and displacing the aorta anteriorly at the same level (Fig. 1A). The mass measured 9.1 × 6.3 cm in greatest dimension on sagittal slice, and 6.4 × 5.8 cm in greatest dimension on axial slice. Magnetic resonance imaging (MRI) revealed similar findings. Serum LDH, CA19–9, and CEA levels were within normal limits, with PSA slightly elevated at 4.95. CBC was within normal limits save for a haematocrit of 35%.

A needle core biopsy showed a spindle cell proliferation involving fat with a focal vague storiiform pattern and low mitotic activity (Fig. 1D). These cells were weakly positive for smooth muscle actin and muscle specific actin, but negative for S-100, myogenin and c-kit. There was no significant pleomorphism or necrosis. These findings were consistent with a low grade spindle cell neoplasm that could not be further classified with limited biopsy material. As the patient had severe neurological pain, but was reluctant to have surgery, he underwent external beam radiation for palliation and minimally invasive tumour management. However, with progressively worsening symptoms and no reduction in tumour size on magnetic resonance imaging (MRI) (Fig. 1B) after 5 months of therapy, the patient agreed to surgical resection.

Gross examination of formalin fixed tissue revealed a 6 cm aortic segment that included the iliac bifurcation distally. There was a 7 × 5 × 4.5 cm mass encircling the aorta with eccentric outgrowth behind it (Fig. 1C). The aortic lumen was occluded by intraluminal extension of the tumour that closely approximated the proximal and distal surgical resection margins. The cut surfaces were tan-white to tan-yellow with gelatinous appearance and focal necrosis and haemorrhage. Microscopically, the tumour showed morphology typical of intimal sarcoma (Fig. 1E–H) with hypercellular and hypocellular areas (Fig. 1F). Thin layers of atypical spindle cells were observed on the blood clot and the luminal surface (Fig. 1G). There was also lobulated fibroblastic proliferation with a focal vague storiiform pattern, consistent with core biopsy findings (Fig. 1F). In addition, there was increased cellularity at the periphery of the lobule (Fig. 1F,H). Interestingly, tumour morphology was similar inside and outside the aorta, with the exception of an absence of blood clot outside.

Retroperitoneal sarcomas are difficult to diagnose even following surgical resection. The most common sarcoma occurring at this site is liposarcoma. Although the current case simulated liposarcoma with a spindle cell proliferation involving fat, no lipoblasts were present. Nevertheless, a dedifferentiated liposarcoma could still explain these findings, especially on initial needle core biopsy, and should still be considered in the differential diagnosis, along with fibromatosis, inflammatory myofibroblastic tumour, leiomyoma, leiomyosarcoma, angiomylolipoma, and schwannoma. However, the imaging findings, overall morphology, and immunohistochemical staining pattern of this case were classic for aortic intimal sarcoma.

Earlier case reports have showed that intimal sarcomas tend to grow intraluminally. Extravascular growth is often seen at local recurrence sites following surgical resection or involving distant metastasis. Unlike their intravascular counterparts, extravascular intimal sarcomas often differentiate toward a distinct cell lineage and have a classifiable histology. In this case, both components demonstrate similar spindle cell proliferation of cell types focally positive for either endothelial or myofibroblastic markers, but not any differentiated histological pattern. The main difference is that the intraluminal tumour is predominantly composed of thrombus.

Intimal sarcoma is known for its resistance to chemotherapy and radiation. This patient had 5 months of external beam radiation without radiological evidence of tumour shrinkage. Subjectively, the patient complained of worsening pain, which may be explained by either tumour progression or radiation associated fibrosis and neuritis. Pathological evaluation did reveal treatment effect with approximately 20% tumour necrosis. This suggests radiation therapy has certain effect on intimal sarcomas, or at least may retard their progression.

The most common presentation of primary intimal sarcoma of the abdominal aorta is pain attributable to ischaemia. This patient’s presentation of pain had a significant neurological element, primarily due to or complicated by nerve root compression. This was supported by the fact that while his peripheral pulses and vascular examination were within normal limits, his neurological examination did elicit some deficits. Although his ‘cramping pain’ relieved by rest is typical for ischaemic pain, his associated weakness, pattern of pain (anteromedial thigh and groin, ‘shooting pain down the leg’) exacerbated by standing and improving with sitting, along with the positive straight leg tests made a stronger case for a neurogenic cause. Therefore, patients with intimal sarcoma may actually experience a mixed picture of vascular and neurogenic claudication, depending on tumour location and extent.

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was found to be the cause in 33 cases.\textsuperscript{1,2} Cystic tumours of the atrioventricular node (CTAVN) are rare. Less than 100 cases have been reported in the literature.\textsuperscript{1} The diagnosis is most often made histologically when examining the cardiac conduction system during autopsy. Atrioventricular block, cardiac arrhythmias and sudden cardiac death are clinical manifestations of this condition. It has rightfully been referred to as the smallest tumour capable of causing sudden cardiac death.\textsuperscript{1,3,4} The following case report is that of a CTAVN discovered during autopsy.

A 19-year-old man suffered a cardiac arrest whilst playing sport. He had been diagnosed 3 years earlier with complete atrioventricular block and a dual chamber cardiac pacemaker was implanted at that time. When the paramedic team arrived at the scene, his ECG trace showed ventricular fibrillation and he was successfully defibrillated. Return of spontaneous circulation was achieved 10 minutes after the initial incident. Subsequent interrogation of the pacemaker revealed that he had suffered four episodes of non-sustained ventricular tachycardia in the preceding week followed by an episode of ventricular fibrillation. No cause for his arrhythmia could be determined. An echocardiogram was performed and was unremarkable. He was admitted to ICU where he was diagnosed with severe hypoxic brain injury. A decision was made to withdraw treatment and he died 10 days later from respiratory failure following aspiration.

A limited autopsy of his lungs and heart was performed. Bilateral purulent consolidation of the lungs was noted. Macroscopically, no abnormalities could be identified in the heart. The pacemaker wires were removed and the device was tested to be in good working order. Tissue blocks were taken from the area around the sinus node and atrioventricular node to examine the conduction system microscopically.

The atrioventricular node was almost completely replaced by a tumour measuring approximately 20 mm, also involving the interventricular septum. The tumour consisted of small and irregular cysts with scattered intervening solid nests of cells (Fig. 1). The cysts were lined by cuboidal and flattened cells. In some areas, a double layer of cells was identified (Fig. 2). Solid nests of polygonal cells with eosinophilic cytoplasm and central round nuclei were present between the cystic spaces. The lesion was highly vascular with multiple capillaries surrounding the cystic spaces. Positivity to cytokeratins (EMA, AE1/3, CK7, CK5/6, Cam5.2, p63, CK-34\textsubscript{beta}E12) confirmed the endodermal origin of the cells, and negative calretinin dismissed a mesothelial origin. Other negative markers were CD34, CD31, SMA and S100. The tumour cells stained focally positive with neuroendocrine marker chromogranin as well as calcitonin. The bi-layered cells lining the cysts had two distinct staining patterns. The luminal cells stained positive with EMA and CK7, whereas the basal cells stained positive with CK5 and p63 (Fig. 3). This is the first report demonstrating both luminal and basal phenotypes in the cyst lining.

\begin{figure}[ht]
\centering
\includegraphics[width=\textwidth]{image1.png}
\caption{Cystic tumour of the atrioventricular node. The main image shows irregular cystic spaces (H&E). The inset shows solid nests of cells (H&E).}
\end{figure}

\begin{figure}[ht]
\centering
\includegraphics[width=\textwidth]{image2.png}
\caption{High power showing bi-layered epithelial lining (H&E).}
\end{figure}

\begin{figure}[ht]
\centering
\includegraphics[width=\textwidth]{image3.png}
\caption{(A) Basal cells are CK5 positive, luminal cells are EMA positive (CK5/EMA dual staining). (B) Basal cells are p63 positive, luminal cells are EMA positive (p63/EMA dual staining).}
\end{figure}
The tumour has been erroneously called ‘mesothelioma of the atrioventricular node’ due to its electron microscopy features, but consistent negativity for mesothelial markers has led to the abandonment of that term. It is postulated that foregut endodermal elements are incorporated into the embryological development of the heart. As with solid cell nests of the thyroid, these elements originate from the ultimobranchial body (UBB). The UBB is part of the fourth pharyngeal pouch that fuses with the thyroid diverticulum during embryological development. Kikukake et al. demonstrated that the UBB comprises p63 positive cells displaying basal/stem cell properties and p63 negative luminal cells.6

Solid cell nests (SCN) of the thyroid gland are known to be remnants of the UBB composed of main cells and calcitonin positive C-cells. The main cells can form either solid nests or cystic structures and express strong p63 nuclear positivity. Luminal cells of the cystic structures are typically p63 negative.6

Cameselle-Teijeiro et al. compared 10 cases of CTAVN with SCN and noticed a resemblance in morphology and antigenicity between the two entities. They postulated that both are remnants of the ultimobranchial body embedded in either the lateral lobes of the thyroid or in the atrioventricular node region of the heart.4

Our case showed similar morphological features to that of the UBB and SCN of the thyroid gland. The cystic structures of our case were lined by a basal monolayer of strongly positive p63/CK5 cells and a luminal layer of p63/CK5 negative cuboidal cells. Single cells stained positive with calcitonin and chromogranin. Scattered solid nests were p63 positive. These findings further support the theory that cystic tumours of the atrioventricular node are indeed the result of UBB remnants incorporated into the heart during embryological development.

The tumour is usually located at the area of the atrioventricular node in Koch’s triangle. In the majority of cases, there are no macroscopic features and the endocardium is intact. Some authors reported seeing multiple tiny cysts filled with fluid or keratinised material.7 Microscopically, the tumour comprises of multiple cysts of variable size. The cysts are lined by epithelium of which columnar, squamous and transitional epithelium are the most common. The epithelial lining can be flattened resembling endothelium. Cytokeratin markers are usually positive, while mesothelial and endothelial markers are negative. In some reported cases, including our case, solid nests of epithelial cells with a similar immunohistochemical profile as the cystic cells are described. The tumour is considered to be benign with symptoms ranging from asymptomatic to variable degrees of heart block requiring cardiac pacing. The tumour has a predilection for females and the mean age of diagnosis is 38 years.8 Most diagnoses are considered to be benign with symptoms ranging from asymptomatic to variable degrees of heart block requiring cardiac pacing. The tumour has a predilection for females asymptomatic to variable degrees of heart block requiring cardiac pacing.

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NSAID-associated protein losing enteropathy with fatal outcome

Sir,

Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most commonly consumed medications. The beneficial effects of NSAIDs have been tempered by the recognition of their toxic effects on the mucosa of the gastrointestinal (GI) tract. The adverse effects of NSAIDs on the upper gastrointestinal tract are well described. Specifically, NSAIDs can be harmful to the small intestine, causing ulcers, perforations and strictures.1–4

Lang and colleagues first used the term ‘diaphragm disease’ (DD) in 1988 to describe the pathological findings of non-specific small-bowel disease associated with use of NSAIDs.5 The prevalence of DD is unknown because of the vague symptoms of this disorder, but radionuclide scanning has revealed small bowel pathology in up to 66% of patients who had taken NSAIDs for longer than 6 months.6,7,8 Furthermore, ulceration rate of 13.5% has been reported in an autopsy specimens from patients who had taken NSAIDs for longer than 6 months.4

Clinical manifestations of DD include obstructive symptoms, abdominal pain, diarrhoea, iron-deficiency anaemia, GI tract blood loss and protein losing enteropathy (PLE).2,4,5,7,8

The patient presented here is a fatal case of PLE due to DD associated with NSAID use. The pathogenetic mechanisms of PLE and DD are discussed.