiltrated with eosinophils, suggesting the patient’s immune system was trying to control the tumour growth (21). Our case represents the first report of eosinophilia associated with ASPS.

CONCLUSIONS
The present report highlights the association of eosinophilia with sarcoma. ASPSs have a poor outcome. In one series, the median survival was 48 months (22). ASPS has a 38% overall five-year survival, and 48% if the disease is localized. A significant reduction in survival is seen in the presence of hematogenous metastases, with a median survival of eight months (range zero to 45 months) (22). With a potential immunomodulatory role in sarcomas, eosinophils are now recognized to have more than a simple presence in tumour biology. Indeed, the role of eosinophils in malignant conditions, particularly sarcoma, will be an important area for future research.

REFERENCES

Figure 3) A Hematoxylin and eosin stain (original magnification ×400) showing malignant cells arranged in an alveolar pattern. B Periodic acid-Schiff stain (original magnification ×1000) showing dark pink, periodic acid-Schiff stain-positive, intracytoplasmic granules